







Assessment of iodine nutrition of schoolchildren in Gonda, India, indicates improvement and effectivity of salt iodisation

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Abstract

Objective: To study the total goitre rate (TGR), urinary iodine concentration (UIC) and salt iodine content among schoolchildren in a previously endemic area for severe iodine deficiency disorder (IDD).

Design: Cross-sectional epidemiological study.

Setting: The study was carried out in the Gonda district (sub-Himalayan region) of North India.

Participants: Nine hundred and seventy-seven schoolchildren (6–12 years) were studied for parameters such as height, weight, UIC and salt iodine content. Thyroid volume (TV) was measured by ultrasonography to estimate TGR.

Results: The overall TGR in the study population was 2.8% (95% CI 1.8, 3.8). No significant difference in TGR was observed between boys and girls (3.5% *v.* 1.9%, $P = 0.2$). There was a non-significant trend of increasing TGR with age ($P = 0.05$). Median UIC was 157.1 µg/l (interquartile range: 94.5–244.9). At the time of the study, 97% of salt sample were iodised and nearly 86% of salt samples had iodine content higher than or equal to 15 part per million. Overall, TGR was significantly lower (2.8% *v.* 31.0%, $P < 0.001$), and median UIC was significantly higher (157.1 *v.* 100.0 µg/l, $P < 0.05$) than that reported in the same area in 2009.

Conclusions: A marked improvement was seen in overall iodine nutrition in the Gonda district after three and a half decades of Universal Salt Iodisation (USI). To sustainably control IDD, USI and other programmes, such as health education, must be continuously implemented along with putting mechanisms to monitor the programme at regular intervals in place.

Keywords
Iodine deficiency disorders
Endemic goitre
Universal salt iodisation
Total goitre rate
Urinary iodine concentration
Salt iodine content
Ultrasonography

Iodine deficiency disorder (IDD) has been a significant public health problem in the Indian landmass for many years. IDD include goitre, cretinism, hypothyroidism, brain damage, learning delays, mental retardation, psychomotor deficits, hearing impairment, lack of speech in children and abortion and stillbirth in pregnant women⁽¹⁾. Using iodised salt may be a simple, inexpensive technique to prevent IDD. In the past 30 years, there has been a steady rise in the number of countries to achieve optimal iodine intake^(2,3). Universal Salt Iodisation (USI) is a promising solution to address iodine deficiency and aims to achieve a target of >90% of households using iodised salt⁽⁴⁾. To

date, thirty-seven countries have reached the USI target and many others are on track^(3,5).

Considering IDD as a significant public health issue in India, the Government of India launched the National IDD Control Program (NIDDCP) in 1962. USI was enforced in 1984, whereby it became mandatory to iodise all the edible salt made within the country^(6–8). Since then, commendable progress in control of IDD was seen in India. According to the data from the National Iodine and Salt Intake survey (years 2014–2015) and the National Family Health Survey-4 (years 2015–2016), 78.6–89.7% of Indian households consumed iodised salt^(9,10). Despite these efforts, a considerable proportion of the population

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continues to consume salt lacking iodine (8%)⁽⁹⁾. Nearly 48 million school-age children of the Indian subcontinent may still be at risk of IDD if they do not consume iodised salt⁽¹¹⁾.

The WHO has recommended the determination of goitre prevalence, urinary iodine concentration (UIC) and estimation of the household penetration of adequately iodised salt among schoolchildren to assess IDD's extent and risk and to evaluate USI's impact^(4,12). While thyroid palpation examination offers a useful estimate of thyroid size in moderately or significantly iodine-deficient areas, serious problems were experienced in areas with mild iodine deficiency (subjective bias in 30–40% of cases) where the majority of goitres were small, and an element of subjectivity creeps in Refs. (4,13,14). Thyroid ultrasound was currently believed to be the foremost reliable method for estimating thyroid volume (TV). In epidemiological surveys, this technique's use was strongly recommended to define goitre prevalence in iodine deficiency areas^(12–14). Although there was no agreement on reference values, more than the upper normal limit of TV (>97th percentile) in children living in normal iodine-supply regions was considered indicative of goitre^(15,16). Only a few studies have used ultrasound in India to estimate goitre prevalence in endemic IDD regions^(17,18).

An earlier survey conducted by Kochupillai *et al.* in year 1982, in the Gonda district (sub-Himalayan region of northern India), previously known as a severe endemic area of IDD, showed a goitre (by palpation) prevalence of 60%^(19,20). Later in the same region in 2009, a goitre (by palpation) prevalence of 31% along with low UIC in a comprehensive household survey on schoolchildren was found⁽²¹⁾. Thus, after a decade, the present study was planned in the same endemic area of iodine deficiency to reassess IDD prevalence in schoolchildren and determine the impact of USI.

Materials and methods

Data collection

The present cross-sectional study was carried out in a known endemic iodine-deficient area of northern India, in the Gonda district of Uttar Pradesh, located approximately 120 km north-east capital city of Lucknow in the state's sub-Himalayan Terai area.

Children from primary schools of rural areas, aged 6–12 years, were selected for the study. The sample size for each of the three parameters, namely goitre prevalence, UIC and salt iodine content determination, was calculated. A sample size of 900 with a power of 95% and a precision of 2% was considered adequate. A multistage sampling technique was applied to select the children from the schools (of the villages). In the first stage of cluster sampling, Gonda District has four subdivisions; one block was selected from each subdivision (total four blocks). In the second-stage cluster sampling, two schools from each three selected block,

whereas three schools from one selected block were chosen randomly (total nine schools). Eligible children list was prepared in each school and proportional to male:female ratio, children were selected (third stage, using stratified random sampling). Nine hundred and seventy-seven children, from nine schools (109 children in each of the eight schools and 105 in another school), were recruited in this study. The Institutional Ethics Committee approved the study. After explaining the study's purpose, written assent and informed consent were obtained from children and their legal guardians.

Schoolchildren were interviewed for the type of salt consumed in the household. Height and weight were measured with the utilisation of standardised procedures. Height was recorded to the closest mm and weight to the closest 100 g. BMI was also calculated with the formula ($BMI = \text{weight (kg)}/\text{height (m}^2\text{)}$), and body surface area (BSA) was calculated using the following formula⁽²²⁾:

$$BSA = (\text{weight (kg)}^{0.425} \times \text{height (cm)}^{0.725}) \times 0.007184$$

Clinical and ultrasound examination of goitre

The goitre assessment and grading were done through clinical examination by clinicians (S.Y. and K.G.). Goitre on palpation was classified according to the revised national guidelines on NIDDCP as grade 0: not visible and not palpable; grade 1: palpable but not visible and grade 2: palpable and visible⁽²³⁾. Volumetric measurement of the thyroid gland was done by a single sonologist (S.K.), using a portable ultrasound machine (Sonosite) with a 7.5 MHz transducer. The intra-observer variation in goitre examination by a sonologist and inter-observer variation between two clinicians were limited by repeated prior training. During the visit to schools, the children were asked to lie in the supine position with the neck hyperextended for thyroid measurement. For measurement of each thyroid lobe's depth and width, the greatest perpendicular antero-posterior and medio-lateral diameters were measured on a transverse image of the largest diameter, respectively.

Similarly, each thyroid lobe's largest cranio-caudal diameter was measured on a longitudinal image to measure length. As per recommendation, the isthmus and thyroid capsule were not included in the measurements. TV was calculated using the Brunn formula: width × length × depth × 0.479 for each lobe⁽²⁴⁾. The volume of the two lobes was added to obtain the total volume. Data from children found to possess a nodule on ultrasound examination were not used for TV assessment.

The prevalence of goitre was quantified using the total goitre rate (TGR), which was calculated as 'the number of goitres in a study population divided by the total number of individuals examined'. In this study, a thyroid gland was identified as goitrous when TV was above the 97th percentile of the TV by using the Indian iodine replete population



reference (TV-for-age and TV-for-BSA)⁽¹⁵⁾. We also calculated TGR using the WHO reference data⁽¹⁶⁾. TGR 0–4.9% was considered as normal, 5–19.9% as mild, 20.0–29.9% as moderate and >30.0% as a severe public health problem⁽¹²⁾.

Measurement of urinary iodine concentration

On the day of TV measurement, each child was asked to give 10–15 ml of urine sample in a wide mouth screw cap plastic bottle with tight lid. UIC assay was performed in endocrinology laboratory, Sanjay Gandhi Postgraduate Institute of Medical Sciences (SGPGI) based on micro plate adaptation of the Sandell–Kolthoff reaction⁽²⁵⁾. The sensitivity of this method was 10 µg/l, with a range of 10–400 µg/l. In the event the UIC values were found outside this range, samples were diluted or used for re-estimation in double volumes. Quality control of the measurement of the iodine content of the urine samples was through participation in the quality assurance programme named 'Ensuring the Quality of Urinary Iodine Procedures (EQUIP)' conducted by Centers for Disease Control and Prevention⁽²⁶⁾.

The prevalence of iodine deficiency for populations was graded according to the WHO classification⁽¹²⁾: No deficiency (adequate iodine nutrition); Median UIC ≥100 µg/l, mild deficiency: Median UIC = 50–99 µg/l, moderate deficiency: Median UIC = 20–49 µg/l, and severe deficiency: Median UIC < 20 µg/l.

Measurement of salt iodine content

On the day of recruitment of schoolchildren for study, they were asked to bring salt (approximately 50.00 g) from their respective households. Salt iodine content was measured following the conventional iodometric titration used for the estimation of iodine in iodised salt in the endocrinology laboratory, SGPGI. Ten gram iodised salt was dissolved in 50 ml distilled water, and the iodine content was determined using a titrimetric method⁽²⁷⁾. The iodine content of salt was expressed in part per million (ppm). Quality control in salt iodine estimation was assessed and ensured in the endocrinology laboratory, SGPGI. The known internal quality control samples were run in duplicate with each batch of the test samples, and the internal quality control was successful when the results of these samples were between the lower (L) and upper (U) limits (i.e. the L-U range obtained through mean ± 2 SD), for 95% of test results. If the results were outside the established range, they were potentially suspicious and the whole batch was repeated.

Statistical analysis

The data were tested for normality using the Shapiro–Wilk test. The TGR by palpation and TV was presented as the number and percentage of schoolchildren. Since TV data, UIC and salt iodine content were not normally distributed,

the median and interquartile ranges (IQR) were reported. TGR in different gender and age groups was compared by using the χ^2 tests. The independent *t* test was used to compare parametric data such as age, weight, height, BMI and BSA of males and females. Mann–Whitney *U* test was used to compare nonparametric data of two classes. Spearman correlations were performed for associations between TV and age, BMI and BSA. The difference was considered significant at *P*-value <0.05. The statistical analysis was performed using the SPSS Statistical Package (version 14.0; SPSS).

Results

A total of 977 children were recruited in the study, and TV was measured by ultrasound. Baseline data are shown in Table 1. Children aged 6–12 years, with a mean age of 9.3 (SD 2.1) years, including 512 boys and 465 girls, were recruited in the survey. The height, weight and BSA of boys were significantly higher than girls (Table 1).

Table 2 shows the age distribution of study participants and TV and TGR among various age groups and BSA. Ultrasonographically measured median (IQR) TV was 2.95 ml (2.18–3.89). While the median volume of the thyroid (IQR) in girls (2.99 ml (2.11–3.96)) was greater than that in boys (2.92 ml (2.22–3.8)), the difference was not statistically significant (*P* > 0.05). There was a strong positive association between the TV and age of children (*r* = 0.63, *P* < 0.001), BMI (*r* = 0.35, *P* < 0.001) and BSA (*r* = 0.63, *P* < 0.001).

TGR by ultrasound based on age (enlarged TV-for-age above the 97th percentile of Indian normative data) was 2.8% (95% CI 1.8, 3.8) in schoolchildren. TGR by ultrasound based on BSA (enlarged TV-for-BSA above 97th percentile of Indian normative data) was 3.0% (95% CI 1.9, 4.1) in schoolchildren (Table 2). Gender-wise, TGR was not significantly different in children (3.5% *v.* 1.9%, *P* = 0.2). No increasing trend in the TGR was observed with the increasing age (*P* = 0.05).

Goitre by palpation was found in 9.7% (95% CI 7.8, 11.6) of children. The TGR of grades 1 and 2 were 7.8% and 1.9%, respectively. While comparing the WHO reference data, TGR based on age and BSA was 9.7% (95% CI 7.8, 11.6) and 15.8% (95% CI 13.5, 18.1), respectively, in schoolchildren.

The children's median UIC (IQR) was 157.1 µg/l (94.5–244.9) and suggested iodine sufficiency. The median UIC (IQR) values were 146.1 µg/l (89.7–231.6) and 169.8 µg/l (91.6–253.7) for males and females, respectively (*P* = 0.05).

In total, 860 salt samples were obtained. The median (IQR) iodine concentration of household salt was 29.5 ppm (21.0–36.0). At the time of the study, 97% of salt sample was iodised and 86.7% of salt samples had iodine content higher than or equal to 15 ppm. Values of median UIC reflected the iodine content in salt. Thus, the median UIC

Table 1 Basic characteristics of participating children (6–12 years)†

Variable	Boys (n 512)		Girls (n 465)		Total (n 977)	
	Mean	SD	Mean	SD	Mean	SD
Age (years)	9.4	2.1	9.3	2.1	9.3	2.1
Height (cm)	142.9***	13.1	139.1	14.6	141.1	14.6
Weight (kg)	27.4*	7.4	26.5	7.2	27.0	7.3
BMI (kg/m ²)	13.5	3.2	13.7	3.2	13.6	3.2
BSA (m ²)	1.07**	0.2	1.03	0.2	1.05	0.2

BSA, body surface area.

P* < 0.05.*P* < 0.01.****P* < 0.001 compared with girls.

†Values of age, height, weight, BMI, and BSA are expressed in mean and standard deviations.

values were 92, 140 and 172 µg/l for salt without iodine, salt with an iodine content between 5 and 15 ppm, and salt with an iodine content equal or higher than 15 ppm, respectively (Table 3).

Children were interviewed for salt use; 91.3% used packet salt, while 8.7% used 'Khada salt' (rock salt) that was not packed. In households using packaged salt, properly iodised salt coverage was substantially higher (84.0%) than households using non-packaged 'Khada salt' (5.7%). It was also found that the median iodine (IQR) content in unpackaged 'Khada salt' was 5.3 (2.1–10.6) ppm. More worryingly, 3.1% of the study participants consumed salt with negligible iodine content (<5 ppm).

Table 2 Thyroid volume measured by ultrasonography and total goitre rate (TGR) in a different age (a) and body surface area (BSA) (b) groups (n 977)

A.						
Age (years)	n	%	TV (ml) median	IQR	TGR (n)	%
6	141	14.4	1.89	1.64–2.32	2	1.4
7	106	10.8	2.11	1.69–2.64	0	
8	123	12.6	2.36	1.90–2.90	4	3.3
9	110	11.3	2.90	2.19–3.65	2	1.8
10	138	14.1	3.11	2.62–3.84	4	2.9
11	137	14.0	3.60	3.04–4.50	8	5.8
12	222	22.7	3.93	3.24–4.95	7	3.2
Total	977		2.95	2.18–3.89	27	2.8
B.						
BSA (m ²)	n	%	TV (ml) median	IQR	TGR (n)	%
0.6	7	0.7	2.06	1.63–3.15	0	
0.7	42	4.3	1.81	1.47–2.18	0	
0.8	90	9.2	2.08	1.75–2.38	1	1.1
0.9	142	14.5	2.24	1.79–3.01	1	0.7
1.0	202	20.7	2.61	1.98–3.31	1	0.5
1.1	193	19.8	3.18	2.60–3.97	8	4.1
1.2	179	18.3	3.83	3.13–4.69	9	5.0
1.3	90	9.2	3.98	3.34–5.19	7	7.8
1.4	24	2.5	4.24	3.62–6.54	2	8.3
1.5	6	0.6	5.16	4.48–6.60	0	
Total	977		2.95	2.18–3.89	29	3.0

TV, thyroid volume; IQR, interquartile range.

Discussion

The war against the ancient and omnipresent scourge of iodine deficiency is at a crucial point. As per the information released by the Ministry of Health and Family Welfare, Government of India (MOHFW), in revised policy guideline of the National Iodine Deficiency Control Program in 2006 (NIDDCP, 2006), the Gonda district was classified as one of the endemic districts for IDD in Uttar Pradesh⁽²³⁾. There was no published study to reassess goitre prevalence in the Gonda district in the past 10 years. A study conducted in the Gonda district in year 2009 found an overall goitre prevalence of 31%, median UIC 100 µg/l, which was too close to the current criteria to consider that a population has an adequate intake of iodine^(12,21). They also found that 23% of households consumed salt that was not iodised and 56% salt with low content of iodine (5–15 ppm). The survey conducted in this district in 2009 spelled the partial success of USI programme.

However, the current study found that TGR in the Gonda district was 2.8%, estimated with ultrasonography in schoolchildren. The present study results showed further success in implementation of USI programme with TGR showing significant decline of <5%⁽¹²⁾. Recent studies have reported a decreasing trend in goitre prevalence among schoolchildren. Some districts in different parts of India have been declared appropriate for iodine, while others remain mild to moderately endemic^(28–32).

**Table 3** Salt iodine content and median urinary iodine concentration in the study populations

Median urinary iodine concentration ($\mu\text{g/l}$)*	157.1 (IQR†: 94.5–244.9)			
Median salt iodine content (ppm)‡	29.5 (IQR†: 21.0–36.0)			
TGR (enlarged TV§ for age above the 97th percentile of Indian normative data)	2.8 % (95 % CI 1.8, 3.8)			
The iodine content of the household's salt sample‡	<i>n</i> †	%†	MUIC in $\mu\text{g/l}$ †	IQR†
Non-iodised (0–4.99 ppm)	27	3.1	91.9	52.2–143.2
Low iodine content (5–14.99 ppm)	88	10.2	139.7	63.8–226.3
Adequate iodine content (≥ 15 ppm)	745	86.7	172.5	106.1–254.4

TGR, total goitre rate; TV, thyroid volume; MUIC, median urine iodine concentration; IQR, interquartile range; ppm: part per million.

Urinary iodine concentration (UIC) in $\mu\text{mol/l} = \text{UIC in } \mu\text{g/l} \times 0.0079$.

*UIC was measured in 944 children.

†Values are given in *n* (%) or median (IQR).

‡Salt iodine content was measured in 860 household salt sample.

§TV measured by ultrasound.

In the present study, we did not observe an increase in the trend of goitre with age; however, a contradictory finding was reported during studies conducted in the Karnataka state where the prevalence of goitre increased significantly with the advancement of age^(33,34).

TGR (using Indian normative TV data) was 2.8 % and 3 % according to age and BSA, respectively. This result was not compatible with the prevalence of goitre ascertained by physical examination (9.7 %). Studies have shown that thyroid ultrasonography is more effective than palpation in assessing the prevalence of goitre in schoolchildren living in slightly iodine-deficient areas and also found that palpation overestimates the actual thyroid size, particularly in children^(12,13,35).

The TGR calculated using WHO normative TV data was found to be 9.7 % and 15.8 % for age and BSA, respectively. However, it was estimated to be higher when calculated using the Indian reference data⁽¹⁶⁾. This difference may be because the Indian reference data cover areas where USI was introduced in 1984, while the WHO reference data include areas with longer established iodine sufficiency^(15,36–38). Variations have been observed in TV among different regions, indicating that population-specific TV estimates may be more reliable than a single international reference^(16,18).

According to the WHO, the IDD eradication measure is a median value of 100 $\mu\text{g/l}$ UIC, 50 % urine sample iodine content $> 100 \mu\text{g/l}$ and not $< 50 \mu\text{g/l}$ in 20 % population⁽¹²⁾. In our study, the median UIC level of 157.1 $\mu\text{g/l}$ indicated no iodine deficiency among the study population.

These findings resembled other studies recorded from the adjacent area. Studies conducted by Neha *et al.* in three hilly districts of Uttarakhand found adequate median UIC of 211 $\mu\text{g/l}$ with iodised salt coverage in half of the study populations⁽³⁹⁾. A recent meta-analysis of studies from different locations showed a substantial reduction in iodine deficiency and goitre prevalence, which indicates that iodine intake has increased globally⁽⁴⁰⁾.

Our study found that almost all samples of salt (97%) were iodised and nearly 86% of salt samples had an iodine content higher than or equal to 15 ppm, which was similar

to the recently published data under National Family Health Survey 4 (2015–2016) showing that 89.7 % of the households consume adequately iodised salt (≥ 15 ppm) in Gonda district, almost reaching the recommended goal of $>90\%$ coverage^(4,10). The momentum towards USI in the district may be acknowledged because around 91.3% of households consume packet salt. Our study shows that iodisation is higher in the refined and packaged salt category (24.3 ppm) than in the non-refined and non-packaged salt category (5.3 ppm). The proportion of salt samples with iodine content between 5 and 15 ppm may be the simple effect of the distribution of iodine contents around the median of 29.5 ppm. In other words, these low iodine values may represent the normal variation of iodine content around the median. These values are inconsequential as the effectiveness of a food fortification programme mainly depends on the median, and not the variation around median.

In India, non-iodised salt is banned under the NIDDCP and the Food Safety and Quality Authority of India^(41,42). Additionally, efforts were made to nudge salt manufacturers away from unrefined and unpackaged salt processing into refined and packaged salt through processing-end interventions.

Gonda was considered to be a district endemic to severe IDD, including cretinism and a very high prevalence of neonatal hypothyroidism^(19,20). The results of the present study showed more progress in the implementation of the USI programme, with both TGR showing a substantial decrease of $<5\%$ and $>85\%$ of salt samples showing an adequate level of iodine. This was also further corroborated by better iodine nutrition status in terms of median UIC of schoolchildren. USI's goal is to cover more than 90 % of the households under adequate iodised salt consumption. The findings from the study indicate that the Gonda district is close to achieving USI. Therefore, the programme must be more vigilant through continuous monitoring of non-iodised salt trade and regular salt testing to achieve its target^(20,21,43,44).

Sustainability was a major priority for many countries with IDD control programmes. In some countries, which

were previously effective in regulating IDD, there was much evidence of IDD relapse^(45,46). We make the following recommendations to the NIDDCP to avoid IDD relapse and to implement successful USI. First, constant efforts to raise awareness among communities to use packet iodised salt. Second, efforts must be made to ensure efficient supply of adequately iodised salt for distribution and sale. Third, a regular monitoring and evaluation must be carried out in all Uttar Pradesh districts, particularly those listed as an IDD-endemic in NIDDCP 2017, on a priority basis, and a continuous re-evaluation/monitoring at every 5 year interval⁽⁶⁾.

The Government of India is committed to implementing USI. Government of India's commitments include improving the implementation of the legal prohibition on the selling of non-iodised salt for edible purposes, updating the NIDDCP policy guidelines and issuing regular gazette notifications, extra-ordinary powers for the Salt Commissioner to track the quality of salt before shipment to railway wagons, and integrating household salt testing in the National Family Health Survey.

Our robust study design to assess and quantify IDD using internationally approved methods was the strength of this research⁽⁴³⁾. This study's results were based on a large sample size representative of the entire district and based on globally agreed guidelines, with an acceptable sampling design and reporting style⁽⁴⁷⁾. Another advantage of our study was that we have quantified TGR with ultrasonography for the first time in India, in the endemic area of IDD. Our study had few limitations. Ideally, the salt had to be obtained by visiting the child's house, but this was not feasible due to logistical reasons. Another limitation was that normative data for ultrasound volume measurement of thyroid were not widely available from India, except for one study⁽¹⁵⁾.

To conclude, the well-monitored salt iodisation programme in India eventually resulted in UIC optimisation and goitre rate decreased dramatically 35 years after USI in the severely iodine-deficient district of the Gonda. With small additional efforts, the identified limitation will be easily overcome. This programme must be permanent as the diet remains low in iodine content. IDD cannot be eliminated but kept under permanent control by continued operation of the salt iodisation programme. A project approach with effective and efficient coordination among all IDD's control stakeholders in India is required.

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