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Etiological Factors for the Persistence of Endemic Goiter in Selected Areas of Siddharthnagar District in Eastern Uttar Pradesh, India

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ABSTRACT

Aim: **To assess the prevalence of goiter, state of iodine nutrition of the population, consumption pattern of common goitrogenic food, and distribution of iodine through edible salt in selected CD Blocks of Siddharthnagar district in Eastern Uttar Pradesh.**

Methods: **Goiter survey among 1,862 school children, aged 6-12 years, of both sexes, and analysis of iodine (I) and thiocyanate (SCN) in 240 urine samples, and iodine content in 210 edible salt samples collected from the selected study areas.**

Results: **The prevalence of goiter was 26.3% (grade 1: 23.2%; grade 2: 3.1%). Median urinary iodine level was 6.0 μg/dl, and 42% had concentration <5 μg/dl. Mean (SD) urinary SCN was 0.75 (0.4) mg/dl. Only17.1% of salt samples had iodine level >15 ppm; 82.9% had <15 ppm.**

Conclusion: **Consumption of inadequately iodized salt and cyanogenic plant foods containing goitrogenic/anti-thyroidal substances by the people of the studied region are possible reasons for the persistence of goiter during the post salt iodination phase.**

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KEY WORDS

iodine deficiency disorders (IDD), goiter prevalence, urinary iodine, urinary thiocyanate, Eastern Uttar Pradesh

INTRODUCTION

Iodine deficiency, through its effects on the developing brain, has condemned millions of people to a life of few prospects and continued underdevelopment. Iodine deficiency disorders (IDD) refer to clinical and subclinical manifestations that are caused by lack of adequate dietary iodine. The school children living in areas with prevalence of mild to moderate iodine deficiency have an average I.Q. 10 points below those of children living in areas where there is no iodine deficiency[1]. IDD constitute a major public health problem in India. Iodine deficiency also affects the socio-economic development of a community[2]. Globally, an estimated 1,571 million people live in iodine deficient environments[3]. In India, about 167 million people are estimated to be at risk for IDD, of whom 54 million have goiter and over 8 million have neurological deficits[4]. In India not a single state or union territory is free from the problem of IDD. Out of 587 districts in the country, 282 districts have been surveyed for IDD, and in 241 districts IDD are endemic[5]. The role of iodine deficiency as an environmental determinant in the development of endemic goiter has been firmly established. However, further observations indicate the existence of other factors in the etiopathogenesis of endemic goiter[6]. Exposure to naturally occurring agents present in several foods, e.g. flavonoids from millet, magnify the severity of goiter endemia[7], and iodine supplementation does not always result in complete eradication and prevention of goiter[8].

Geographically, Siddharthnagar district in Eastern Uttar Pradesh is located in the foothills of the Himalayas and made up of tarai (flat lands). The entire sub-Himalayan Tarai region is in the classical endemic goiter belt of India[9]. During the post salt iodination phase, reports on endemic goiter and the current state of iodine nutrition are not available. Thus the present study was conducted using quantifiable indicators and standardized methodology to assess the prevalence of goiter, state of iodine nutrition of the population, consumption pattern of common goitrogenic foods that generally interfere with iodine nutrition, and the distribution of iodine through edible salt in certain selected community development blocks of Siddharthnagar district in Uttar Pradesh.

POPULATION AND METHODS

Selection of study area

The Siddharthnagar district lies between the Maharajganj district on the east and Gonda on the west; on the south district Basti separates it, while on the north the boundary marches with Nepal. It has 14 Community Development (CD) Blocks, of which ten are rural and four are urban. The total area of the district is about 2,895 km^2 and the population is about 2 million. In the present study six areas/localities - three from urban blocks and three from rural blocks - were selected[10].

Selection of study population

School children in the age group 6-12 years from both sexes were selected, because of their high vulnerability to goiter, easy accessibility, and that they are representative of their age group in the community[1]. This age group truly reflects the correct status of iodine nutrition in the general population[11]. As there was no available information on the prevalence of goiter in the study areas, the sample size was calculated based on the assumed goiter prevalence of 20%, 95% confidence interval (CI) and allowable/permissible error of 10%. Using these parameters, a sample size of 1,600 was obtained. In our study, a total of 1,862 (53.8% [1,001] male and 46.2% [861] females) school children in the age group 6-12 years were included from six study areas. To provide adequate representation of the target population, in each selected study area, one primary school annexed to a nearby junior high school was randomly chosen for detailed survey. Identified schools were informed one week before the survey to ensure attendance of students. School children and teachers were briefed about the activities to be undertaken during the survey.

Clinical goiter survey/prevalence of goiter

Eighteen hundred and sixty-two school children of the recommended age group were clinically examined for the enlargement of thyroid (goiter) by trained research staff using palpation as per the recommendation of Dunn and Van dar Haar[12]. Goiter grading was carried out using the criteria of WHO/UNICEF/ICCIDD[1] as follows:

Grade 0: No palpable or visible goiter.

Grade 1: A goiter that is palpable but not visible when the neck is in the normal position. It moves upwards in the neck as the subject swallows.

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.

The sum of grades 1 and 2 provided the total goiter rate (TGR).

The age of the students was recorded from the school register and was rounded off to the nearest whole number.

Iodine in urine/state of iodine nutrition

In each study area, 40 urine samples were collected because measurement of iodine content in 40 samples at random gives a clear idea regarding the consumption pattern of iodine intake of that locality[12]. Samples were collected from children of both sexes irrespective of their thyroid status from the clinically examined enrolled students at a definite interval maintaining proportionate representation from the entire population of the studied schools following WHO/UNICEF/ICCIDD criteria[12]. Urine samples were kept in wide-mouth screw-capped plastic bottles with a drop of toluene added to inhibit bacterial growth and minimize bad odor. The samples were brought to the laboratory and kept at 4°C till analyzed. Iodine in the urine was determined by the arsenite method following dry ashing in the presence of potassium carbonate[13]. Internal quality control was maintained by processing standards with a known concentration range of iodine content with each batch of test samples.

Thiocyanate in urine/consumption pattern of common goitrogenic foods

Thiocyanate content in urine was measured from the collected urine samples used for the analysis of iodine by the method of Aldridge[14] and modified by Michajlovskij and Langer[15]. The iodine/thiocyanate ratio (I/SCN) was calculated by the division of each iodine concentration (μg/dl) by the same sample's thiocyanate concentration (mg/dl).

Iodine in salt/distribution of iodine through edible salt

The iodine content of at least 35 salt samples collected at random from a locality represent a valid estimate about the iodine content of the edible salt of the locality[16]. Therefore to measure the iodine content of edible salt samples available in the area, 35 marked airtight plastic containers were distributed at random to the students of the studied schools and they were asked to bring about 20 g of salt from their households the next day. The salt samples were kept at room temperature in the laboratory and iodine content was measured within one week by the iodometric titration method[17].

Study period

The study was conducted during from August to December 2006.

Statistical analysis

The data were collected in a pre-tested proforma. Mean, standard deviation and median values were used to describe the data as appropriate. Two-tailed χ^2 test was applied to determine whether or not there was a significant association between prevalence of goiter with age and sex of the school children, to compare the nature/texture of salt samples and their iodination. P values of less than 0.05 were considered statistically significant.

RESULTS

Prevalence of goiter

Overall TGR was found to be 26.3%, though in most of the children goiter was palpable or Grade 1 (23.2%), but visible goiter or Grade 2 was prevalent (3.1%) in the studied sample. Goiter prevalence was maximum in Mithwal (36.6%) followed by Khesraha (33%), and minimal in Bansi Block (17.2%) (Table 1). Goiter prevalence was significantly higher in rural study areas (31.1%) than in urban areas (21.8%) ($p < 0.001$). Goiter prevalence among girls was 29.4% and in boys 23.6%, and the difference was statistically significant ($p < 0.01$). It was found to be maximal (31.5%) in the age group of 8 years. The difference in goiter prevalence among different age groups was not statistically significant (Table 2).

Urinary iodine and thiocyanate excretion level

The median value for urinary iodine (MUI) concentration was 6 μg/dl. Overall, 9.1% of the studied population had an iodine excretion level below 2.0 μg/dl, showing severe iodine deficiency; 32.9% had a level in the range of 2.0-4.9 μg/dl, indicating moderate iodine deficiency; 30.8% had an iodine level in the range of 5.0-9.9 μg/dl, indicating mild iodine deficiency; while 27% of the population showed no iodine deficiency - their iodine excretion level was ≥10 μg/dl, as per WHO/UNICEF/ICCIDD criteria (Table 3).

In the 240 urine samples were analyzed, the mean (SD) urinary thiocyanate level was 0.7 (0.4) mg/dl (Table 3), indicating that the entire studied population is further exposed to thiocyanate load.

TABLE 1

Goiter prevalence in different study areas of Siddharthnagar District

Study area (CD Block)	Rural/ Urban	Total no. of children	No. of children with goiter			Severity of public health problem
			Grade 1	Grade 2	Total (1+2)	
Bansi	urban	326	51 (15.6%)	5 (1.5%)	56 (17.2%)	mild
Barhni	urban	341	64 (18.8%)	6 (1.7%)	70 (20.5%)	moderate
Sourathgarh	urban	306	71 (23.2%)	15 (4.9%)	86 (28.1%)	moderate
Itwa	rural	297	65 (21.8%)	6 (2.0%)	71 (23.6%)	moderate
Mithwal	rural	292	100 (34.2%)	7 (2.3%)	107 (36.6%)	severe
Khesraha	rural	300	81 (27.0%)	18 (6.0%)	99 (33%)	severe
Total		1,862	432 (23.2%)	57 (3.1%)	489 (26.3%)	moderate

Severity of public heath problem: 5.0-19.9% = mild; 20.0-29.9% = moderate; >30% = severe.

TABLE 2

Goiter prevalence by age and sex in selected areas of Siddharthnagar District

Age (years)	Males (n = 1,001)				Females (n = 861)				Combined TGR (%) (n = 1,862)
	Goiter grade			TGR (%)	Goiter grade			TGR (%)	
	0	1	2		0	1	2		
6 (n = 383)	167	38	2	19.3	129	45	2	26.7	22.7**
7 (n = 413)	174	49	2	22.6	135	48	5	28.2	25.2**
8 (n = 349)	137	46	6	27.5	102	50	8	36.25	31.5**
9 (n = 194)	75	27	3	28.6	63	21	5	29.2	28.9**
10 (n = 184)	80	21	5	24.5	55	19	4	29.4	26.6**
11 (n = 173)	70	17	2	21.3	64	16	4	23.8	22.5**
12 (n = 166)	62	14	4	22.5	60	21	5	30.2	26.5**
Total (n = 1,862)	765	212	24	23.6*	608	220	33	29.4*	26.3

* χ^2 = 8.04, d.f. = 1, p <0.01; ** χ^2 = 9.1, d.f = 6, p >0.05.

TABLE 3

Urinary iodine (I) and thiocyanate (SCN) excretion pattern of the studied school children of Siddharthnagar District

Study area (CD Blocks)	Urinary iodine excretion levels (μg/dl)					SCN⁺ (mg/dl)	I/SCN ratio⁺	I/SCN*	
	median	% Urine samples							
		<2.0	2.0-4.9	5.0-9.9	≥10			<3	3-7
Bansi (n = 40)	5.25	10	37.5	42.5	10	0.4 (0.1)	14.9 (11.5)	2	10
Barhni (n = 40)	10.62	2.5	20	25	52.5	1.1 (0.5)	11.9 (8.7)	4	9
Souratgarh (n = 40)	10	0	12.5	35	52.5	0.8 (0.3)	18.8 (18.7)	1	8
Itwa (n = 40)	4.37	10	45	35	10	0.5 (0.1)	10.6 (8.7)	3	13
Mithwal (n = 40)	3.75	25	57.5	12.5	5	0.8 (0.3)	5.3 (7.0)	16	14
Khesraha (n = 40)	7.5	7.5	25	35	32.5	0.6 (0.3)	27.1 (35.1)	2	7
Total (n = 240)	6	9.1	32.9	30.8	27	0.7 (0.4)	14.8 (18.9)	28 (11.6%)	61 (25.4%)

⁺ Mean (SD); * No. of individuals with I/SCN ratio <3 or 3-7.

TABLE 4

Iodine content of salt samples from selected studied areas of Siddharthnagar District

Study area (CD Block)	No. of salt samples	Iodine content in salt (ppm)			
		0	<15	15-29.9	≥30
Bansi	35	0	35 (100%)	0	0
Barhni	35	1 (2.8%)	31 (88.6%)	3 (8.6%)	0
Sourathgarh	35	3 (8.6%)	24 (68.5%)	3 (8.6%)	5 (14.3%)
Itwa	35	0	34 (97.2%)	0	1 (2.8%)
Mithwal	35	0	31 (88.6%)	4 (11.4%)	0
Khesraha	35	0	15 (42.8%)	15 (42.8%)	5 (14.3%)
All	210	4 (1.9%)	170 (81.0%)	25 (11.9%)	11 (5.2%)

TABLE 5

Iodine content in different categories of salt

Texture of salt	Iodine content in salt	
	<15 ppm	>15 ppm
Powder (n = 52)	26 (50.0%)	26 (50.0%)
Crystalline (n = 158)	148 (93.7%)	10 (6.3%)
Total (n = 210)	174 (82.9%)	36 (17.1%)

$\chi^2 = 52.53$, d.f. = 1, $p < 0.001$.

A significant positive correlation (r = 0.19, p <0.01) was found between urinary iodine level and urinary thiocyanate concentration.

Iodine thiocyanate ratios (I/SCN)

It was found that the mean I/SCN ratio obtained from all study areas was 14.8, which is well above the critical level of 7; 25.4% of the studied individuals had I/SCN ratios ≤7, but more than 3; and 11.6% had I/SCN ratios ≤3. Therefore a total of 37% studied individuals had I/SCN ratios below or equal to the critical level of 7.

Iodine in edible salt

Tables 4 and 5 depict the iodine content of edible household salt. Out of 210 collected edible salt samples, 75.2% (158) were crystal and 24.8% (52) were powder salt. All salt samples were analyzed for iodine; 82.9% had iodine levels below 15 ppm, of which 1.9% had no iodine, 11.9% had an iodine level above 15 ppm but below 30 ppm, and only 5.2% salt samples had an iodine level equal to or more than 30 ppm. Fifty percent of the powdered salt samples and 6.3% of the crystal salt samples had an adequate (>15 ppm) iodine level. A significant difference was found in iodine content between powdered salt and crystal salt (p <0.001).

DISCUSSION

The prevalence of endemic goiter in school children in the age group of 6-12 years is the most widely accepted marker to evaluate the severity of IDD in a region. It indicates the long-term iodine nutritional status in a population[18]. On the basis of goiter prevalence, WHO/UNICEF/ICCIDD[16] recommended criteria to understand the severity of IDD as a public health problem in a region. According to these criteria, a prevalence rate of 5.0-19.9% is considered a mild public health problem; 20.0-29.9% moderate; and above 30% severe. The overall TGR of 26.3% (Grade 1 23.2%; Grade 2 3.1%) indicated that IDD are a moderate public health problem in this region. Out of the six studied areas, in two rural areas, namely Mithwal and Khesraha, IDD are severe. In the present study, the prevalence of goiter among girls (29.4%) was found to be greater than in boys (23.6%), and the difference was statistically significant, which is almost consistent with earlier observations[19,20]. However, a progressive increase in goiter prevalence was found from the age group of 6 years till the age group of 8 years, followed by a decline from the age group of 9 years to 11 years, but no significant association was found between the age of school children and prevalence of goiter.

The urinary iodine level is used as a valuable indicator for the assessment of IDD, as 90% of the body's iodine is excreted through the urine[12]. The median urinary iodine (MUI) level indicates the state of iodine nutrition of a study area when it is based on at least 40 urine samples taken at random[12]. The WHO/UNICEF/ICCIDD have also recommended that no iodine deficiency is indicated in a population when the MUI level is 10 μg/dl or more, i.e. more than 50% of the urine samples should have urinary iodine excretion (UIE) level ≥10 μg/dl, and not more than 20% of the samples have UIE level less than 5 μg/dl[16]. In the present study, the median urinary iodine concentration in the studied areas was 6 μg/dl which is much lower than the recommended level of 10 μg/dl. Overall, only 27% of the children had UIE in the range of optimal iodine nutrition, i.e. ≥10 μg/dl, and 42% had UIE <5 μg/dl. Thus according to the above recommendation, these results indicate that the studied area is biochemically iodine deficient at present. However, in two CD Blocks, namely Itwa and Mithwal, MUI is extremely low (4.37 μg/dl and 3.75 μg/dl, respectively) and more than 50% of the urine samples had iodine <5 μg/dl, indicating extreme iodine deficiency. There may be discrepancies between urinary iodine concentration and the prevalence of goiter, because the UIE level reflects the current iodine status, while the prevalence of goiter indicates the long-term iodine status in a population[18]. In most of our earlier studies in India, findings of high TGR in spite of optimal urinary iodine excretion have been reported[21], suggesting a transition from iodine deficient to iodine sufficient state, or the involvement of factors other than iodine deficiency for the persistence of endemic goiter. The observations of the present study are different; the studied population is still in a state of iodine deficiency.

The uptake and metabolism of iodine by the thyroid gland can be impaired by the pseudohalide thiocyanate (SCN). Urinary excretion of SCN indicates the consumption of cyanogenic plant foods (such as cabbage, cauliflower, radish, mustard, maze, turnip, sweet potato, etc.). In India, large numbers of cyanogenic plants (SCN precursors) are used as common vegetables and thus IDD persist in many such regions in spite of recommended iodine intake[22]. Indian cyanogenic plant foods that are used as common vegetables have potent anti-thyroid activity, and even supplementation with extra iodine fails to counteract their effect[23]. In a recent countrywide survey, Marwaha *et al.*[24] reported that SCN appears to play an important role in goiter formation during the post salt iodination phase, especially among poor children. It has been mentioned that the mean (SD) value in the non-endemic population was 0.5 (0.1) mg/dl[24]. In the present study, the mean (SD) urinary SCN value was 0.7 (0.4) mg/dl. This finding indicates that the consumption of cyanogenic plant foods containing a large amount of SCN precursors, namely, cyanogenic glucosides and thioglucosides, in the region studied is relatively high.

There is a relationship between urinary iodine and SCN concentrations: when the consumption of SCN is increased, as shown by increased urinary SCN level, the excretion of iodine is also increased. Therefore the body's SCN level may be considered as one of the regulators to maintain iodine level in the body.

The available literature suggests that the development of goiter does not necessarily depend upon the consumption of large quantities of food containing SCN precursors but is critically related to the balance between the dietary supplies of iodine and SCN[25]. The I/SCN ratio has been recommended as an indicator of the combined effect on the thyroid of low iodine intake and high SCN exposure. The mean ratio is higher than 7 under normal conditions, and endemic goiter develops when it reaches a critical threshold of 3[26]. In the present study, the mean I/SCN ratio in the Mithwal CD Block was below the critical level of 7, whereas in the other five study areas it was above this critical level. However, it was found that in each study area there were individuals with an I/SCN ratio below 7 or even below 3. A total of 37% of the studied population had I/SCN ratios below or equal to 7, indicating their susceptibility for the development of goiter. Therefore, involvement of SCN or SCN precursors, such as goitrin and isothiocyanates, present in the food consumed by the people of the studied region may have an additional role along with iodine deficiency for the persistence of endemic goiter.

It has been recommended by WHO/UNICEF/ICCIDD that 90% of households should get iodized salt at the recommended level of 15 ppm[27]. The people of this region consume both crystal and powdered (refined) salt. Three-quarters of households (75.2%) consume crystal salt of low iodine content, and the other 24.8% consume powdered salt. Only 11.9% of households consume salt with the recommended iodine level (>15 ppm). This observation revealed that, although salt was being iodized, either an inadequate quantity of iodine was added at the time of fortification at the point of production, or there were losses of iodine at the different points of distribution, such as packaging (jute bags), transportation and storage conditions (open air under sunlight), length of time in distribution (a period of 9 months is required to reach the household level) and climate (humid conditions may reduce iodine by 30-98%). Cultural practices, such as washing salt, may reduce the iodine content in many areas[17]. An earlier study in this district on iodine content in salt suggested that 64.7% of households were consuming salt below the recommended level of 15 ppm[28], and our recent study on another five CD Blocks of this district showed that 83.4% of households were consuming salt with inadequate iodine (<15 ppm)[29]. Comparing the present observation with earlier findings during the post salt iodization phase it has been suggested that there is an urgent need to strengthen the system of monitoring the quality of salt at the household as well as the retailer level to ensure the availability of 15 ppm of iodine at the consumption point, i.e. household level.

In conclusion, the findings of the present study revealed that intake of inadequately iodized crystal salt by the majority of the population is the main cause of biochemical iodine deficiency which is shown by low UIE. In addition, consumption of antithyroidal/goitrogenic substances present in cyanogenic plant foods may have a possible role in the persistence of endemic goiter that may be considered as a moderate public health problem in the studied region during the post salt iodization phase. Strategies need to be developed, involving different government departments, non-governmental organizations as well as members of the community, to increase awareness for both sale and consumption of adequately iodized salts, and regular monitoring of the quality of salt at the household as well as the retailer level to ensure the availability of 15 ppm of iodine at the consumption point/household level. To substantiate the involvement of goitrogenic factors in association with biochemical iodine deficiency for the persistence of these disorders in the region, further studies are important.

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REFERENCES

1. WHO/UNICEF/ICCIDD. Indicators for assessing iodine deficiency disorders and their control through salt iodization. WHO/NUT/94.6, 1994.
2. Levin HM. Economic dimension of iodine deficiency disorders. In: Hetzel BS, Dunn JT, Stanbury JB, eds. The Prevention and Control of Iodine Deficiency Disorders. Amsterdam: Elsevier, 1987; 195-208.
3. United Nations Children's Fund. The State of the World's Children: Focus on Nutrition. New York: Oxford University Press, 1998; pp 15.
4. Ramji S. Iodine deficiency disorders - epidemiology, clinical profile and diagnosis. In: Sachdev HPS, Choudhury P, eds. Nutrition in Children - Developing Country Concern. New Delhi: Department of Paediatrics, Moulana Azad Medical College, 1995; 245-254.
5. Kapil U. Progress made in elimination of IDD and possible impact of lifting ban on sale of non-iodized salt. J Acad Hospital Admin 2000; 12: 33-41.
6. Stanbury JB, Hetzel B. Endemic Goiter and Endemic Cretinism: Iodine Nutrition in Health and Disease. New York: Wiley & Sons, 1980; pp 606.
7. Ermans AM, Mbulamonko NM, Delange F, Ahluwalia R, eds. Role of Cassava in the Etiology of Endemic Goiter and Cretinism. Ottawa: IDRC, IDRC-136e, 1980; 13-16.
8. Gaitan E, Nelson NC, Poole GV. Endemic goiter and endemic thyroid disorders. World J Surg 1991; 15: 205-215.
9. WHO/SEARO. Iodine deficiency disorder in South East Asia. SEARO Regional Health, New Delhi, 1985; paper no. 10.
10. Cochran WG. Sampling Technique, 3rd Ed. Calcutta: Wiley Eastern Ltd, 1977.
11. WHO/UNICEF/ICCIDD. Global Prevalence of Iodine Deficiency Disorders, Micronutrient Deficiency Information System (MDIS). Working Paper No. 1, 1993; pp 5.
12. Dunn JT, Van dar Haar F. Detection of iodine deficiency. In: A Practical Guide to the Correction of Iodine Deficiency - Technical Manual no. 3. The Netherlands: ICCIDD/UNICEF/WHO Publication, 1990; 13-20.
13. Karmarkar MG, Pandav CS, Krishnamachari KAVR. Principle and Procedure for Iodine Estimation; A Laboratory Manual. New Delhi: Indian Council of Medical Research, 1986; 10-12.
14. Aldridge WN. The Estimation of Micro Quantities of Cyanide and Thiocyanate. Analyst London 1945; 70: pp 474.
15. Michajlovskij N, Langer P. Studien uber Benzie Hungen zwischen Rhodanbildung and Kropfbildender Eigenschaft von Nahrungsmitteln. In: Gehalt Einiger Nahrungs Mittel an Praformierten Rhodanid. Hoppe Seyless. Z Physiol Chem 1958; 26-30.
16. Indicators of Tracking Progress in IDD Elimination. IDD Newsletter 1994; 10: 37-41.
17. Sullivan KM, Houston E, Gorestein J, Cervinskas J. Titration methods for salt iodine analysis. In: Sullivan KM, Houston E, Gorestein J, Cervinskas J, eds. Monitoring Universal Salt Iodization Programme. UNICEF/ICCIDD/PAMM/WHO, 1995; pp 11.
18. Sebosta MLD, Dannhauser A, Jooste PL, et al. Prevalence of goiter and urinary iodine status of primary school children in Lesotho. Bull WHO 2003; 81: 28-34.
19. Hetzel BS. An overview of the prevention and control of iodine deficiency disorders. In: Hetzel BS, Dunn JT, Stanbury JB, eds. The Prevention and Control of Iodine Deficiency Disorders. Amsterdam: Elsevier, 1987; 7-31.
20. Chandra AK, Ray I. Influence of age, sex and caste on goiter prevalence of the people in Tripura, North East India. J Hum Ecol 2001; 12: 313-317.
21. Chandra AK, Tripathy S, Ghosh D, Debnath A, Mukhopadhyay S. Goiter prevalence and the state of iodine nutrition in Sundarban delta of North 24-

Parganas in West Bengal. Asia Pac J Clin Nutr 2006; 15: 357-361.
22. Chandra AK, Ray I. Evaluation of the effectiveness of salt iodization status in Tripura, North East India. Indian J Med Res 2002; 115: 22-27.
23. Chandra AK, Mukhopadhay S, Lahari D, Tripathy S. Goitrogenic content of cyanogenic plant foods of Indian origin and their anti-thyroidal activity in vitro. Indian J Med Res 2004; 119: 180-185.
24. Marwaha RK, Tandon N, Gupta N, Karak AK, Verma K, Kochupillai N. Residual goitre in the post iodization phase: iodine status, thiocyanate exposure and autoimmunity. Clin Endocrinol (Oxf) 2003; 59: 672-681.
25. Delange F, Vigneri R, Trimachi F, Filetti S, Pezzino V, et al. Etiological factors of endemic goiter in North Eastern Sicily. J Endocrinol Invest 1978; 2: 137-142.
26. Delange F, Bourdoux P, Colinet E, et al. Nutritional factors involved in the goitrogenic action of cassava. In: Delange F, Ahluwalia R, eds. Cassava Toxicity and Thyroid Research and Public Health Issues. Ottawa: IDRC, 1982; 17-26.
27. ICCIDD/UNICEF/WHO. Assessment of Iodine Deficiency Disorders and Monitoring their Elimination. A Guide for Programme Managers, 2nd Ed. WHO/NHD/01.1, 2001.
28. Kapil U, Singh P. Status of iodine content of salt and urinary iodine excretion in India. Pak J Nutr 2003; 2: 361-373.
29. Chandra AK, Bhattacharjee A, Malik T, Ghosh S. Goiter prevalence and iodine nutritional status of school children in a sub-Himalayan tarai (flat land) region of eastern Uttar Pradesh. Indian Pediatr 2008; 45: 469-474.