

Iodine nutritional status in Uttarakhand State, India

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ABSTRACT

Introduction: Uttarakhand (UK) state is a known endemic region to iodine deficiency (ID). **Objective:** To assess the current status of iodine nutrition in a population of UK. **Methodology:** Three districts, namely Udham Singh Nagar (USN), Nainital (N), and Pauri Garhwal (PG) were selected. In each district, 30 clusters were identified by utilizing the population proportional to size cluster sampling methodology. Total of 6143 school age children (SAC) (USN; 1807, N; 2269, PG: 2067), 5430 adolescent girls (AGs) (USN; 1823, N; 1811, PG: 1796), 1727 pregnant mothers (PMs) (USN; 632, N; 614, PG: 481), and 2013 Neonates (USN; 649, N; 670, PG: 694), were included in the study. Clinical examination of thyroid of each child, AG and PM was conducted. Spot urine and salt samples were collected from children, AGs and PMs. Cord blood samples were collected from neonates for estimation of thyroid stimulating hormone (TSH). **Results:** In SAC, total goiter rate (TGR) was 13.2% (USN), 15.9% (N), and 16.8% (PG). Median urinary iodine concentration (UIC) level was 150 µg/l (USN), 125 µg/l (N), and 115 µg/l (PG). In AGs, TGR was 6.8% (USN), 8.2% (N) and 5.6% (PG). Median UIC level was 250 µg/l (USN), 200 µg/l (N), and 183 µg/l (PG). In PMs, TGR was 16.1% (USN), 20.2% (N), and 24.9% (PG). Median UIC level was 124 µg/l (USN), 117.5 µg/l (N) and 110 µg/l (PG), respectively. In Neonates, TSH levels of >5 mIU/L were found in 55.3 (USN), 76.4 (N) and 72.8 (PG) percent of neonates. **Conclusion:** UIC level in PMs and TSH levels among neonates indicate the prevalence of ID in three districts surveyed.

Key words: Adolescent girls, iodine-deficiency disorders, neonates, pregnant mothers, school age children

INTRODUCTION

Iodine deficiency (ID) is the single most important and preventable cause of mental retardation worldwide. Iodine deficiency disorders (IDDs) refer to all of the consequences of iodine deficiency in a population that can be prevented by ensuring an adequate intake of iodine. ID in the fetus results in miscarriages, stillbirths, brain disorders, retarded psychomotor development, speech, and hearing

impairments.^[1] The thyroid hormones are crucial for brain and neurological development. If the pregnant mother (PM) is iodine deficient, there is a decreased synthesis of thyroxin by the fetal thyroid that leads to compromised mental and physical development of the fetus.^[2]

People living in areas affected by severe ID may have an intelligence quotient (IQ) of up to 13.5 points below that of those from areas where there is no ID.^[1] ID has been found to be associated with at least six of the 8 millennium development goals.^[3] ID directly affects human resource development that in turn greatly affects the human productivity and country's development at large. School

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age children (SAC) (6–12 years), adolescent girls (AGs), PM and neonates are the most vulnerable groups as they are sensitive to even marginal ID.^[1]

Iodine deficiency is a major public health problem in Uttarakhand (UK), India. In 1962, the National Goitre Control Programme was launched in eight hilly districts (Uttarkashi, Chamoli, Pithoragarh, Tehri Garhwal, Pauri Garhwal (PG), Dehradun, Nainital, and Almora) and in Bijnor District in UK.^[4] In the state of UK, according to National Family Health Survey (NFHS)-3 survey only 46% households were using iodized salt with an iodine content of 15 ppm or more.^[5] Earlier surveys conducted among SAC in UK Districts reported a prevalence of goiter as 38.1% Udham Singh Nagar (USN) and 6.9% (Nainital), respectively.^[6,7] Another study conducted among adolescent PMs in Uttaranchal (2003) reported total goiter rate (TGR) of 15% and median urinary iodine concentration (UIC) level of 95 µg/L indicating the presence of ID.^[8]

The daily recommended dietary allowance (RDA) of iodine required by PM is higher (250 µg/day) as compared to normal adult (150 µg/day).^[1] During pregnancy, RDA of iodine is increased by 50% due to (1) physiological increase in maternal and fetal thyroid hormone production and (2) increase in renal iodine losses.^[9]

There is a lack of recent data on the magnitude of ID in the vulnerable groups (SAC, AGs, PMs and Neonates) of UK state. Hence, the present study was conducted to assess the current iodine nutritional status among SAC, AGs, PMs and neonates in three districts of UK.

METHODOLOGY

Study participants

A cross-sectional survey was conducted in the year 2013–2014. The study was undertaken in the state of UK which has three geographical regions namely: (1) Kumaon (2) Terai (Plain) and (3) Garhwal. One district was selected randomly from each region, i.e. Nainital (Kumaon region), USN (Terai region) and PG (Garhwal region). In each district, iodine status was assessed amongst; SAC (6–12 years), AGs (12–≤18 years), PMs and neonates.

School age children

The 30 clusters (schools) in each district were selected by using population proportionate to size sampling (PPS) methodology recommended by WHO/UNICEF/ICCIDD.^[1] In each school, the children were briefed about the objectives of the study and the informed consent was undertaken.

Sample size

Keeping in view the anticipated prevalence of 15%, a confidence level of 95%, absolute precision of 2.0, and a design effect of 1.5, a total sample size of 1800 was calculated for each district. We included 1807 (USN), 2269 (N), and 2067 (PG) of SAC in the present study.

Adolescent girls

The 30 clusters (schools) in each district were selected by using PPS methodology recommended by WHO/UNICEF/ICCIDD.^[1] In each school, the AGs were briefed about the objectives of the study and the informed consent was undertaken. AGs, who were menstruating on the day of the survey, were excluded.

Sample size

Keeping in view the anticipated prevalence of 11.6%, a confidence level of 95%, absolute precision of 1.5, a total sample size of 1751 was calculated for each district. We included 1823 (USN), 1811 (N) and 1796 (PG) of AGs in this study.

Pregnant mothers

The study participants were selected by adopting two-stage sampling technique. In each district, first 30 clusters (villages) were identified by utilizing PPS methodology as recommended by WHO/UNICEF/ICCIDD.^[1] In the second stage, in each cluster (village), sixteen PMs who were attending the antenatal clinics were included. PMs who were consuming drugs that could influence their thyroid status were excluded from the study.

Sample size

Keeping in view the anticipated prevalence of 5%, a confidence level of 90%, absolute precision of 15.0, and a design effect of 2, a total sample size of 510 from each district as calculated. We included 632 (USN), 614 (N), and 481 (PG) of PMs in this study.

Neonates

In selected districts, all the hospitals/Community Health Centres (CHCs)/Primary Health Centres (PHCs) catering to the population for obstetric services were identified and enlisted. Out of which six hospitals/CHCs/PHCs that catered maximum deliveries were randomly selected. A total of 510 births occurred in these government institutions during the study period were included from each district. The informed consents were undertaken from the mother of the neonates. Cesarean deliveries, deliveries in which iodine preparations were used and PMs who were on anti-thyroid therapies were excluded from the study.

Sample size

Keeping in view the anticipated prevalence of 2.9%, a confidence level of 95%, absolute precision of 2.0, and a design effect of 2, a total sample size of 541 from each district was calculated. We included 649 (USN), 670 (N), and 694 (PG) of neonates in the present study.

Clinical thyroid examination

Clinical examination of the thyroid of each child, AGs and PMs was conducted by trained field investigator. The grading of the goiter was done according to the criteria recommended jointly by WHO/UNICEF/ICCIDD (a) grade 0-not palpable and not visible (b) grade I-palpable but not visible (c) grade II-palpable and visible.^[1] The sum of grades I and II provided the TGR of the study population. When in doubt, the investigators recorded the immediate lower grade. The intra- and inter-observer variation was minimized by repeated training of the investigator and by random examinations of goiter grades by the authors.

Laboratory measurements

Urine sample

In each cluster, a minimum of nineteen SAC, AGs, and thirteen PMs were selected (from the subjects who were enrolled for clinical thyroid examination), and casual urine samples were collected from them in the plastic bottles with the screw caps. The urine samples were stored in the refrigerator until analysis. The UIC analysis was done within 2 months using the wet digestion method.^[10]

Salt sample

Similarly, a minimum of eighteen SAC, twenty AGs and eleven PMs were selected, and salt samples were collected from them in the auto-seal polythene pouches. They were requested to bring four teaspoons of salt (about 20 g) from their kitchen. The iodine content of the salt was analyzed by using standard Iodometric Titration (IT) method.^[11]

Quality control measures

We adopted Internal Quality Control (IQC) methodology, in which a pooled urine sample was prepared. This pooled sample was analyzed 25 times with standards and blank in duplicate. The mean (X) UIC and standard deviation (SD) of this pooled sample was calculated. This was considered as IQC sample. The IQC sample was stored in the refrigerator and analyzed with every batch of UIC estimation. The 95% confidence interval for the mean of UIC of IQC sample was then calculated. This was used as the operating control range. The methodology adopted was as follows:

Sample mean (X) ± 2 (standard deviation)

The $X - 2 (SD)$ = the lower confidence limit or lower concentration value (LCV).

$X + 2 (SD)$ = the upper confidence limit or upper concentration value (UCV).

The operating control range for IQC sample was between LCV and UCV.

A regular linear graph paper was utilized to prepare Levey-Jennings plots. The mean UIC of the IQC sample was plotted as a continuous horizontal line on the Y-axis. The LCV was plotted below the mean line on the Y-axis scale, and the UCV was plotted above the mean line on the Y-axis scale. The X-axis was used to plot the date on which the IQC sample was analyzed. This chart was used to plot the date specific analysis. The UIC obtained for the IQC sample for each batch. If the value of the IQC sample was between the two limit lines of LCV and UCV, then the UIC test was deemed in control, and all results were accepted. If any value of the IQC sample was plotted outside the two limit lines of LCV and UCV then, the test was considered as out-of-control, and the entire batch was repeated.^[12]

Umbilical cord blood collection for estimation of thyroid stimulating hormone

Cord blood was collected before placental delivery within five minutes after birth to avoid clotting. One drop of blood was applied to filter paper. The spots were dried at room temperature, and the filter papers were sealed and kept in a freezer until assayed in the laboratory. The samples were stored at 4°C before analysis.

The samples were estimated for thyroid stimulating hormone (TSH) by using sandwich enzyme linked immunosorbent assay method. Dry Blood Spots were eluted in anti-TSH antibodies coated with microwells and were incubated with peroxidase labeled anti-TSH monoclonal antibodies. After washing, the unbound antibodies were washed off, and the bound conjugate remained in the micro well. These bound conjugates further react with substrate 3,3',5,5'-tetramethylbenzidine and produce a color product. The concentration of TSH is directly proportional to the color produced. Absorbance was read at 450 nm, and a value of TSH was expressed in the units' mIU/l of blood. To measure the concentration of TSH in the test sample, the calibration standards and controls were used. The calibration standards and controls were assayed for producing a standard curve of TSH by optical density (O.D) versus TSH concentration (mIU/l). Therefore, by comparing the O.D of the test samples to this standard curve, the concentration of the TSH was determined.^[13-15]

Ethical clearance

The project was approved by Ethical Committee of All India Institute of Medical Sciences, New Delhi.

RESULTS

Total goiter rate

School age children

A total of 6143 SAC were included in the study for the clinical examination of the thyroid gland from the districts of USN ($n = 1807$), Nainital ($n = 2269$) and PG ($n = 2067$). The TGR was found to be 13.2% (USN), 15.9% (N) and 16.8% (PG), respectively [Table 1].

Adolescent girls

A total of 5430 AGs were included in the study for the clinical examination of the thyroid gland from the districts of USN ($n = 1823$), Nainital ($n = 1811$) and PG ($n = 1796$). The TGR was found to be 6.8% (USN), 8.2% (N) and 5.6% (PG), respectively [Table 1].

Pregnant mothers

A total of 1727 PMs were included in the study for clinical examination of the thyroid gland from the districts of USN ($n = 632$), Nainital ($n = 614$) and PG ($n = 481$) in UK. The TGR was found to be 16.1% (USN), 20.2% (N) and 24.9% (P), respectively [Table 1].

Urinary iodine concentration

The median UIC levels and percentage of iodized salt

(salt with an iodine content of less than 15 ppm) consumed by SAC, AGs, and PMs is depicted in Table 1.

School age children

A total of 1778 urine samples were collected from districts of USN ($n = 587$), Nainital ($n = 611$) and PG ($n = 580$). The median UIC levels were 150 $\mu\text{g/l}$ (USN), 125 $\mu\text{g/l}$ (N) and 115 $\mu\text{g/l}$ (PG), respectively.

Adolescent girls

A total of 1816 urine samples were collected from districts of USN ($n = 622$), Nainital ($n = 600$) and PG ($n = 594$). The median UIC levels were 250 $\mu\text{g/l}$ (USN), 200 $\mu\text{g/l}$ (N), and 183 $\mu\text{g/l}$ (PG), respectively.

Pregnant mothers

A total of 1404 urine samples were collected from districts of USN ($n = 532$), Nainital ($n = 468$) and PG ($n = 404$). The median UIC levels were 124 $\mu\text{g/l}$ (USN), 117.5 $\mu\text{g/l}$ (N), and 110 $\mu\text{g/l}$ (P), respectively.

Thyroid stimulating hormone levels

A total of 2013 cord blood samples were collected from districts of USN ($n = 649$), Nainital ($n = 670$) and PG ($n = 694$). The TSH levels of more than 5 mIU/l were found in 55.3 (USN), 76.4 (N) and 72.8 (P) percent of neonates, indicating a high prevalence of ID in the population studied [Table 1].

Table 1: Total Goitre Rate, Median Urinary Iodine Concentration, Percentage of Families Consuming Adequately Iodized Salt and Thyroid Stimulating Hormone among School Age Children, Adolescent Girls, Pregnant Mothers and Neonates in Udham Singh Nagar, Nainital and Pauri Garhwal Districts of Uttarakhand, India

Parameters	Udham Singh Nagar	Nainital	Pauri Garhwal
School age children			
TGR	13.2 (1807)	15.9 (2269)	16.8 (2067)
Median UIC	150 (587)	125 (611)	115 (580)
Percentage consuming adequately iodized salt (>15 ppm)	46.7 (660)	57.7 (642)	40.4 (562)
Adolescent girls			
TGR	6.8 (1823)	8.2 (1811)	5.6 (1796)
Median UIC	250 (622)	200 (600)	183 (594)
Percentage consuming adequately iodized salt (>15 ppm)	40.5 (748)	56.0 (608)	53.3 (600)
Pregnant mothers			
TGR	16.1 (632)	20.2 (614)	24.9 (481)
Median UIC	124 (532)	117.5 (468)	110 (404)
Percentage consuming adequately iodized salt (>15 ppm)	50.3 (597)	67.0 (548)	57.9 (349)
Neonates			
TSH (>5 mIU/L)	55.3 (649)	76.4 (670)	72.8 (694)

Figures in parenthesis denotes total subjects enrolled. TGR: Total goiter rate, UIC: Urinary iodine concentration

DISCUSSION

Urinary iodine concentration is currently the most practical biochemical marker for iodine nutrition. UIC is an indicator of recent dietary intake of iodine in last 24 h, as most of the iodine absorbed in the body appears in the urine. According to WHO/UNICEF/ICCIDD, the median UIC level of <100 $\mu\text{g/l}$ amongst SAC and AGs indicates ID in the community.^[1] The present study found median UIC level of >100 $\mu\text{g/l}$ in all the three districts surveyed amongst SACs and AGs indicating adequate iodine status. Earlier studies conducted amongst SAC in the year 1999 and 2003 from adjoining districts reported the median UIC level of 175 $\mu\text{g/L}$ and 110 $\mu\text{g/L}$, respectively.^[16,17]

AGs are the future mothers. The deficiency during pregnancy leads to adverse health consequences among newborns. A recent study published in lancet among 14–15 years girls reported the presence of mild iodine deficiency (51.0%), moderate deficiency (16.0%) and severe deficiency (1.0%) in the subjects' studied.^[18]

PMs are the most vulnerable to ID as they have increased the requirement for iodine due to the increase in BMR

and increased renal excretion of iodine that accompanies pregnancy. The assessment of UIC in PMs provides their current nutritional status. It also suggests the likely occurrence of IDD among the newborns. Pregnant women are also a prime target group for IDD control activities because they are especially sensitive to even marginal ID. Inadequate iodine status during early pregnancy is adversely associated with child cognitive development. The thyroid hormones are crucial for brain and neurological development. The severe form of ID leads to cretinism and mental retardation. These outcomes are irreversible.^[1]

The present study reported a high prevalence of ID amongst PMs as indicated by low median UIC level (<150 µg/L) in all the three districts surveyed. The median UIC levels among PMs were found to be 124 µg/L (USN), 117.5 µg/L (N), and 110 µg/L (P), respectively indicating the presence of insufficient iodine intake by the PMs in all the three districts. An earlier study conducted among PMs in district USN reported the median UIC level of 95.0 µg/L.^[8] Earlier similar studies conducted amongst the PMs in the neighboring state (Himachal Pradesh) reported median UIC levels as 200 µg/L (Kangra), 149 µg/L (Kullu) and 130 µg/L (Solan) respectively.^[19]

The findings of the present study were substantiated by the low percentage of consumption of salt with adequate iodine content. It was observed that only 50.3% (USN), 67.0% (N) and 57.9% (P) of families were consuming salt with an iodine content of more than 15 ppm. A study conducted in the United Kingdom has documented that children of mothers who had ID during pregnancy are more likely to have low verbal IQ and poor reading accuracy and comprehension.^[20]

In this study, the prevalence of goiter was found to be 16.1% (USN), 20.2% (N) and 24.9% (P) indicating ID as a moderate public health problem among PMs in UK. The TGR illustrates past iodine status and a decrease in iodine intake. Earlier studies conducted amongst PMs in Uttaranchal (2003) and Rajasthan (2008) revealed a goiter prevalence of 15.0% and 3.1%, respectively.^[8,21] In UK, the use of adequately iodized salt by the population has decreased from 60% in NFHS-2 (1989–1999) to 46% in NFHS-3 (2005–2006).^[5] The increase in TGR could be due to consumption of salt with low iodine content by a higher percentage of the population.

Iodine deficiency in Neonates leads to cretinism including mental deficiency with a mixture of Mutism, spastic diplegia, squint, hypothyroidism, and short stature. Neonates are the most vulnerable group for ID. Raised TSH in neonates is an indicator for ID.

WHO (2007) reported that a <3% frequency of TSH concentrations above 5 mIU/L in samples collected 3–4 days after birth indicates iodine sufficiency in a population.^[1] In this study, 55.3 (USN), 76.4 (Nainital) and 72.8 (PG) percent of neonates reported TSH level of >5 mIU/L, indicating the presence of ID. Earlier studies conducted in the districts of Himachal Pradesh, i.e. Kangra and Solan reported that 73.4 and 63.7 percent of the neonates had TSH level of 5 mIU/L and more.^[22,23] Another study conducted in district Kangra had reported that 4.4% of neonates were suffering from neonatal hypothyroidism.^[24] A study conducted in West Bengal reported TSH levels of more than 5 mIU/L in 2.9% of the neonates.^[25]

Several studies have attempted to apply the frequency of neonatal TSH values of more than 5 mIU/L in determining population iodine status and monitoring intervention programs.^[26–28] Studies conducted amongst neonates have documented that ID during the initial phase of life affects the developing brain. Thyroid stimulating hormone affects proper development of the central nervous system.^[1]

CONCLUSION

Findings of this study substantiated that there is a high prevalence of ID amongst PMs and neonates of UK state. Moreover, there is an urgent need to strengthen the IDD control program for prevention of ID in UK. Thus, there is also a need to review the implementation of the iodized salt program in UK. Furthermore, there is an urgent need for a neonatal screening program for early detection of children with ID.

Limitations of the study

- The intra- and inter-observer variation in goiter examination was controlled by repeated training and random examination of goiter grades by an expert. However, despite all of the training for quality control, there is still the possibility of misclassification of a normal thyroid gland as goiter grades I and vice versa
- We could not assess the size of the thyroid gland using ultrasound due to a lack of resources
- Iodine deficiency can be detected using maternal free thyroxine during the first trimester of pregnancy. We could not assess the same due to a lack of resources for this investigation.

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Conflicts of interest

There are no conflicts of interest.

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