Original Article

Iodine nutritional status in Himachal Pradesh state, India

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ABSTRACT

Introduction: Iodine deficiency (ID) is the preventable causes of mental retardation worldwide. Himachal Pradesh (HP) state is a known endemic region to ID. **Objective:** the objective was to assess the current status of iodine nutrition in a population of HP, India. **Methodology:** There are three regions in HP namely: Kangra, Mandi, and Shimla. In each region, one district was selected namely: Kangra, Kullu, and Solan. In each district, 30 clusters were identified by utilizing population proportional-to-size cluster sampling methodology. A total of 5748 school-age children (SAC) (Kangra; 1864, Kullu; 1986, Solan: 1898), 1711 pregnant mothers (PMs) (Kangra; 647, Kullu; 551, Solan: 513), and 1934 neonates (Kangra; 613, Kullu; 638, Solan: 683), were included in study. Clinical examination of thyroid of each child and PM was conducted. Casual urine samples were collected from children and PMs. Cord blood samples were collected for estimation of thyroid stimulating hormone (TSH) among neonates. **Results:** In SAC, total goiter rate (TGR) was 15.8% (Kangra), 23.4% (Kullu), and 15.4% (Solan). Median urinary iodine concentration (UIC) level was 200 μg/l (Kangra), 175 μg/l (Kullu), and 62.5 μg/l (Solan). In PMs, TGR was 42.2% (Kangra), 42.0% (Kullu), and 19.9% (Solan). Median UIC level was 200 μg/l (Kangra), 149 μg/l (Kullu), and 130 μg/l (Solan). In Neonates, TSH levels of > 5 mIU/L were found in 73.4 (Kangra), 79.8 (Kullu), and 63.2 (Solan) percent of neonates. **Conclusion:** As per, UIC level (<100 μg/l) in SAC, ID was found in district Solan. In Kullu and Solan districts, there were ID (UIC level < 150 μg/l) among PMs. TSH levels indicated ID in all districts surveyed.

Key words: Goiter, Himachal Pradesh, iodine deficiency, thyroid stimulating hormone

Introduction

Iodine deficiency (ID) is the single most important and preventable cause of mental retardation worldwide. ID disorders (IDDs) refer to all of the consequences of ID in a population that can be prevented by ensuring an adequate intake of iodine. ID in 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 ID, there is a decreased synthesis of thyroxin by the fetal thyroid, which 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] IDDs have been found to be associated with at least 6 of the 8-millennium development goals.[3] ID directly affects human resource development, which in turn greatly affects

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the human productivity and country's development at large. School-age children (SAC) (6–12 years), PM, and Neonates are the most vulnerable groups as they are sensitive to even marginal ID.[1]

Himachal Pradesh (HP) in India is a known endemic to ID. Kangra Valley experiment (1956–1961) conducted by Indian scientists led to initiation of the National Goiter Control Program, in 1962.[4] A significant progress has been made in the control of IDD through the supply of iodized salt. However, the recent studies conducted on SAC have revealed that total goiter rate (TGR) in many districts are still in the range of 5–20% indicating that the population continues to suffer from chronic iodine insufficiency.[5,6] Earlier surveys conducted among SAC in HP reported a prevalence of goiter as 12.1% (Kangra), 19.8% (Kangra), and 11.3% (Solan), respectively.[5-7]

During pregnancy, recommended dietary allowance (RDA) of iodine is increased by 50% due to: (i) Physiological increase in maternal and fetal thyroid hormone production, and (ii) increase in renal iodine losses.[8] Hence, the daily RDA of iodine required by PM is higher (250 μg/day) as compared to normal adult (150 μg/day).[1]

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

Methodology

Study participants

A cross-sectional survey was conducted in the year 2012–2014. The study was undertaken in The State of HP, which has three geographical regions namely: (i) Kangra, (ii) Mandi, and (iii) Shimla. One district was selected randomly from each region, that is, Kangra (Kangra region), Kullu (Mandi region), and Solan (Shimla region). In each district, iodine status was assessed among; SAC (6–12 years), PMs and neonates.

SAC: The 30 clusters (schools) in each district were selected by using population proportionate to size sampling methodology recommended by WHO/UNICEF/ICCIDD.[1] These 30 schools were selected from rural, urban, and semi-urban areas. 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 1864 (Kangra), 1986 (Kullu), and 1898 (Solan) of SAC in the present study.

PMs: In each cluster seventeen PMs who were attending the antenatal clinics were included. These clusters were selected from rural, urban, and semi-urban areas. 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 647 (Kangra), 551 (Kullu), and 513 (Solan) of PMs in the present study. PMs who were consuming drugs that could influence their thyroid status were excluded from the study.

Neonates: In selected districts, all the hospitals/institutions providing obstetric services were identified and enlisted. Of which 5 hospitals/institutions that provided maximum deliveries were selected. These hospitals were selected from rural, urban, and semi-urban areas. A total of 510 births occurred in these institutions during the study period were included from each district. The informed consents were undertaken from the mother of the neonates. Cesarean 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 613 (Kangra), 638 (Kullu), and 683 (Solan) of neonates in the present study.

Clinical thyroid examination

Clinical examination of the thyroid of each child and PM 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 1 - palpable but not visible, [c] Grade 2 - palpable and visible).[1] The sum of Grades 1 and 2 provided the TGR of the study population. When in doubt, the investigators recorded the immediate lower grade. The intra- and inter-observer variation were minimized by repeated training of the investigator and by random examinations of goiter grades by the first author.

Laboratory measurements

Urine sample

In each cluster, a minimum of fifteen SAC and ten PMs (from the subjects who were enrolled for clinical thyroid examination) were requested to provide casual urine samples in the plastic bottles with the screw caps provided to them. The urine samples were stored in the refrigerator until analysis. The urinary iodine concentration (UIC) analysis was done within 2 months using the wet digestion

method.[9] The median UIC level of < 100 μg/l in SAC and < 150 μg/l in PMs is prescribed cut-off by WHO for defining a population with ID.

Salt sample

A minimum of eleven SAC and eleven PMs were selected and were requested to bring four teaspoons of salt (about 20 g) in the auto seal polythene pouches from their kitchen. The iodine content of the salt was analyzed by using standard iodometric titration method.[10]

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 were 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 (SD)

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.[11]

Umbilical cord blood collection

Cord blood was collected before placental delivery within 5 min 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 (ELISA) method. The ELISA kit was manufactured by Bio-Rad laboratories, Gurgaon, India. 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 microwell. 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' mlU/l of blood. In order 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 (OD) versus TSH concentration (mlU/l). Therefore, by comparing the OD of the test samples to this standard curve, the concentration of the TSH was determined.[12-14] 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.

Ethical clearance

The project was approved by ethical committee of All India Institute of Medical Sciences, New Delhi.

Results

Total goiter rate

1. SAC: A total of 5748 SAC were included in the study for the clinical examination of the thyroid gland from three districts of HP. The enrolled school children in district Kangra of age 6 ≤ 8 years, 8 ≤ 10 years, and 10-12 years were 27.0%, 33.5%, and 39.5%; in Kullu were 31.5%, 41.8%, and 26.7%; and in district Solan were 24.9%, 38.1%, and 37.0%, respectively. The prevalence of goiter Grade 0 was found to be 84.2% (Kangra), 76.6% (Kullu), and 84.6% (Solan); goiter Grade 1 was found to be 15.6% (Kangra), 23.1% (Kullu), and 15.3% (Solan); and goiter Grade 2 was found to be 0.2% (Kangra), 0.3% (Kullu), and 0.1% (Solan), respectively. The TGR was found to be 15.8% (Kangra), 23.4% (Kullu), and 15.4% (Solan), respectively [Table 1].
2. PMs: A total of 1711 PMs were included in the study for the clinical examination of the thyroid

Table 1: TGR, median UIC, percentage consuming adequately iodized salt and TSH among school-age children, pregnant mothers and neonates in Kangra, Kullu, and Solan districts of Himachal Pradesh, India

Parameters	Kangra	Kullu	Solan
School-age children			
TGR	15.8 (1864)	23.4 (1986)	15.4 (1898)
Median UIC (μg/L)	200 (463)	175 (532)	62.5 (513)
Percentage consuming adequately iodized salt (>15 ppm)	82.3 (327)	51.3 (683)	39.5 (557)
Pregnant mothers			
TGR	42.2 (647)	42.0 (551)	19.9 (513)
Median UIC (μg/L)	200 (368)	149 (439)	130 (311)
Percentage consuming adequately iodized salt (>15 ppm)	68.3 (511)	60.3 (436)	48.5 (336)
Neonates			
TSH (>5 mIU/L)	73.4 (613)	79.8 (638)	63.2 (683)

*Figures in parenthesis indicate the number of total subjects surveyed. TGR: Total goiter rate, UIC: Urinary iodine concentration, TSH: Thyroid stimulating hormone

gland from three districts in HP. The PMs from the age of 18 to 42 years were enrolled in the study. The prevalence of goiter Grade 0 was found to be 57.8% (Kangra), 57.9% (Kullu), and 80.1% (Solan); goiter Grade 1 was found to be 40.2% (Kangra), 41.0% (Kullu), and 19.7% (Solan); and goiter Grade 2 was found to be 2.0% (Kangra), 1.0% (Kullu), and 0.2% (Solan), respectively. The TGR was found to be 42.2% (Kangra), 42.0% (Kullu), and 19.9% (Solan), respectively [Table 1].

Urinary iodine concentration

The UIC levels and percentage of iodized salt (salt with an iodine content of 15 ppm or more) consumed by SAC and PMs are depicted in Table 1 and Figure 1.

1. SAC: The median UIC Levels were 200 μg/l (Kangra), 175 μg/l (Kullu), and 62.5 μg/l (Solan), respectively.
2. PMs: The median UIC Levels were 200 μg/l (Kangra), 149 μg/l (Kullu), and 130 μg/l (Solan), respectively.

Thyroid stimulating hormone levels

The TSH levels of more than 5 mIU/L were found in 73.4 (Kangra), 79.8 (Kullu), and 63.2 (Solan) percent of neonates indicating high prevalence of ID in the population studied.

Discussion

The present study reported a high prevalence of ID among SAC and PMs as indicated by high TGR level and low median UIC level. The TGR in a population indicates past iodine status and chronic low intake of iodine. Whereas, 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. UIC is currently the most practical biochemical

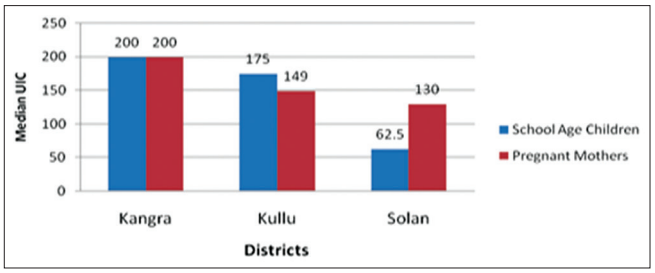

Figure 1: Median urinary iodine concentration level among school-age children and pregnant mothers in Kangra, Kullu, and Solan districts of Himachal Pradesh

marker for iodine nutrition. According to WHO/UNICEF/ICCIDD, the median UIC level of < 100 μg/l among SAC indicates ID in the community.[1] The present study found low iodine status among SAC in district Solan as indicated by median UIC level of < 100 μg/l. This could be possibly due to consumption of salt with < 15 ppm of iodine. An earlier study conducted in district Solan had reported the median UIC level as 150 μg/l.[7] The lower median UIC level in the present study could be due to a higher percentage of the population consuming salt with inadequate iodine (26.7%[1999] vs. 60.5%, in the present study).[7]

A recent 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.[15] PMs are the most vulnerable group for IDD as they have increased the requirement for iodine due to the increase in basal metabolic rate and increased renal excretion of iodine that accompany pregnancy. The assessment of UIC in PM provides their current nutritional status. It also suggests the likely occurrence of IDD among the newborns.[1] The present study found low iodine status in PMs of districts Kullu and Solan as indicated by median UIC level of < 150 μg/l. We are unable to compare the findings of our study on iodine status among PMs with other similar studies due to a lack of published data. Earlier studies conducted among the PMs in the neighboring states reported median UIC levels as: 110 μg/l (Pauri), 117.5 μg/l (Nainital), 124 μg/l (Udham Singh Nagar), and 95 μg/l (Udham Singh Nagar), respectively.[16,17]

ID 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. According to WHO, raised TSH in neonates at birth 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 the present study, 73.4 (Kangra), 79.8 (Kullu), and 63.2 (Solan) percent of neonates reported TSH level of 5 mlU/l and more indicating the presence of ID in three districts surveyed. This could be possibly due to a higher percentage of families consuming salt with an iodine content of < 15 ppm.

The earlier studies conducted over a period of time in the district of Kangra, Kullu, and Solan have shown that iodine nutritional status depends upon the iodine content of salt consumed by the population. The UIC levels were low when the population was consuming salt with low iodine intake and vice versa.[5-7]

Several studies have attempted to apply the frequency of neonatal TSH values of more than 5 mIU/L in determining the population iodine status and monitoring intervention programs.[18-20] Studies conducted among neonates have documented that ID during the initial phase of life affects the developing brain. TSH affects proper development of the central nervous system.[1] An earlier study conducted in West Bengal reported TSH levels of more than 5 mIU/L in 2.9% of the neonates.[21] Our earlier study conducted in district Kangra have documented 4.4% of neonates were suffering from neonatal hypothyroidism.[22]

Conclusion

The findings of the present study indicate that there is an urgent need to strengthen the IDD control program for prevention of ID in HP. There is a high prevalence of ID among SAC, PMs, and neonates of HP. Thus, there is a need to review the implementation of the iodized salt program in HP. Furthermore, there is an urgent need for a neonatal screening program for early detection if children with ID.

Limitations of the Study

1. 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 for misclassification of a normal thyroid gland as goiter Grades 1 and vice versa
2. We could not assess the size of the thyroid gland using ultrasound due to a lack of resources
3. ID 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
4. Cord blood sample taken immediately after delivery could have false positive high values of TSH due to physiological neonatal TSH surge that elevates TSH level

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