Brief Communication
Lab Med Online
Vol. 9, No. 4: 232-235, October 2019
https://doi.org/10.3343/lmo.2019.9.4.232

Clinical Chemistry

Iodine Deficiency in Neonates: Where Do We Stand After a Quarter Century of Initiating Iodization Programs?

Lena Jafri, F.C.P.S., Hafsa Majid, F.C.P.S., Sibtain Ahmed, F.C.P.S., Imran Siddiqui, F.C.P.S., Farooq Ghani, Ph.D., Aysha Habib Khan, F.C.P.S.

Department of Pathology and Laboratory Medicine, Aga Khan University, Karachi, Pakistan

An observational study was conducted at the Section of Clinical Chemistry, Department of Pathology and Laboratory Medicine, to assess the iodine status using the World Health Organization (WHO), United Nations International Children's Emergency Fund (UNICEF), and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) consensus criteria, which state that >3% prevalence of serum thyroid stimulating hormone (TSH) ≥10 mIU/L in the population is an indicator of iodine deficiency. Serum neonatal TSH was analyzed from January to December 2013. In a period of one year, a total of 11,597 neonates with the mean (25 percentile, 75 percentile value) age of 2.0 days (0.5–3.5) were tested for serum TSH. The overall mean TSH level was 3.38 mIU/L (5.63–1.96), with optimal levels (1–39 mIU/L) in 93%, <1 mIU/L in 6.3%, and ≥40 mIU/L in 0.3% neonates. Of all the neonates, 7.9% (N=916) showed TSH ≥10 mIU/L which is higher than the recommended WHO/UNICEF/ICCIDD criteria for mild endemicity for iodine deficiency in the population. These results suggest that iodine deficiency is still prevalent in our population, indicating a need for effective intervention programs and increasing awareness regarding the use of iodized salt and supplementation in all reproductive-aged women to prevent iodine deficiency in neonates.

Key Words: Iodine, Deficiency, Congenital hypothyroidism, Neonates, Thyroid stimulating hormone

Iodine deficiency constitutes a major nutrition problem worldwide [1]. The youth are the most susceptible to iodine deficiency and its consequences, as iodine is essential for normal growth and development. The most deleterious effect of iodine deficiency is mental retardation and it is reported to be associated with a loss of intelligence quotient [2]. In Pakistan, iodine deficiency is known to exist in the northern region including the Khyber Pakhtunkhwa province and Azad Jammu and Kashmir [3]. For preventing this, salt iodization programs were started in 1989 by the National Iodine Deficiency Disorder (NIDD) program in Pakistan, but a high number of the rural population still uses non-iodized salt [4]. Consumption of iodized salt in Pakistan, last measured in 2011, was found in 69.20% of the households, according to the World Bank [5]. Iodine deficiency lowers the circulating T4 and raises the serum thyroid stimulating hormone (TSH), due to which iodine-deficient populations generally have higher serum TSH concentrations compared to iodine-sufficient groups. Screening in developed countries is directed at detecting neonates with congenital hypothyroidism (TSH >40 mIU/L in serum) and not at assessing iodine status. However, serum TSH can also be used to assess the iodine status of a population.

Serum TSH is not a practical marker for iodine deficiency in school-going children and adolescents, as the serum TSH values of iodine sufficient and insufficient groups overlap. Serum TSH is reported to be a valuable indicator for iodine deficiency in neonates as they have low total body iodine content and high turnover. This higher turnover of iodine leads to increased TSH levels, and its response is enhanced in iodine deficiency [6]. Hence, TSH levels are increased in iodine-deficient neonates and this phenomenon is called transient hypothyroidism [7]. Therefore, evaluating elevated TSH level is a valuable indicator of the severity of

Corresponding author: Hafsa Majid, F.C.P.S.
https://orcid.org/0000-0001-7506-7988
Section of Chemical Pathology, Department of Pathology and Laboratory Medicine, Aga Khan University, Stadium Road, Karachi 74800, Pakistan
Tel: +92-21-3486-1945, Fax: +92-21-34934294, E-mail: hafsa.majid@aku.edu

Received: August 10, 2018
Revision received: January 28, 2019
Accepted: February 12, 2019

This article is available from http://www.labmedonline.org

iodine deficiency in neonates, if performed within 48–72 hours of life [7].

The World Health Organization (WHO) in collaboration with United Nations International Children's Emergency Fund (UNICEF), and the International Council for Control of Iodine Deficiency Disorders (ICCIDD) recommend that serum TSH levels >10 mlU/L are mild elevations and are proportional to the degree of iodine deficiency [8]. The consensus statement states that when a sensitive TSH assay is used on samples collected three to four days after birth, a <3% frequency of TSH values >10 mlU/L indicates iodine sufficiency in a population [9].

The present study aimed to evaluate the iodine status in neonates tested at our center using the current WHO/UNICEF/ICCIDD criteria for iodine deficiency, i.e., >3% of neonates exhibiting TSH values >10 mIU/L indicates iodine deficiency.

Retrospective analysis of laboratory data from patients tested for serum NTSH from January to December 2013 was conducted at the Section of Chemical Pathology, Department of Pathology and Laboratory Medicine, Aga Khan University Hospital. For all subjects, only initial test results were included and repeated testing results were excluded. Our center is a tertiary care center based in Karachi with both urban and rural patients. Most females registered for delivery belong to urban areas. Additionally complicated cases from rural areas and peripheral regions are also referred to our center. In the present study, neonates were discharged after 48 hours and samples are obtained right before discharge. To maintain confidentiality, instead of the patient identification details a code was assigned. Exemption was sought from the institutional ethical review committee (3344-Pat-ERC-14).

For TSH analysis, 2 mL of blood was collected in a gel separator tube and sent to a laboratory. At the laboratory, serum was separated and analyzed by an automated analyzer ADVIA Centaur (Siemens Diagnostics, NY, USA), using a chemiluminescence immunoassay technique. Three levels of quality control materials were run with each batch of samples and the laboratory participated in a proficiency testing surveys of the College of American Pathologist twice a year with >80% performance compared with peer group. The optimal TSH was 1–39 mIU/L, while a value ≥40 mIU/L was labeled as congenital hypothyroidism.

According to the WHO/UNICEF/ICCIDD 'consensus criteria' more than 3% prevalence of serum TSH ≥10 mIU/L in a population is considered as an indicator of iodine deficiency. A frequency of 3–19.9% indicates mild iodine deficiency. Frequencies of 20–39.9% and above 40% indicate moderate and severe iodine deficiency, respectively [5].

The statistical analysis was performed using the Statistical Package of Social Sciences (SPSS) version 19. For examining the distribution of data, Kolmogorov-Smirnov test was performed. Statistical analyses were performed for continuous variables whereas data were analyzed for the frequency of samples from each group (<1 mIU/L, 1–10 mIU/L, 10–40 mIU/L, >40 mIU/L).

Within a period of one year, a total of 11,597 samples were analyzed for neonatal serum TSH, the median (25 percentile, 75 percentile value) age of neonates was 2.0 days (0.5–3.5). Nearly 90% (N=10,441) of the neonates tested for serum NTSH were born at the Aga Khan University Hospital, whereas the remaining samples were received from outpatient clinics. The distribution of data was skewed on Kolmogorov-Smirnov test ($P<0.001$).

The overall median TSH level was 3.38 mIU/L (149.99). Optimal levels of TSH were found in 86% of the neonates, and TSH level <1 mIU/L was found in 6.4% of the neonates Congenital hypothyroidism was suspected in 0.3% of the neonates with a serum TSH value ≥40 mIU/L. Hyperthyroidism was suspected in 0.1% of the neonates with serum TSH <0.1 mIU/L. Of the neonates, 7% (N=916) showed TSH ≥10 mIU/L, which is higher than the recommended WHO criteria for mild endemicity for iodine deficiency in the population. The distribution of serum TSH and the frequency of subjects with deficiency are shown in Table 1.

In the present study, we observed that despite implementation of NIDD programs, iodine deficiency is still prevalent in our pop-

Table 1. Distribution of Serum TSH in children tested at the Clinical Laboratory over a period of 1 year (N=11,597)

	Serum TSH (mIU/L)				
	<0.1	0.1–<1	1–10	10–<40	≥40
Frequency of neonates (%)	11 (0.1)	743 (6.4)	9,927 (86)	884 (7)	32 (0.3)
Median (IQR) serum TSH	0.016 (0.010–0.057)	0.75 (0.56–0.88)	3.325 (2.11–5.11)	12.61 (11.21–15.56)	100 (59.5–146.7)

Data are represented as frequency (%) and median (25 percentile, 75 percentile value). The conversion factor of mIU/L to uIU/mL is 1.

ulation, with nearly 8% neonates tested at 2nd day of life exhibiting serum TSH >10 mIU/L. This indicates a 'mild iodine deficiency' according to the criteria. The national nutrition survey 2011 (NNS 2011) conducted in Pakistan, reported that children aged 6–12 years had median urinary iodine levels of 126 μg/L, but adequate iodine levels (>100 μg/L) were found in only 63.3% of the children [10, 11]. This survey also reported that 7% of school-going children (6–12 years) had either palpable or visible goiters on clinical examination, which is another indicator for iodine deficiency status. Our study findings are comparable with the prevalence of goiter reported by NNS in 2011; however, the actual figures of iodine status in our population may be much poorer as the urinary iodine estimation shows a higher prevalence of iodine deficiency.

Our TSH method is a fourth generation or ultrasensitive assay that detects very low quantities of NTSH.

Pakistan is the 6th most populous country in the world, with a population of about 180 million. More than 42% of the Pakistani population is aged <14 years [12]. Priorities for child healthcare have focused on infectious diseases, malnutrition, and other communicable diseases. There is lack of government commitment to invest in correcting the micronutrient status. Salt iodization programs in our country were started in 1989, but the reported use of iodized salt for cooking is 39.8% (NNS 2011) [10]. The main reasons for this include the absence of legislations regarding salt iodization and the introduction of these programs only in large scale salt processors. Since 70% of our population resides in rural areas and uses salt sourced from small scale salt processors, our population is not benefitting from these programs. Moreover, there is no proper mechanism for assessing the efficiency of such programs and for educating the public regarding the benefits of using iodized salt in regular diet. Although the main responsibility for a successful national salt iodization programme rests with government officials and international agencies to assist governments with appropriate advice, funding, and training, it is high time that private sector agencies come forward and spread this message.

There are some limitations to our study. Here, urinary iodine concentration was not measured for assessing iodine status. Although urinary iodine measurement is superior to serum TSH for assessment of iodine status, but the method for its measurement is inductively coupled with Mass Spectrometry, and thus, requires expertise and cannot be performed routinely [13]. Contrarily, serum TSH assessment can reliably replace urine iodine estimation if performed using an accurate and precise methodology with neonatal samples collected less than 48 hours after birth [14]. Since the current study included only laboratory data of serum TSH and the prevalence of iodine deficiency can be increased or decreased if actual urinary iodine is measured.

In conclusion, iodine deficiency is prevalent in Pakistan as shown by the frequency of high serum TSH levels in this study. Eradication of iodine deficiency must be made a national goal, indicating that there is a need for effective intervention programs and increasing awareness among the public regarding the use of iodized salt. We should particularly aim to improve the iodine status of young children and pregnant ladies to prevent consequences of iodine deficiency and improve fetal outcomes [15].

AUTHORS' DISCLOSURES OF POTENTIAL CONFLICTS OF INTEREST

No potential conflicts of interest relevant to this article were reported.

REFERENCES

1. Delange F. Iodine deficiency as a cause of brain damage. Postgrad Med J 2001;77:217-20.
2. Qian M, Wang D, Watkins WE, Gebski V, Yan YQ, Li M, et al. The effects of iodine on intelligence in children: a meta-analysis of studies conducted in China. Asia Pac J Clin Nutr 2005;14:32-42.
3. Sarwar S, Aslam M, Waqar MA, Hussain M, Butt IF. Iodized salt: a risk factor for hyperthyroidism. JRMC 2013;17:284-7.
4. Azizi F and Mehran L. Experiences in the prevention, control and elimination of iodine deficiency disorders: a regional perspective. East Mediterr Health J 2004;6:761-70.
5. De Benoist B, Maria A, Ines E, Bahi T, Henrietta A. Iodine status worldwide: WHO global database on iodine deficiency. Geneva: World Health Organization, 2004.
6. Delange F. Screening for congenital hypothyroidism used as an indicator of the degree of iodine deficiency and of its control. Thyroid 1998; 8:1185-92.
7. Sağlam H, Büyükuysal L, Köksal N, Ercan I, Tarim O. Increased incidence of congenital hypothyroidism due to iodine deficiency. Pediatr Int 2007;49:76-9.
8. Kapil U. WHO indicators for valid assessment of iodine deficiency

https://doi.org/10.3343/lmo.2019.9.4.232

disorders. Indian J Community Med 2009;34:268.

9. Sullivan KM, May W, Nordenberg D, Houston R, Maberly GF. Use of thyroid stimulating hormone testing in newborns to identify iodine deficiency. J Nutr 1997;127:55-8.
10. Aga Khan University, Pakistan, Pakistan Medical Research Council (PMRC), Nutrition Wing, Ministry of Health, Pakistan, Pakistan National Nutrition Survey 2011. http://www.mhinnovation.net/sites/default/files/downloads/innovation/research/Pakistan%20National%20Nutrition%20Survey%202011.pdf (draft May 2012).
11. Bhutta Z, Soofi S, Zaidi S, Habib A, Hussain M. Pakistan National Nutrition Survey, 2011. Available at: https://ecommons.aku.edu/pakistan_fhs_mc_women_childhealth_paediatr/262
12. Sarwar S, Saeed I, Razzaq Z. Urinary iodine levels in residents of Azad Jammu and Kashmir. JRMC 2014;18:142-4.
13. Zimmermann MB. Methods to assess iron and iodine status. Br J Nutr 2008;99:S2-9.
14. Eastman CJ. Screening for thyroid disease and iodine deficiency. Pathology 2012;44:153-9.
15. Zimmermann MB. Iodine deficiency in pregnancy and the effects of maternal iodine supplementation on the offspring: a review. Am J Clin Nutr 2009;89:668S-72S.