

# Relationship Between Maternal Iodine Status and Cord Blood Thyroid Function Profile in an Iodine Sufficient Environment

Jibril M El-Bashir<sup>1</sup>, Abbiyesuku M. Fayeofori<sup>2</sup>, Adamu Sani Gombe<sup>3</sup>, Abdullahi.J. Randawa<sup>4</sup>, Abdurrahman B. Muhammad<sup>5</sup>, Aliyu S. Ibrahim<sup>1</sup>, Adamu Rabiu<sup>1</sup>, Suleiman M. Hafsatu<sup>1</sup>, Yahya Anisa<sup>4</sup>, Lawal B. Kankia<sup>4</sup>

<sup>1</sup>Department of Chemical Pathology ABU Zaria, <sup>2</sup>Department of Chemical Pathology Babcock University, <sup>3</sup>Department of Chemical Pathology FTH Gombe, <sup>4</sup>Department of Obstetrics and Gynaecology ABU Zaria, <sup>5</sup>Department of Chemical Pathology Usmanu Danfodio University Sokoto.

\*Correspondence: Dr. Jibril Mohammed El-Bashir. Department of Chemical Pathology ABU Zaria **Email:** mejibril@abu.edu.ng. **Tel:** +2348058095678.

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## ABSTRACT

**Background:** During the 10th to 12th week of gestation, foetal TSH appears and the foetal thyroid gland is capable of concentrating iodine and synthesizing iodothyronines. However, little hormone synthesis occurs until the 18th to 20th week. Thereafter, foetal thyroid secretion increases gradually. Foetal iodine is obtained from maternal sources and the extent to which maternal thyroid hormones cross the placenta is controversial. **Aim:** To determine the relationship between maternal iodine status with cord blood thyroid function test. **Method:** A prospective longitudinal study of two hundred and thirteen apparently healthy pregnant women was conducted consisting of 58, 87 and 68 in first, second and third trimesters respectively. Cord blood thyroid function tests (TSH, free T<sub>3</sub> and free T<sub>4</sub>) were assayed using commercial ELISA kits while urinary iodine concentration (UIC) was assayed using modified Sandell – Kolthoff reaction. Median UIC of less than 150, 150 – 249 and above 249 µg/L were considered inadequate, adequate and more than adequate respectively. Data was analysed using Epi – info 3.5.3 and p – value less than 0.05 was considered significant. **Results:** Cord blood TSH mean (SD) was significantly elevated 9.44(7.4) µIU/L in cord blood of mothers with inadequate iodine status compare with those having adequate 7.21(8.4) µIU/L and more than adequate 6.81 (5.5) µIU/L (p = 0.0029). There was a significantly positive correlation between maternal UIC and cord blood TSH (P = 0.0000, r = 0.26) but not with free T<sub>4</sub>. Cord blood TSH suggestive of congenital hypothyroidism (> 20 µIU/L) was seen in 9 out of 90 (10 %) of those with insufficient, 2/31 (6.5 %) of those with sufficient and 3/92 (3.3 %) of those with more than adequate iodine statuses. **Conclusion:** Cord blood TSH relates positively with maternal iodine status.

**Key words:** Cord Blood, Thyroid, Iodine, Placenta, Hypothyroidism

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## INTRODUCTION

Iodine deficiency is a significant public health problem throughout the world.<sup>[1]</sup> The effect is particularly clearer among pregnant women and young children.<sup>1</sup> The most devastating outcomes are increased perinatal mortality and mental retardation.<sup>[1]</sup> The main factor responsible for iodine deficiency is low dietary iodine which is usually due to low iodine level in the soil as a result of repeated leaching effects of snow, running water and heavy rainfall.<sup>[1,2]</sup> Crops grown on this soil do not provide adequate amounts of iodine to the body when eaten.<sup>[1]</sup>

Iodine is normally present in the body in minute amounts.<sup>1</sup> It is mainly found in the thyroid gland serving its main role in the synthesis of thyroid hormones. When body iodine content is inadequate, thyroid hormone synthesis is impaired, resulting in hypothyroidism and a series of functional and developmental abnormalities known as Iodine Deficiency Disorders.<sup>[1]</sup> Spectrum of iodine deficiency disorders in foetus and neonates include abortions, stillbirths, congenital anomalies, increased perinatal mortality, endemic cretinism, deaf, mutism, neonatal goiter, neonatal hypothyroidism and endemic mental retardation.<sup>[1]</sup> Zaria is an iodine sufficient environment.<sup>[3]</sup> Its median urinary iodine concentration was reported to be 193 µg/L among pregnant women and 205 µg/L in non-pregnant women within reproductive age group.<sup>[3]</sup> This fall within the iodine sufficiency range of 150 – 250 µg/L as recommended by WHO.<sup>[1,2,4]</sup>

The anatomy of the thyroid gland is evident around seven weeks of intrauterine life by appearance of bilobed thyroid shape.<sup>[5]</sup> Histologically, thyroid follicles containing colloid are seen by 10 weeks. Iodine trapping begins by 10 weeks,<sup>6</sup> thyroid hormones (T<sub>4</sub> and T<sub>3</sub>) synthesis and secretion at 12 weeks and TSH secretion can be detected at 12 weeks.<sup>[5,7]</sup>

During intrauterine life, the foetus is completely dependent on the mother for supply of thyroid hormones until mid-gestation when foetal thyroid hormone synthesis begins.<sup>[3,5,6]</sup> However, mother's

iodine continues to be its only source.

Congenital hypothyroidism, occurs in approximately 1:2000 – 1:4000 newborns.<sup>[4,9,10]</sup> It is the most common treatable cause of mental retardation in children.<sup>[4]</sup> Most new-born babies with congenital hypothyroidism have no clinical manifestations of thyroid deficiency.<sup>[4]</sup> As a result, it is difficult to predict which infants are likely to be affected.<sup>[4]</sup> For these reasons, new-born screening programs in which either thyroxine (T<sub>4</sub>) or thyrotropin (TSH) are measured in heel-stick blood specimens were developed to detect this condition as early as possible.<sup>[4]</sup>

## MATERIALS AND METHODS

A longitudinal prospective study that involved 213 pregnant women (58 in first trimester, 87 in second trimester and 68 in third trimester). The study subjects were recruited from ABU Teaching Hospital, Audu Kwari Primary healthcare and Kofan Gayan general hospital, all in Zaria. Their ages ranged between 14 and 45 years. All subjects were apparently healthy with no evidence of renal, hepatic, endocrine or other metabolic diseases that would affect thyroid function. None of the participants was on restricted salt intake or smokes cigarette. They were also not on any drug that may affect thyroid function or iodine metabolism except for the iodized table salt. Each subject had resided in the locality for at least six months before enrollment into the study. Ethical approval was obtained from Kaduna State ministry of health and informed written consent was obtained from the subjects. About 5 milliliters of urine specimens were collected between 9 and 11:00 am. They were kept frozen at -20 °C until analysis. Urinary iodine concentration was determined using modified Sandell – Kolthoff reaction. The method has within run and between run coefficient of variations of 5.5 % and 9.2 % respectively.<sup>[8]</sup> Cord bloods were carefully collected from umbilical veins after delivery of placenta using a wide bore needle and syringe. The specimens were transferred to 10 ml plain bottles and allowed to stand at room temperature for one

hour to clot before centrifuging at 5000 rpm for 5 minutes to separate sera which was then frozen at -20 °C until analysis.

Data was analysed using EPI – INFO 3.5.3 software. Difference in mean values was analysed using Mann – Whitney test, Chi – square or Wilcoxon rank test. Correlation between cord blood TSH, free T<sub>4</sub> and free T<sub>3</sub> with urinary iodine concentration was done using Spearman correlation coefficient. Urinary iodine concentrations were described using medians and ranges as recommended by W.H.O.<sup>[1,2]</sup> P – Values of < 0.05 were considered significant.

### RESULTS

Table 1 shows socio-demographic characteristics of the participants. All the participants are within reproductive age group of 15 – 40 years with mean age (SD) of 25.13 (6.0) years. Parity, mean (SD) was 2.23 (2.2) ranging between 1 and 10 childbirths. The mean (SD) systolic and diastolic blood pressures were 117.72 (10.3) and 77.49 (10.4) respectively. Gestational age mean (SD) was 21.05 (10.8) with the range between 4 weeks and 44 weeks. The overall mean (SD) cord blood TSH was 7.98 (6.9) mIU/L and the range was between 0.54 and 44.1 mIU/L.

Ninety of the participants (42.3 %) had inadequate, 31 (14.6 %) had adequate and 92 (43.2 %) had more than adequate nutritional iodine statuses. The median (range) urinary iodine concentrations were 57 (13 - 145), 200 (150 – 242) and 367 (250 – 660) µg/L for those having inadequate, adequate and more than adequate iodine statuses respectively. Cord blood TSH was significantly lower among those having more than adequate iodine levels compare with those having inadequate iodine statuses (6.8 (5.5) vs 9.44 (7.4), *P* = 0.0029). Cord blood free T<sub>3</sub> and free T<sub>4</sub> were similar among the groups having inadequate, adequate and more than adequate iodine levels, *P* > 0.05 (See table 2).

Among the 14 participants with cord blood TSH of more than 20 mIU/L, nine (64.3 %) belonged to the group having inadequate iodine, 2 (14.3 %) were from the group with adequate iodine levels while

3 (21.4 %) from those having more than adequate iodine (see table 3).

Linear regression showed that urinary iodine concentration correlated significantly and positively with TSH (*r* = 0.26, *P* = 0.0000) but not with free T<sub>3</sub> and free T<sub>4</sub> (see table 4).

**Table 1. Socio - Demographic characteristics of the mothers**

	Mean (SD)	Range
Age (years)	25.13 (6.0)	15 – 40
Parity	2.23 (2.2)	1 – 10
Systolic BP (mmHg)	117.72 (10.3)	80 – 170
Diastolic BP (mmHg)	77.49 (10.4)	60 – 120
Gestational Age (weeks)	21.05 (10.8)	4 – 44
Cord blood TSH (mIU/L)	7.98 (6.9)	0.54 – 44.1

SD = Standard deviation, BP = Blood Pressure

**Table 2: Relationship between maternal iodine status and cord blood thyroid function profile**

	n	Cord TSH mIU/L	Cord FT <sub>3</sub> ng/dl	Cord FT <sub>4</sub> Pg/mL	Median (range) UIC µg/L
Inadequate	90	9.44±7.4	1.16±0.4	1.27±0.7	57 (13-145)
Adequate	31	7.21±8.4	1.58±2.4	1.40±1.3	200(150-242)
More than adequate	92	6.8±5.5	1.12±0.3	1.38±0.8	367(250-660)
<i>P-value</i>		0.0029	0.6184	0.4223	

**Table 3: Maternal iodine status and cord blood TSH cut-off values for congenital hypothyroidism**

	Cord Blood TSH mIU/L		
	0–20	>20	TOTAL
Maternal iodine status			
Inadequate (%)	81 (90.0)	9 (10.0)	90 (100)
Adequate (%)	29 (93.5)	2 (6.5)	31 (100)
More than adequate (%)	89 (96.7)	3 (3.3)	92 (100)
<b>Total</b>	<b>199</b>	<b>14</b>	<b>213</b>

**Table 4: Correlation between maternal urinary iodine concentration and cord blood thyroid function parameters**

	Pearson's correlation	<i>P-Value</i>
TSH	0.26	0.0000
Free T <sub>3</sub>	0.10	0.1221
Free T <sub>4</sub>	0.00	0.6964

## DISCUSSION

Congenital hypothyroidism is inadequate production of thyroid hormone in the newborns.<sup>[9,11,12]</sup> Its worldwide incidence is between 1:2,000– 1:4,000 live births.<sup>[4,11,12]</sup> Maternal iodine deficiency is one of the major causes.<sup>[4]</sup> Due to its severe and irreversible nature and difficulty in clinical diagnosis, newborn screening programs were developed in mid 1970s requiring either thyroxine (T<sub>4</sub>) or thyroid stimulating hormone (TSH) measurements in heel-stick blood specimens for early detection and treatment.<sup>[12]</sup>

Another screening method is the use of cord blood for the measurement of TSH. Cord blood has a high sensitivity with a high false positive rate.<sup>[10]</sup> It is non-invasive, easy to collect with decreased turnaround time for results, thus giving room for quick intervention.<sup>[13]</sup> It almost eliminates loss of patients to follow up as the result is usually available almost immediately before the mother leaves the hospital.<sup>[12]</sup> Various studies adopted cut – off value of above 20 mIU/L.<sup>[12,14,15]</sup> The participants were within reproductive age group with mean age of 25.1 years. This is contrary to a similar study in Ghana where the participants were older with mean maternal age of 29.6 years.<sup>[4]</sup>

Median urinary iodine concentration in pregnancy is normally 150 – 250 µg/L according WHO.<sup>[1,2]</sup> In the current study, the group having inadequate iodine status constituting about 42.3 % of the study population had 57 µg/L as its median urinary iodine concentration. This is agreement to a study in Accra and Tamale where about one third of the study population had biochemical evidence of iodine deficiency.<sup>[4]</sup> Thyroid stimulating hormone concentration is significantly elevated in the iodine deficient group compared with the iodine sufficient groups. This could be due to the fact that lack of iodine from the maternal sources results in foetal hypothyroidism characterised by elevated TSH.

Fourteen participants (6.6 %) had cord blood TSH above 20 mIU/L. This was suggestive of congenital hypothyroidism and therefore need confirmatory tests during follow-up. Nine of them (64.3 %) belonged to those having inadequate iodine status.

Those with adequate and more than adequate iodine status had 2 (14.3 %) and 3 (21.4 %) respectively. This finding confirms that congenital hypothyroidism has other causes apart from iodine deficiency.<sup>[9]</sup> As iodine deficiency is the commonest and most important cause of congenital hypothyroidism, significant number should be seen in the iodine deficiency group. This is in agreement with the findings of Dei Tutu et.al (2020) where congenital hypothyroidism was associated with low maternal iodine status.<sup>[4]</sup>

Maternal iodine status related significantly and positively with Cord blood TSH ( $r = 0.26$ ,  $P = 0.0000$ ) but there was no significant relationship with free T<sub>3</sub> and free T<sub>4</sub>. Dei Tutu et.al (2020)<sup>[4]</sup> also found significant positive correlation between maternal iodine status and infant TSH which is in agreement with the current study.

## CONCLUSION

Maternal iodine status correlates significantly with cord blood TSH. Cord blood TSH is significantly higher among those with inadequate nutritional iodine status.

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