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Original Research Article

INTERRELATIONSHIP BETWEEN THE URINARY LEVEL (UI) IN PREGNANT WOMEN, THEIR BREAST MILK IODINE (MI) LEVELS POST DELIVERY AND URINARY IODINE (UI) LEVELS IN THEIR OFFSPRINGS- A HOSPITAL BASED, NON-INTERVENTIONAL, CROSS-SECTIONAL VOLUNTARY SCREENING STUDY IN IODINE DEFICIENT HIMALAYAN REGION IN NORTH INDIA

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ABSTRACT

Background: Iodine deficiency in the postpartum period has the potential to affect neonatal neuropsychointellectual development. In the neonatal period, milk is the only source of iodine. Urinary iodine estimation has been the traditional definitive method for assessment of iodine status in a population including that of neonates.

Material and Methods: A total of 57 mothers and their neonates were included in the study. During their third trimester outpatient visit, 5 mL random spot urine samples were collected. After childbirth, approximately 5 ml of manually expressed breast milk samples were collected from the same mothers. Within first 28 days of birth, random urine samples were collected from the neonates. Subsequently the maternal urinary iodine, maternal breastmilk iodine & the neonatal urinary iodine were estimated.

Results: The mean maternal urinary iodine level was 157.7±81.56 mcg/L. The mean maternal breast milk iodine levels were 204.5±113.65 mcg/L. The mean neonatal urinary iodine levels were 157.7±81.56mcg/L. There was a significantly positive correlation between maternal urinary iodine and maternal breastmilk iodine ($r=0.860$;$p<0.001$). A positive correlation was found between maternal urinary iodine secretion and neonatal urinary iodine secretion ($r=0.608$, $p<0.001$). There was a significant positive correlation between Breastmilk iodine and neonatal urinary iodine levels ($r=0.567$; $p<0.001$).

Conclusion: It was concluded that women who had deficient urinary iodine had low breastmilk iodine levels and like urinary iodine, breastmilk iodine can serve as a proxy marker for thyroid hormone status of the body. Breastfed neonatal iodine status parallels their maternal iodine status and thus their maternal thyroid status since urinary iodine is a marker of thyroid hormonal status.

Key Words: Breast milk iodine levels, maternal urinary iodine levels, neonatal urinary iodine levels.

INTRODUCTION

Iodine is a trace element required for the biosynthesis of thyroid hormones and is obtained solely from external source.[1] Thyroid hormones regulate various processes of cellular metabolism, influencing all cells throughout life. Particularly important is the role of thyroid hormones in normal brain development and cognition1. Iodine deficiency in the postpartum period has the potential to affect neonatal neuropsychointellectual development. In the neonatal period, milk is the only source of iodine. Pregnant & lactating women and infants are the most susceptible to iodine deficiency disorders. In the pregnant and lactating women, iodine deficiency is related to disorders that affect mothers and their fetuses viz increased early and late miscarriages, intellectual disability, endemic cretinism, neonatal hypothyroidism, neonatal hypothyroitropenemia, increased perinatal and infant mortality and, growth retardation.[2]

Iodine is considered unique among trace elements in milk because it is avidly concentrated in the mammary gland.[3] Iodine in human milk is often found at concentrations that are 20-50 times higher than that in plasma. Sodium iodide symporter (NIS), an intrinsic membrane protein, mediates the transport of iodide into the thyroid gland.There is a dearth of reports on the iodine content of human milk in the scientific literature. Generally, these studies show that the mean iodine content of human milk is relatively low in women from areas with a high prevalence of goiter (9-32µg/L), and among the women diagnosed with goiter (13-18 µg/L).[3] Human milk iodine concentrations are higher in areas where salt iodization occurs.

Urinary iodine estimation has been the traditional definitive method for assessment of iodine status in a population including that of neonates. Median urinary iodine levels in a population below 100µg/L indicate iodine deficiency.[4] WHO recommends measuring the median urinary iodine (UI) concentration for assessing iodine intake in non-pregnant and pregnant women.[5] It recommends that a median UI concentration of 150–249 mcg/L in a population of pregnant women indicates adequate iodine intake. Daily iodine intake can be extrapolated from the UI concentration assuming 24-h urine volumes and iodine bioavailability of 92%. The recommended daily iodine intake during pregnancy of 220–250 mcg/day would correspond to a median UI concentration of 135–155 mcg/L during pregnancy.[6,7]

WHO recommends that infants aged 0-12 months receive 90 µg iodine/day. The Estimated Average Requirement (EAR) of iodine for pregnant women is 160 µg iodine/day. The Recommended Dietary Allowance (RDA) of iodine for pregnant women is defined as the EAR plus twice the coefficient of variation (CV) to cover 97-98% of individuals in this group. Thus, the new RDA for pregnant women is 220 µg iodine/day,[6,7] which is close to the WHO recommendation of 200 µg iodine/day for pregnant women.

MATERIAL AND METHODS

Subject Selection

This was a hospital based, non-interventional, cross-sectional voluntary screening study conducted at a tertiary care hospital in the Himalayan region of north India. Duration of study was 2 years. A total of 57 mothers and their neonates were included in the study.

Inclusion Criteria

- Pregnant women in the age group of 20-40 years in third trimester of pregnancy for UI estimation.
- Mothers in the age group of 20-40 years for breast milk iodine estimation during first 28 days of lactation.
- Exclusively breastfed neonates for urinary iodine estimation.

Exclusion Criteria

- Subjects with any sign or symptom of hypothyroidism or hyperthyroidism.
- Mothers taking any iodine supplement other than iodized salt.
- Mothers who were cigarette smokers or ex-smokers.
- Mothers suffering from any other systemic disorders or taking drugs that affect thyroid status.
- Mothers having complicated pregnancy or delivery.
- Any neonatal complication that needed admission in the hospital NICU.
- Any neonate on supplementary diet/formula milk/drug.

Study women population was selected from the pregnant patients registered in the Department of Obstetrics and a written informed consent was taken from all the enrolled subjects. A thorough history was taken from the subjects and examination was done to rule out any thyroid or systemic disorder. During their third trimester outpatient visit, 5mL random spot urine samples were collected in 10 ml labeled iodine free plastic tubes and aliquots were stored at −20 °C for further analysis. After childbirth, approximately 5 ml of manually expressed breast milk samples were collected from the same mothers in 10 ml labeled iodine free plastic tubes and aliquots were stored at −20 °C for analysis. Within first 28 days of birth, random urine samples were collected from the neonates in urine collection bags according to the detailed instructions provided. The genital region of the newborns was cleansed by chlorhexidine. For male neonates, entire penis was placed in the bag, attaching the adhesive to the skin and for female neonates the bag was attached over the labia for collection. Approximately 5ml of spot urine samples were

transferred into 10 ml labeled iodine free plastic tubes and aliquots were stored at −20 °C for analysis. Breast milk and corresponding neonatal urinary samples were collected on the same day.

BIOCHEMICAL ANALYSIS

Urinary Iodine Estimation

Urine is digested with ammonium persulfate. Iodide being the catalyst in the reduction of ceric ammonium sulphate(yellow) to cerous form(colorless), is detected by rate of color disappearance (Sandell-Kolthoff reaction)[8]. Iodine concentrations were measured at least twice. In 95% of the samples, the initial two measurements were within 15% of each other, and the two values were averaged. In the case where the initial two measurements were not within 15% of each other, a third measurement was obtained, and the average of all measurements was reported.

Iodine Estimation from breast milk[9]

Milk samples and calibrators were added to test tubes, and 2000mL of digestion acid solution was added. After being covered with plastic caps, the tubes were placed into the wells of the heating block for 10 min at 230°C in a fume hood. For safe cooling, the tubes were left under the hood for cooling to room temperature. Then 50mL of the digested samples was transferred to another tube and the same procedure was followed thereon as was used for the estimation of urinary iodine.

The results were grouped into following categories

BREAST MILK IODINE LEVELS (mcg/l),[7]

<100----------Severe deficiency
100-199-------Inadequate
200-400-------Adequate
>/=400------- More than adequate

MATERNAL URINARY IODINE LEVELS,[6,7,10]

<50-------Severe deficiency
50-149-----Inadequate
150-249-----Adequate
>/=250------More than adequate

NEONATAL URINARY IODINE LEVELS (mcg/l)[5,7,11]

<50------Severe deficiency
50-99----Inadequate
100-200----Adequate
>/=200-----More than adequate

Statistical Analysis: The recorded data was compiled and entered in a spreadsheet (Microsoft Excel) and then exported to data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Continuous variables were expressed as Mean±SD and categorical variables were summarized as frequencies and percentages. Karl Pearson's correlation coefficient and Scatter Plots were employed to establish correlation between various variables. Student's independent t-test and ANOVA were used for comparing various parametric data. A *P*-value of less than 0.05 was considered statistically significant. All *P*-values were two tailed.

RESULTS

A total of 57 mother- neonate pairs were enrolled in the study over a period of 2 years. The mean age of mothers in this study was 30.2 ± 3.06 years. In our study, 36.8% (21) neonates had a gestational age of 37 weeks, 31.6% (18) neonates had a gestational age of 38 weeks, 17.5% (10) neonates had a gestational age of 39 weeks and 14% (8) neonates had a gestational age of 40 weeks.

40.35% (23) of neonates were males and 59.65% (34) were females. 12.3% (7) of the neonates weighted less than 2.5 kgs, 77.2% (44) weighted between 2.5 and 3.5 kgs and 10.5% (6) weighed more than 3.5 kgs. The mean weight of the neonates in our study was 2.97±0.39Kg.

19.3%(11) of the neonateswere first in birth order, 36.8%(21) of neonateswere second in birth order,31.6%(18) of neonateswere third in birth order and 12.3%(7) of neonateswere fourth in birth order.

29.2% (17) of neonates were born by vaginal delivery and 70.2% (40) of neonates were born by LSCS.

A positive significant correlation was seen in our study between maternal urinary iodine and breast milk iodine (r=0.869, p <0.001) as depicted in Fig.1

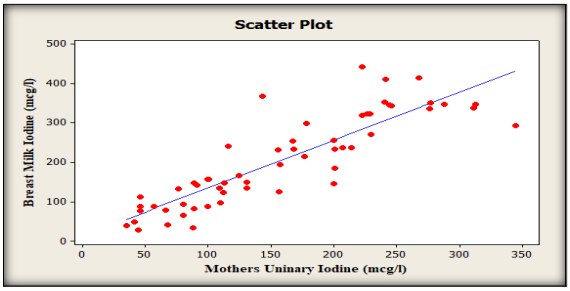

Figure 1: Scatter plot showing correlation between maternal urinary iodine and breast milk iodine

A positive significant correlation was seen in our study between maternal urinary iodine and neonatal urinary iodine (p=0.608 ,r<0.001) as depicted in Figure 2.

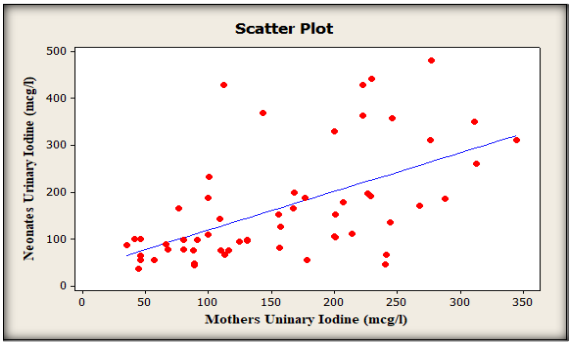

Figure 2: Scatter plot showing correlation between maternal urinary iodine and neonatal urinary iodine

A positive significant correlation was seen in our study between breast milk iodine and neonatal urinary iodine (p=0.567 , r<0.001) as shown in Fig 3.

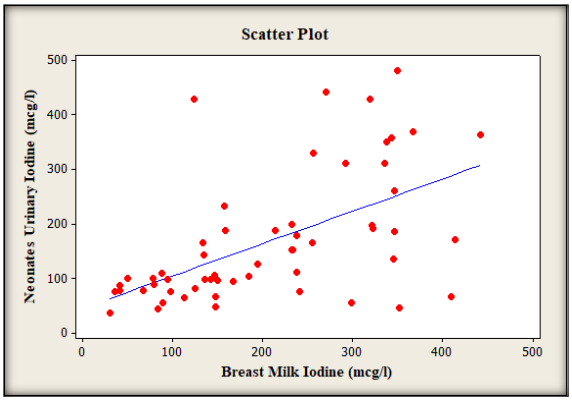

Figure 3: Scatter plot showing correlation between neonatal urinary iodine and breast milk iodine

There was no significant correlation of maternal age with maternal urinary iodine and breast milk iodine. Similarly, there was no significant correlation of gestational age with maternal urinary iodine, breast milk iodine and neonatal urinary iodine. Also, there was no significant correlation of neonatal birth weight with neonatal urinary iodine.

A statistically insignificant association (p=0.669) was seen between gender of the neonate and the neonatal urinary iodine.

A statistically insignificant association was seen between birth order of the neonate and the maternal urinary iodine (p=0.517), breast milk iodine (p=0.941) and neonatal urinary iodine (p=0.391) respectively.

Maternal urinary Iodine (mcg/l) levels in the study group are shown in table 1

Table 1: Maternal urinary Iodine (mcg/l)

Iodine (mcg/l)	Frequency	Percentage
Severe Deficiency (< 50)	6	10.5
Inadequate (50-149)	22	38.6
Adequate (150-249)	22	38.6
More Than Adequate (≥ 250)	7	12.3
Mean±SD (Range)=157.7±81.56 (34.7-344.7)		

The Breast milk iodine levels in study mothers are shown in table 2.

Table 2: Maternal breast milk iodine (mcg/l)

Iodine (mcg/l)	Frequency	Percentage
Severe Deficiency (< 100)	14	24.6
Inadequate (100-199)	16	28.1
Adequate (200-400)	24	42.1
More Than Adequate (> 400)	3	5.3
Mean±SD (Range)=204.5±113.65 (29.6-441.5)		

The Neonatal urinary iodine levels (mcg/L) in the study group are shown in table 3.

Table 3: Neonatal urinary iodine levels (mcg/l)

Iodine (mcg/l)	Frequency	Percentage
Severe Deficiency (< 50)	4	7.0
Inadequate (50-99)	19	33.3
Adequate (100-200)	21	36.8
More Than Adequate (> 200)	13	22.8
Mean±SD (Range)=167.5±118.23 (37-481)		

Correlation between Maternal urinary iodine, Breast milk iodine and Neonatal urinary iodine is shown in table 4

Table 4: Showing correlation between maternal urinary iodine, breast milk iodine and neonates urinary iodine

Parameter	Pearson Correlation (r)	P-value
Maternal Urinary Iodine-Maternal Breast Milk	0.869	<0.001*
Maternal Urinary Iodine-Neonates Urinary Iodine	0.608	<0.001*
Neonates Urinary Iodine-Maternal Breast Milk	0.567	<0.001*

DISCUSSION

Iodine deficiency disorders (IDD) are a major public health problem worldwide in all age groups, but infants and pregnant and lactating women are the most vulnerable.[12] During pregnancy and lactation, the fetus and infants are sensitive to maternal iodine intake and an adequate iodine concentration in breast milk (BMIC) is essential for optimal growth and neurological development. Exclusively breastfed infants depend entirely on their mother's milk iodine content for thyroid hormone synthesis since they, unlike adults, lack significant thyroxine stores.The median urinary iodine excretion is the recommended biomarker to monitor daily iodine intake in a given population, and in non-lactating women, approximately 90% of the ingested iodine is excreted through urine.[12] The Himalayan region is one of the most iodine-deficient areas in the world and for many decades, iodine deficiency disorders have been a public health problem in this region.Despite the importance of iodine for the infant's growth and development, scientific literature has only a few studies about the iodine content of human milk. This study aimed to measure maternal urinary iodine and breast milk iodine levels and the neonatal urinary iodine concentration (UIC) in a random sample of lactating women and their neonates in our part of the world.

In our study, the mean maternal urinary iodine level was 157.7±81.56 mcg/L.

Similar results were seen by Yan Ling Wang et al,[13] who reported a mean urinary iodine level of 147 mcg/L in pregnant women in their third trimester in areas of China where salt supplementation with Iodine was being done.

In an iodine deficient belt of Saki in Nigeria, Ojule AC et al,[14] found that the mean maternal urinary iodine excretion was 144.76 +/- 14.68 which is close to our results. Almost similar results were seen by P.P.A Smyth et al,[15] (132 ± 6.8 ug/L), Anibal Aguayo et al,[16] (140 µg/L) &Ane Miren Castilla et al,[17] (133 µg/L).

Yozen Fuse et al,[18] found that urinary iodine excretion increased from 220.0 µg/liter in the first trimester to 258.0 µg/liter in the second trimester & decreased to 195.0 µg/liter in the third trimester. This is close to our study where third trimester maternal urinary iodine levels were 157.7±81.56.

In our study, in 49.1% of cases the maternal urinary iodine levels were below recommended levels (severe deficiency or inadequate). The results are close to the ones obtained by Pongpaew P et al,[19] in Thailand where 52.0 per cent of the women investigated had a low urinary iodine excretion.

In our study, the mean maternal breast milk iodine levels were 204.5±113.65 mcg/L. In a study conducted by Colette A. Gushurst et al (1980)20 in 37 American women living in areas of adequate nutritional iodine intake, mean breast milk iodide levels were 178 µg/L (range 29 to 490 µg/L) which are close to our study results. Yan Ling Wang et al,[13] found a mean breast milk iodine level of 163 µg/L in areas of salt supplementation of China. In our study, in 52.7% of cases the maternal breast milk iodine levels were below recommended levels (severe deficiency or inadequate). The results are close to the ones obtained by Pongpaew P et al,[19] where the breast milk iodine from 46.7 % of mothers was found to be below recommended standards. We found that in 43.85% of study mothers, breast milk iodine concentration was <150 mcg/L.Arash Ordookhani et al,[20] also saw that 52% of mothers in their study had breast milk iodine concentration <150mcg/L.

In our study, the mean neonatal urinary iodine levels were 157.7±81.56mcg/L. In a study by Delange F et al (1986)21 while studying variations of Iodine Nutrition and Thyroid Function during the Neonatal Period in Europe, the mean iodine level in neonatal urine in Rotterdam, the Netherland was 162.0 mcg/L which is close to our results. In a study by PPA Smyth et al,[22] (2017), median urinary iodine obtained from breast feeding babies was 148 µg/L which is close to our results.

In our study, there was a significantly positive correlation between maternal urinary iodine and maternal breast milk iodine (r=0.860 ;p<0.001).

A positive significant correlation was found between Breast milk iodine and maternal urinary iodine concentration (r=0.533, P= 0.000) by Majid Mobasseri et al 23(2015). Similar results were obtained by Hamid R. Bazrafshan et al (2005)24 who found that maternal urinary iodine and maternal breast milk iodine level were significantly correlated (r = 0.44, p < 0.0001). Also, there was a positive correlation (r = 0.44, p less than 0.01) between the milk iodide concentration and the iodine of maternal urine specimen in a study conducted by Johnson LA et al,[25] in mothers living in the Wellington area of New Zealand. Iodine in breast milk of lactating mothers was positively correlated with their urinary iodine excretion (p<0.001) in a study conducted by Golam Morshed Molla et al,[12] (2005).

In our study, maternal urinary iodine levels and breast milk iodine levels were deficient in 49.1% (severe deficiency + inadequate) and in 52.7% (severe deficiency + inadequate) respectively. The results are close to those obtained in 75 women in Khon Kaen province, Northeast of Thailand by Pongpaew P et al,[19] where urine from 52.0 per cent and breast milk from 46.7 per cent of the women investigated were below recommended levels.

In our study, a positive correlation was found between maternal urinary iodine secretion and neonatal urinary iodine secretion (r=0.608, p<0.001). A closely similar significant correlation between neonatal UIC and maternal UIC (r=0.462, P= 0.000) was found by Majid Mobasseri et al.[23] A direct significant correlation was noted between the urinary iodine excretion of neonates and that of their mothers (r = 0.37; P<0.01) by Mahin Hashemipoor et al,[26] who concluded that urinary iodine excretion

in mothers paralleled the urinary iodine concentration of their neonates. There was a significant positive correlation between maternal and neonatal urine iodine levels ($r = 0.34$, $p < 0.001$) in a study conducted by Chatchai Suesirisawad et al,[27] in Thailand.

In our study, there was a significant positive correlation between Breast milk iodine and neonatal urinary iodine levels ($r=0.567$; $p<0.001$). In a study conducted by Yan Ling Wang et al,[13] in 2009 in areas of salt supplementation of China, there was a positive correlation between urine iodine of infants and breast milk iodine of lactating women ($r = 0.526$, $p = 0.000$), closely related to our study. Breast milk iodine was significantly correlated with urine iodine ($r =0.52$, $p < 0.001$) in a study conducted by Sophie S.Y. Chan et al28 at a tertiary referral hospital in Sydney, Australia. A closely similar significant correlation between neonatal UIC and Breast milk iodine concentration ($r=0.414$, $P= 0.000$) by Majid Mobasseri et al.[23] Neonatal urinary iodine was positively correlated with iodine concentration in breast milk ($p<0.01$) in a study conducted by Golam Morshed Molla et al.[12]

A similar significant positive correlation was found between Breast milk iodine and neonatal urinary iodine levels by Mahin Hashemipour et al (2010),[29] while studying Urine and breast milk iodine concentrations in healthy and congenitally hypothyroid neonates and their mothers in Iran.

In our study, there was no significant correlation between mothers age and Maternal urinary iodine ($r= -0.238$, $p=0.074$) or Breast milk iodine ($r= -0.148$, $p=0.272$).

Also, there was no significant correlation between Gestational age and maternal urinary iodine ($r=0.036$, $p=0.792$), Breast milk iodine ($r=0.129$, $p=0.340$) or Neonatal urinary iodine ($r= -0.108$, $p=0.425$).

In our study, there was no significant correlation between Neonatal Birth weight and Neonatal urinary iodine ($r=0.225$, $p=0.093$).

There was no significant association between Gender of neonate and Neonatal urinary iodine in our study ($p=0.669$).

Also there was no significant association between Birth order with maternal urinary iodine ($p=0.517$), Breast milk iodine ($p=0.941$) and Neonatal urinary iodine($p=0.391$).

Due to paucity of literature regarding correlation or association of Maternal age, Gestational age, Birth weight, Gender of neonate and Birth order with Iodine levels, the results could not be compared to our study.

In summary, about half of the mothers had deficient iodine levels in their urine and breast milk while about 40% of the neonates had deficient iodine levels in their urine despite the adequacy of salt iodine supplementation in our part of the world.

Therefore, it is imperative that iodine supplementation of other foods such as edible oil, cereals and bakery products should be done to ensure adequate iodine intake by pregnant and lactating mothers which is about 200-250 mcg/day as recommended by WHO. Neonates, who are exclusively breastfed need not be supplemented by dietary iodine if their mothers are receiving adequate dietary iodine.

CONCLUSION

There was a highly significant correlation between maternal urinary iodine and breast milk iodine levels ($r=0.869$, $p<0.001$) and thus it was concluded that women who had deficient urinary iodine had low breast milk iodine levels and like urinary iodine, breast milk iodine can serve as a proxy marker for thyroid hormone status of the body.

There was a highly significant correlation between maternal urinary iodine and neonatal urinary iodine levels ($r=0.608$, $p<0.001$) in our study and thus it was concluded that breastfed neonatal iodine status parallels their maternal iodine status and thus their maternal thyroid status since urinary iodine is a marker of thyroid hormonal status.

A highly significant correlation between breast milk iodine and neonatal urinary iodine levels was seen in our study ($r= 0.567$, $p<0.001$) signifying that exclusively breastfed infants are dependent on their mother's milk for maintaining the iodine status and therefore the thyroid hormone status of their bodies.

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