**Iodine concentrations in milk and in urine during breastfeeding are differently affected by maternal fluid intake**

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Background: Breastfed infants are dependent on iodine transport into breast milk for production of thyroid hormones. Thyroid hormones are important regulators of brain development. It has been considered whether breast milk iodine concentration (MIC) could be predicted by maternal urinary iodine concentration (UIC), but reports on correlations have been inconsistent. We used urinary creatinine concentration as a proxy for maternal fluid intake and speculated if this might differently influence on UIC and MIC.

Methods: We examined 127 breastfeeding women after the introduction of the mandatory iodine fortification of salt in Denmark. Maternal spot urine and a breast milk sample were obtained at median 31 days after delivery (interquartile range: 25-42), and the women were asked about intake of iodine containing supplements postpartum.

Results: Median UIC was 72 µg/l (46-107 µg/l) and higher in iodine-supplemented mothers (47.2% of participants); 83 µg/l (63-127 µg/l) vs. 65 µg/l (40-91 µg/l), p=0.004. Median MIC was 83 µg/l (61-125 µg/l) and also higher in iodine-supplemented mothers; 112 µg/l (80-154 µg/l) vs. 72 µg/l (47-87 µg/l), p<0.001. There was a weak correlation between UIC and MIC (r=0.28, p=0.015). A strong correlation was present between UIC and urinary creatinine concentration (r=0.76, p<0.001), whereas urinary creatinine concentration was not correlated to MIC (r=-0.049, p=0.58). When UIC and urinary creatinine were used to estimate 24-hour urinary iodine excretion, the correlation between this estimate and breast milk iodine excretion was stronger (r=0.48, p<0.001).

Conclusions: Iodine supplement intake in Danish breastfeeding women should be recommended. Results indicate that UIC, but not MIC, depends on maternal fluid intake and that maternal estimated 24-hour iodine excretion may be a better indicator of iodine supply to the breastfed infant than UIC.
Iodine concentrations in milk and in urine during breastfeeding are differently affected by maternal fluid intake

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Conclusions: Iodine supplement intake in Danish breastfeeding women should be recommended. Results indicate that UIC, but not MIC, depends on maternal fluid intake and that maternal estimated 24-hour iodine excretion may be a better indicator of iodine supply to the breastfed infant than UIC.
Introduction

Iodine is obligatory for thyroid hormone production and lack of thyroid hormones during infant brain development may lead to permanent brain damage (1). Thus, maternal iodine requirements are increased during the period of breastfeeding to ensure an adequate supply of iodine both via breast milk to the developing infant and to the mother. Consequently, WHO, United Nations Children’s Fund (UNICEF) and the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) define an adequate maternal intake of iodine as 250 µg/day during breastfeeding (2).

Population median urinary iodine concentration (UIC) is the recommended method to assess population iodine intake (2). In non-lactating women, around 90% of ingested iodine is excreted into urine, whereas in lactating women part of plasma inorganic iodine is transported into breast milk by the sodium iodide transporter (NIS) (3). Urinary iodine excretion is consequently lower, and the median UIC indicating sufficient iodine intake in breastfeeding women is similar to the non-pregnant state (≥100 µg/l), although maternal iodine requirements are increased (2).

WHO, UNICEF and ICCIDD define an adequate intake of iodine in children less than two years old as 90 µg/day (2). As previously reviewed in details (3-5), a number of studies have measured breast milk iodine concentration (MIC) and found a wide range of median or mean concentrations. As recently highlighted by Leung et al (6), physiological mechanisms may challenge the interpretation of studies of breast milk iodine measurements. These authors illustrated a rise in MIC following acute maternal dietary iodine intake.

Another aspect previously considered is how reliably the iodine supply to the breastfed infant can be evaluated by maternal UIC (7,8). It has been illustrated that UIC adjusted by urinary creatinine as a proxy for fluid intake might more precisely estimate iodine intake in non-lactating women and in men (9-11), and in a study from Australia of 50 breastfeeding women, there was no significant correlation between UIC and MIC, but MIC was significantly correlated to the urinary iodine/creatinine ratio (12).
In Denmark, information on maternal iodine nutrition during breastfeeding and infant iodine nutrition only exist in studies (13,14) performed before the mandatory iodine fortification of salt introduced in the year 2000 (15). In the present study we examined if Danish women living in an area with previously moderate iodine deficiency took iodine containing supplements postpartum and evaluated iodine status in breastfeeding women by measurement of maternal urinary iodine excretion. In addition, we studied iodine content of infant feeding by measuring breast milk iodine excretion and iodine content of infant formulas. Data were used to investigate the relationship between urinary iodine excretion and breast milk iodine excretion in breastfeeding women and to study the feasibility of using urinary creatinine excretion to adjust for differences in maternal fluid intake.

Materials and methods

Study population and design

The study is a postpartum follow-up of women initially included in the Obstetric Department, Aalborg University Hospital in pregnancy. From June to August 2012, we consecutively recruited 245 healthy, pregnant women referred to the Obstetric Department for ultrasound as part of the antenatal investigation programme. The initial examination aimed to evaluate if Danish pregnant women living in an area of Denmark with previously moderate iodine deficiency took iodine containing supplements and to evaluate iodine intake by measurement of urinary iodine concentration in a spot urine sample (16).

In the present follow-up study, the women were contacted by phone in the postpartum period after birth of a live-born child. If willing to participate, a telephone interview was performed, and the women were asked about intake of iodine containing supplements in the postpartum period, smoking habits, breastfeeding and/or use of infant formulas. The same interviewer performed all interviews.

Additionally, the women were asked to make a spot urine and a breast milk sample at home and if infant formulas were used, they were also asked to sample prepared infant formula. Vials for
sampling were mailed to the women willing to participate, and they were instructed to make the
urine and breast milk sample non-fasting and as close together in time as possible. The women were
asked about the timing of sampling in relation to breastfeeding of the child and whether milk was
from one or both breasts. A small group of women (n=13) were instructed to make breast milk
samples from the same breast both immediately before and after breastfeeding of the child.

The study protocol was approved by the local ethical committee.

Laboratory procedures

Urine and raw breast milk samples were stored at -20 °C from time of sampling until collection at
home and until measurement of UIC and MIC in runs during the time of the study inclusion.

After thawing and brief mixing of samples, UIC and MIC were determined by the
cerium/arsenite method after alkaline ashing to dryness (combusting organic material), as
previously described (17). The analytical sensitivity of the assay was 2 µg/l and the lowest standard
above the zero blank contained 10 µg iodine/litre. For urine samples, the recovery of iodine was
95.5% (SEM 2.4%) and inter-assay CV was 2.7%, as previously described (15). For breast milk
samples, the recovery of iodine was 93.6% (SEM 1.04%), when 75 µg iodine/litre was added to 10
breast milk samples with a median iodine concentration of 78 µg/l (range 51-118 µg/l). Serial
dilution of 10 breast milk samples containing 51-118 µg iodine/litre gave curves parallel to the
standard curve. Inter-assay CV was 3.6% when 7 breast milk samples were measured in triplicate.

The iodine laboratory was certified by the U.S. Centers for Disease Control and Prevention EQUIP
program which includes twice yearly measurement of ‘blind’ external controls.

Urinary creatinine concentrations were measured on a Cobas 8,000 system (Roche, Switzerland).

Equipment was calibrated according to the manufacturer’s instructions and external standards were
included.
Statistical analyses

Characteristics of the women according to intake of iodine supplements were compared using Chi-square test or Fisher’s exact test and multivariate logistic regression was used to examine predictors of iodine supplement intake postpartum.

Urinary iodine excretion was expressed as spot urine concentration (µg iodine/litre) and as estimated 24-hour iodine excretion (µg iodine/24 hours) calculated from the mean 24-hour urinary creatinine excretion (1.09 gram creatinine/24 hours), previously measured in a group of Danish pregnant women (18). This calculation was used for both pregnancy and postpartum urinary iodine concentrations as the 24-hour urinary creatinine excretion was almost identical to that found in a general female population age 25-34 years (19). For calculation of 24-hour breast milk iodine excretion, a breast milk volume of 800 ml/24 hours was used (20).

UIC, MIC and urinary creatinine concentrations showed skewed distributions, and results were expressed as medians with 25th and 75th percentiles (interquartile range, IQR). The Mann-Whitney test was used to compare urinary iodine excretion stratified by iodine supplement intake and time of sampling. The Wilcoxon signed rank test was used for comparison of related samples (pregnancy versus postpartum and before versus after breastfeeding of the child). Urinary and breast milk iodine and urinary creatinine measurements were log-transformed for illustration of correlations and calculation of Pearson’s correlation. The ratio between 24-hour estimated breast milk iodine excretion and urinary iodine excretion was log-transformed for calculation of geometric mean with 95% confidence interval (95% CI). The Student’s t-test was used to compare the geometric mean ratio by iodine supplement intake.

Statistical analyses were performed using Stata 11 (StataCorp, College Station, TX, USA) and a 5% level of significance was chosen.
Results

Study population

Figure 1 illustrates the selection of the women included in the follow-up study postpartum. Among women included in pregnancy, 85.3% were interviewed by phone in the postpartum period (median day 22 postpartum (range 9-146)), and in this group of women, 70.3% sampled breast milk and/or urine at home. A total of 130 women delivered both a urine sample in pregnancy and postpartum and a breast milk sample. Three women were excluded because they reported they were smokers. Thus, leaving 127 women for urine- and breast milk analyses (figure 1). The time interval between samplings (milk - urine) was median 0 minutes (IQR - 30 to 7 minutes).

Iodine supplement intake

At the time of the postpartum interview, 117 of 209 women (56.0%) reported intake of dietary supplements, and 98 of the 209 women (46.9%) took a vitamin and/or mineral supplement containing iodine. In pregnancy, 174 of these 209 women (83.3%) were iodine supplement users.

Table 1 presents characteristics of the women interviewed according to intake of iodine supplements postpartum. Only iodine supplement use in pregnancy significantly predicted iodine supplement intake postpartum with similar findings in multivariate analyses examining all variables in table 1 as categoricals. In addition, maternal cohabitation, ethnicity, occupation and pre-pregnancy BMI as reported in pregnancy were examined in univariate and multivariate analyses. Neither did any of these variables significantly predict iodine supplement intake postpartum.

In pregnancy, the iodine supplements used almost all contained 150 or 175 µg iodine/day and most women continued such supplement postpartum. However, a subgroup of the iodine supplement users (n=15) took a multivitamin pill that was labeled by the manufacturer as ‘supplement for breastfeeding women’ and contained only 45 µg iodine/day.
Urinary and breast milk iodine

Table 2 presents time of sampling and results of urinary iodine and creatinine excretion and breast milk iodine excretion in pregnancy and postpartum stratified by maternal intake of iodine supplements.

UIC postpartum ranged from 8-422 µg/l. In comparison to women not taking iodine supplements, median UIC and estimated 24-hour urinary iodine excretion were significantly higher in iodine supplement users both in pregnancy and postpartum. When comparing related urine samples in pregnancy and postpartum in individual mothers (table 2), UIC was lower (p<0.001) and urinary creatinine higher (p<0.001) in the postpartum period than in pregnancy.

MIC ranged from 19-301 µg/l as illustrated in figure 2. Median MIC and estimated 24-hour breast milk iodine excretion was higher in women taking iodine supplements postpartum in compare to non-users (table 2). When evaluating related urine and breast milk samples postpartum in individual mothers (table 2), MIC was higher than UIC (p=0.013), but when stratified by iodine supplement intake, only iodine supplement users had significantly higher MIC (iodine supplement intake: p=0.016, no iodine supplement intake: p=0.33). Estimated 24-hour breast milk iodine excretion was not significantly different from estimated 24-hour urinary iodine excretion (p=0.29), neither when stratified by iodine supplement intake.

Iodine content of the supplements differed, and urine and breast milk iodine excretion was considerably lower in women with the lowest iodine supplement intake (45 µg/ day (n=9)) in comparison to women with a higher intake of iodine from supplements (150 or 175 µg/ day (n=49)): estimated 24-hour urinary iodine excretion: 58 µg (IQR 50-87 µg) vs. 89 µg (61-147 µg), p=0.030; 24-hour breast milk iodine excretion: 54 µg (51-85 µg) vs. 98 µg (74-123 µg), p=0.048.

Among women with no iodine supplement intake postpartum (n=67), UIC and MIC were not significantly higher in the group of women (n=49) who had used iodine supplements in pregnancy in compare to women (n=18) with no iodine supplement intake both in pregnancy and postpartum (data not shown).
Correlations between urinary iodine, urinary creatinine and breast milk iodine

Figure 3 illustrates the relationship between maternal urinary iodine excretion postpartum, maternal urinary creatinine excretion postpartum and breast milk iodine excretion. Figure 3a depicts that UIC and MIC were only modestly correlated. We hypothesized that this relatively weak correlation might be caused by differences in maternal fluid intake. As illustrated in figure 3c, a strong correlation was observed between urinary creatinine (a proxy for fluid intake) and UIC, whereas no correlation was observed between MIC and urinary creatinine concentrations (figure 3d). Thus, fluid intake as evaluated by urinary creatinine influenced strongly on UIC, but had no influence on MIC (figure 3c versus figure 3d). As a consequence of this disparity, the correlation between iodine excretion in urine and breast milk was stronger, when UIC was adjusted by urinary creatinine and expressed as 24-hour urinary iodine excretion (figure 3b versus figure 3a).

To evaluate at the level of the individual how breast milk iodine excretion could be determined from maternal urinary iodine excretion postpartum, we calculated the ratio between estimated 24-hour breast milk iodine excretion and maternal 24-hour urinary iodine excretion. The geometric mean ratio was 0.93 (95% CI: 0.85-1.03) and not significantly different when stratified by iodine supplement intake (iodine supplement intake: 1.02 (0.90-1.15), no iodine supplement intake: 0.86 (0.75-0.99), p=0.076).

Sampling time

Time from delivery to sampling of urine and breast milk ranged from 14-135 days. UIC (r=0.20, p=0.026) and urinary creatinine concentration (r=0.24, p=0.008) correlated with time from delivery, but when UIC was adjusted by urinary creatinine to calculate 24-hour urinary iodine excretion, no correlation with time from delivery was observed (r=-0.044 p=0.62). Similarly, estimated 24-hour breast milk iodine excretion did not correlate with time from delivery to sampling neither in iodine supplement users (r=-0.17, p=0.19), nor in iodine supplement non-users (r=-0.11, p=0.37).
Time of sampling during the day ranged from 00:20 to 23:50. Median estimated 24-hour urinary iodine excretion was slightly higher when sampling was performed in the late afternoon/evening (16:00-24:00 (n=34): 83 µg (65-122 µg), 08:00 to 16:00 (n=81): 62 µg (48-94 µg), 24:00-08:00 (n=12): 63 µg (49-93 µg), p=0.031). Time of sampling did not influence on estimated 24-hour breast milk iodine excretion (p=0.42).

Breast milk sampling from one or both breasts did not influence on median MIC, and no difference in median MIC was observed when sampling was performed before or after breastfeeding of the child (data not shown). A small group of women sampled breast milk both immediately before and after breastfeeding of the child (n=13). The difference in MIC (before – after) was small (median 4 µg/l (IQR: 2-13 µg/l)), but the concentration was significantly higher before breastfeeding, p=0.017.

Infant formulas

A total of 35 infant formulas were obtained. The iodine concentrations ranged from 62-167 µg/l, and the overall median iodine concentration was 122 µg/l (IQR: 93-155 µg/l). Stratified by brand, the median iodine concentrations were: Nan-1 (n=20): 155 µg/l (137-158 µg/l), Allomin-1 (n=9): 87 µg/l (86-92 µg/l), Althera (n=5): 102 µg/l (98-103 µg/l), Hipp organic (n=1): 98 µg/l.

Discussion

Principal findings

In a follow-up study of women giving birth in an area of Denmark with previously moderate iodine deficiency, iodine supplement use postpartum was less frequent than in pregnancy. Urinary iodine and breast milk iodine concentrations were below the levels recommended, but significantly higher with iodine supplement intake and higher than the levels reported before the iodine fortification of salt in Denmark. Among iodine supplement users, the subgroup of women with the lowest iodine supplement intake was in particular at risk of iodine deficiency.
Maternal UIC, but not MIC, was strongly dependent on urinary creatinine concentration as a proxy for maternal fluid intake, and results indicate that UIC adjusted for creatinine more precisely predicts iodine content of breast milk.

Comparison with previous Danish studies

Iodine content of breast milk was previously evaluated in Denmark before the mandatory iodine fortification of salt introduced in the year 2000 (15). In a study by Pedersen et al (13) performed in an area of Denmark with previously moderate iodine deficiency, 53 pregnant women (30% smokers) were randomized to 200 µg/iodine/day (n=27) or controls (n=26) from gestational week 17-18 until 12 months after delivery. Median MIC day 5 postpartum was significantly higher in iodine-supplemented mothers (41 vs. 28 µg/l in controls). In another study by Nohr et al (14), 148 mothers in 5 cities of Denmark were included (35% smokers). The women reported on intake of iodine supplements at arrival for delivery and were instructed to continue their current supplement intake in the postpartum period. Sampling of breast milk was also in this study performed 5 days after delivery. Median MIC was significantly higher in iodine supplemented mothers (57 vs. 34 µg/l) with regional differences (higher values in East Denmark with previously mild iodine deficiency). In addition to this, it was illustrated, that smoking mothers had considerably lower MIC than nonsmoking mothers (26 vs. 54 µg/l) (21).

Median MIC was also in our study higher in iodine supplemented mothers (112 vs. 72 µg/l) and had increased in compare to the previous studies. In our study, breast milk samples were collected later in the postpartum period, but our results were not dependent on time from delivery to sampling, neither in iodine supplement users nor in non-users. Studies evaluating breast milk iodine content at different time points postpartum either reported a significant decrease or no difference according to time after delivery (22-24).
Mechanisms of iodine excretion in breast milk

Iodide is transported into breast milk by the sodium iodide transporter (NIS) (25). NIS is present in various tissues including the thyroid gland and the placenta (26). NIS is competitively inhibited by a number of chemicals and in Denmark the most frequent NIS inhibitor is thiocyanate from smoking. In the thyroid gland (26), and presumably also the placenta (27), inhibition of NIS-mediated iodide transport is autoregulated by iodide. However, in the lactating mammary gland, no autoregulation of NIS seems to occur as illustrated by lower breast milk iodine concentrations in smokers (21). The frequency of maternal smoking was much lower in our present study than in the previous Danish studies. Smokers (n=3) were excluded from urine and breast milk analyses in our study. Among women included, one woman had a low UIC (23 µg/l) in comparison to MIC (94 µg/l). She reported smoking cessation a few weeks before the interview.

Maternal fluid balance

Iodine status should be assessed by measurement of urinary iodine concentration rather than dietary intake (28). Spot urine samples are the easiest and recommended method in population studies and median UIC is considered a valid marker for population iodine intake (2). In general, it has been much discussed whether urinary iodine concentration should be adjusted for differences in fluid intake by urinary creatinine (11). Our study suggests that urinary iodine concentrations are dependent on fluid intake in breastfeeding women, whereas milk iodine concentration is not. Thus, MIC was not dependent on maternal fluid intake in line with studies indicating that breast milk volume is not influenced by maternal fluid intake (29,30). On the other hand, maternal fluid intake influenced on UIC as illustrated by the strong correlation with urinary creatinine concentration. Thus, the iodine status of breastfeeding women might be more precisely estimated when UIC is adjusted by differences in fluid intake, as previously suggested for non-lactating women and for men (9,10). Furthermore, the correlation with breast milk iodine excretion was stronger, when urinary iodine content was adjusted by creatinine in accordance with a previous (12).
Infant formulas

Iodine content of infant formulas used in Denmark was previously reported in 1999 (31). In that study, infant formulas in dry preparation were prepared using iodine-free demineralized water, whereas in our study, the mothers prepared the infant formulas at home according to the manufacturer’s instructions. The median iodine concentration was considerably higher in our study (122 vs. 57 µg/l) also for the individual brands that were measurement in both studies and even taking the iodine content of tap water into account.

Strength and limitations

The strength of our study is the high rate of participation among invited women in the postpartum interview and the relatively large number of urine- and breast milk samples obtained (10). We are aware that the study is a postpartum follow-up of women initially included in pregnancy and that the women according to ethical requirements were informed about the importance of iodine intake at the initial visit. This information was kept low-grade, and data on urinary iodine concentrations in pregnancy and press releases were not reported until after the last inclusion postpartum. Our study only included women in one region of Denmark, however, we found no significant predictors of iodine supplement intake beside iodine supplement intake in pregnancy and we find it unlikely that iodine supplement use in Danish women would considerably differ between regions (32). We did not have information on maternal dietary habits postpartum, and we do not know if differences in maternal fluid intake were caused by differences in intake of iodine containing drinks such as dairy products or water-based drinks such as tea or coffee. The level of iodine in drinking water in the region investigated is low and corresponds to the level in West Denmark (31).

National perspective

Women with no intake of iodine supplements and women with an intake of iodine supplements with low iodine content (45 µg/day) were in particular at risk of being iodine deficient. Thus, iodine supplement intake in Danish breastfeeding women should be officially recommended. One of the
concerns about iodine intake in pregnancy and postpartum has been the risk of exaggerating of thyroid autoimmunity (33). A previous study in Denmark did, however, not detect an increased risk of postpartum thyroiditis from iodine supplement in thyroid peroxidase antibody-positive mothers (34). Median urinary iodine concentration and 24-hour iodine excretion in breast milk were below the level recommended both in iodine supplement users and non-users. Together with the findings in Danish pregnant women (16) and findings from the general Danish population (35), results may indicate a need for a modest increase in the level of iodine added to salt in Denmark.

Conclusion

Maternal estimated 24-hour urinary iodine excretion showed a better correlation to maternal milk iodine concentration than did maternal urinary iodine concentration. This may suggest that estimated 24-hour urinary iodine excretion is a useful indicator of maternal iodine status during breastfeeding and of iodine supply to the breastfed infant. However, more studies on the usefulness of this indicator are warranted in populations with different dietary or environmental habits.

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Disclosure statement

The authors declare that they have no conflict of interest.
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Figure legends

**Figure 1** Flowchart illustrating the selection of the women participating in the postpartum follow-up study.

**Figure 2** Dotplot illustrating all breast milk iodine concentrations (n = 127). Black dots illustrate iodine supplement users, white dots illustrate iodine supplement non-users. Solid line is median, dotted lines are 25th and 75th percentiles. Values were stratified into 30 bands, in the range from 19-301 µg/l, each band corresponding to 9.4 µg/l.

**Figure 3** Scatter plots of 127 samples illustrating the correlation between (a) maternal postpartum urinary iodine concentration and breast milk iodine concentration, (b) estimated 24-hour breast milk iodine excretion and maternal postpartum 24-hour urinary iodine excretion, (c) maternal postpartum urinary creatinine and urinary iodine concentrations and (d) maternal postpartum urinary creatinine and breast milk iodine concentrations. All values were log-transformed for illustration and calculation of Pearson’s correlation. Values on the axes are anti-logged.
Table 1 Characteristics of the mothers participating in the postpartum interview (n = 209) at initial inclusion in pregnancy, at delivery and at the time of the postpartum interview according to maternal intake of iodine supplements postpartum.

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<tr>
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<td>15-28</td>
<td>46</td>
<td>46.9</td>
<td>57</td>
</tr>
<tr>
<td>&gt; 28</td>
<td>35</td>
<td>35.7</td>
<td>41</td>
</tr>
<tr>
<td>Maternal smoking</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>92</td>
<td>93.9</td>
<td>105</td>
</tr>
<tr>
<td>Yes</td>
<td>6</td>
<td>6.1</td>
<td>6</td>
</tr>
<tr>
<td>Breast-feeding</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Full</td>
<td>73</td>
<td>74.5</td>
<td>75</td>
</tr>
<tr>
<td>Partly</td>
<td>14</td>
<td>14.3</td>
<td>21</td>
</tr>
<tr>
<td>No</td>
<td>11</td>
<td>11.2</td>
<td>15</td>
</tr>
</tbody>
</table>

\(^a\) Chi-square test or Fishers’ exact test: iodine supplement postpartum vs. no iodine supplement postpartum.

\(^b\) Previous live- and stillbirths including index pregnancy.

\(^c\) Highest educational level full-filled or initiated. General education: ‘basic’ (primary/secondary education only; 9-13 years). General education and education qualifying for a profession: ‘low’ (vocational education and training: 9-13 years), ‘middle’ (short- or medium cycle higher education: 14-16 years), ‘high’ (long-cycle higher education: ≥ 17 years).
Table 2 Urinary iodine and breast milk iodine excretion according to maternal iodine supplement intake in women who delivered a urine sample both in pregnancy and postpartum and a breast milk sample.

<table>
<thead>
<tr>
<th>In pregnancy</th>
<th>All women</th>
<th>Iodine supplement in pregnancy</th>
<th>No iodine supplement in pregnancy</th>
<th>p&lt;sup&gt;a&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>Pregnant women</td>
<td>127</td>
<td>100</td>
<td>106</td>
<td>83.5</td>
</tr>
<tr>
<td>Median IQR</td>
<td></td>
<td>Gestational week at sampling</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>20</td>
<td>13-20</td>
<td>20</td>
<td>13-20</td>
</tr>
<tr>
<td>Urinary iodine (µg/l)&lt;sup&gt;b&lt;/sup&gt;</td>
<td>91</td>
<td>61-140</td>
<td>98</td>
<td>66-150</td>
</tr>
<tr>
<td>Estimated 24-hour urinary iodine (µg)&lt;sup&gt;c&lt;/sup&gt;</td>
<td>147</td>
<td>93-260</td>
<td>163</td>
<td>113-278</td>
</tr>
<tr>
<td>Postpartum</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Breastfeeding women</td>
<td>127</td>
<td>100</td>
<td>60</td>
<td>47.2</td>
</tr>
<tr>
<td>Days after delivery at sampling</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>31</td>
<td>25-42</td>
<td>34</td>
<td>26-44</td>
</tr>
<tr>
<td>Urinary iodine (µg/l)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>72</td>
<td>46-107</td>
<td>83</td>
<td>63-127</td>
</tr>
<tr>
<td>Estimated 24-hour urinary iodine (µg)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>10.1</td>
<td>5.0-15.9</td>
<td>9.6</td>
<td>4.9-15.9</td>
</tr>
<tr>
<td>估算24小时尿碘(µg/l)&lt;sup&gt;d&lt;/sup&gt;</td>
<td>63</td>
<td>46-92</td>
<td>80</td>
<td>51-132</td>
</tr>
<tr>
<td>Breast milk iodine (µg/l)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>69</td>
<td>50-100</td>
<td>87</td>
<td>55-144</td>
</tr>
<tr>
<td>Estimated 24-hour breast milk iodine (µg)&lt;sup&gt;e&lt;/sup&gt;</td>
<td>83</td>
<td>61-125</td>
<td>112</td>
<td>80-154</td>
</tr>
</tbody>
</table>

IQR, interquartile range (25th-75th percentile).

<sup>a</sup>Mann-Whitney test: iodine supplement in pregnancy vs. no iodine supplement in pregnancy.

<sup>b</sup>Urinary creatinine: 1 mmol/l = 0.1131 µg/l.

<sup>c</sup>Calculated from 24-hour urinary creatinine previously measured in a group of Danish pregnant women: 1.09 gram creatinine/24 hours (18).

<sup>d</sup>Mann-Whitney test: iodine supplement postpartum vs. no iodine supplement postpartum.

<sup>e</sup>Calculated from previously estimated average daily breast milk intake: 800 ml/24 hours (20).
Figure 2

Breast milk iodine concentration (µg/l)

254x190mm (96 x 96 DPI)