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Iodine status in lactating women in Norway

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Abstract

Background: Iodine is an essential element for foetal and infant growth and for development of the central nervous system. Lactating women and infants are exceptionally vulnerable to iodine deficiency and lack of thyroid hormones during infancy may lead to permanent brain damage. Despite the importance of iodine for infant health, few studies have assessed iodine concentration in human milk and there is currently no existing data on iodine status of lactating women in Norway.

Objective: The overall aim of this study was to assess iodine status in lactating women by assessing iodine concentrations in breast milk (BMIC) and urine (UIC) and compare them with WHO cut-offs, and by evaluating estimated iodine intake from food and dietary supplements.

Methods: A cross-sectional survey was performed in lactating women in five randomly selected Mother and Child Health Centres in Oslo during October and December 2016. A total of 175 lactating women between 2nd and 28th weeks postpartum participated. Iodine concentration in breast milk and spot urine samples were analyzed by inductively coupled plasma mass spectrometry (ICPMS-QQQ). Participants also provided information on iodine intake from food and supplements covering the last 24-hour (24h) and the habitual iodine intake (food frequency questions).

Results: The median and 25th and 75th percentiles (P25, P75) BMIC was 68 (45, 98) µg/L and median UIC was 64 (39, 95) µg/L. A total of 76% had BMIC <100µg/L, 18% had BMIC between 100-200µg/L and only 6% women had BMIC between 200-600µg/L. A total of 81% had UIC <100µg/L. Habitual iodine supplement use was reported by 29%, of which 18% had taken an iodine-containing supplement the last 24-hour. The median (P25, P75) habitual iodine intake from food and total iodine intake (food and supplements) was 106 (79, 138) µg/day and 135 (94, 212) µg/day, respectively. The median (P25, P75) 24-hour iodine intake from food and total iodine intake (food and supplements) was 121 (82, 162) µg/day and 134 (95, 222) µg/day, respectively. Infant's age, iodine-containing supplement intake in the last 24-hours, smoking status and UIC predicted BMIC, explaining 33% of the variance.

Conclusions: Approximately ¾ of the lactating women had inadequate iodine concentration in breast milk and urine. This was supported by inadequate iodine intake from food and supplements. Findings of this study indicate inadequate iodine status in lactating women and claim for further attention to iodine status during lactation.

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Abbreviations

BMI	Body Mass Index
EAR	Estimated Average Requirement
EFSA	European Food Safety Authority
FCT	The Norwegian Food Composition Table
FFQ	Food Frequency Questionnaire
HiOA	Oslo and Akershus University College
I	Iodine
ICCIDD	International Council for the Control of Iodine Deficiency Disorders
ID	Iodine deficiency
IDD	Iodine-deficiency disorders
IOM	Institute of Medicine
IQ	Intelligence quotient
BMIC	Breast milk iodine concentration
MIT	Monoiodotyrosine
MoBa	The Norwegian Mother and Child Cohort Study
NHMRC	National Health and Medical Research Council
NIS	Sodium-iodide symporter
NMBU	Norwegian University of Life Sciencies
NNR	Nordic Nutrition Recommendations
REK	Regional Committees for Medical and Health Research Ethics, Norway
SPSS	Statistical Package for the Social Sciences
T3	Triiodothyronine
T4	Thyroxine
Tg	Thyroglobulin
TSH	Thyroid stimulating hormone
UIC	Urinary iodine concentration
UNICEF	United Nations Children’s Fund
WHO	World Health Organization

1. Introduction

For several decades, the Norwegian population has been considered iodine sufficient. However, during the last years reports of insufficient iodine nutrition among pregnant women have been published (Brantsæter et al., 2013; National Nutrition Council, 2016; Azizi & Smyth, 2009). The latest rapport of iodine status in Norway was published in June 2016 (National Nutrition Council, 2016). Three comprehensive studies in pregnant and lactating women provide background information about the current iodine status in Norway: 1) Small in Norway (LiN) - longitudinal study of dietary data, urine, blood and hair samples from 1036 pregnant women and their children, conducted during the period 2011-2014 (Sanchez, 2015). The families were followed from pregnancy until the child is 18 months. 2) The 'Fjell studien' includes dietary data and urine samples from 64 pregnant women and 76 women three months postpartum, conducted in the period 2009-2011 (Seldal, 2012). Mother and child were followed from pregnancy until the child was 12 months old. 3) The Norwegian Mother and Child Cohort Study (acronym MoBa) is a large pregnancy cohort with dietary data from approximately 95,000 pregnant women, and urine samples from 119 women obtained in the years 2002-2008 (Brantsaeter et al., 2008; Meltzer et al., 2008). Results from a master thesis on "Determination of 12 elements in breast milk from Norwegian mothers" were used as well, where 301 samples of breast milk were analysed (Vollset, 2015). Results from MoBa that a surprisingly high proportion (54%) of pregnant women had total iodine intake (iodine from food and supplements) well under the recommendations for pregnant and lactating women. Insufficient iodine intake was confirmed by low urinary iodine concentration in the subsample of 119 MoBa participants and low urinary iodine concentrations in the 'Fjell studien'. Furthermore, mothers with low dietary iodine intake had the lowest iodine concentration in urine and breast milk (Bransæter et al., 2008; Vollset, 2015). The MoBa study also showed that during this period (2002-2008) there was a decline both in the intake of milk, yogurt and seafood among Norwegian women (Bransæter et al., 2013). The main determinants of low iodine intake (<100µg/day) were "no dietary supplements", "less than 2 dl milk / yoghurt per day" and "less than 20 g of seafood per day" (Brantsaeter et al., 2013).

During 2016, Associate Professor Sigrun Henjum at Oslo and Akershus University College (HiOA) initiated a study on iodine status in pregnant and lactating women to evaluate iodine status. Two master students participated in the research; I was given the opportunity to be a part of the study on iodine status among lactating women. From October to December 2016 I participated in the data collection which included recruitment of participants at Mother and Child Health Centres, and I was responsible for collecting breast milk and urine samples and for checking completeness of questionnaire answers and interviewing the participants regarding iodine intake.

The main purpose of the present study was to assess iodine status in lactating women through breast milk and urinary iodine concentrations, as well as through iodine intake from food and supplements. The iodine study in lactating women was undertaken to increase the knowledge and to provide new and important insight regarding iodine status in this vulnerable group.

2. Theoretical background

In this chapter, I will describe the importance of iodine, the recommended iodine intake and main sources of iodine, as well as iodine deficiency and its consequences. I will pay a special attention to iodine status in Nordic countries.

2.1 The importance of iodine

IODINE is an essential nutrient required for the synthesis of thyroid hormones that are critical for development of the brain and central nervous system (Zimmermann, 2009). The thyroid hormones help to regulate a wide range of physiological processes (Andersen, 2014). Iodine deficiency occurs when iodine intake is insufficient for the body to produce adequate amounts of thyroid hormones (Zimmermann, 2009). Iodine deficiency is a major public health problem for populations throughout the world, particularly for pregnant and lactating women and young children (WHO, 2004). More than one third of the world's population has insufficient iodine intake and iodine deficiency poses a threat throughout the lifecycle and has been associated with mental impairment (WHO, 2013).

Iodine deficiency during pregnancy and lactating may impair growth and brain development of the offspring and increase infant mortality (Zimmermann, 2009). Thus, maternal iodine requirement is increased during the period of breastfeeding to ensure an adequate supply of iodine both to the infant via breast milk and to the mother (WHO, 2007). If iodine intake is not increased during lactation, women may not excrete enough iodine into their breast milk to cover the infant's requirements (Dold et al, 2017). To protect those at risk, pregnant, lactating women and infants less than two years old are targeted in iodine deficiency disorders (IDD) prevention and control programs (WHO, 2013). Despite the importance of iodine for infant health, there are limited scientific publications reporting iodine concentrations in human milk.

2.2 Recommendations for daily iodine intake

The recommended intake is the average daily dietary intake that is sufficient to meet the requirement of nearly all (97%) healthy individuals in a particular life stage or group. Recommendations include a safety margin accounting for variations in the requirement of the group of individuals, while the Estimated Average Requirement (EAR) is the daily intake value that is estimated to meet the requirement of half of the apparently healthy individuals in a life stage or group (Nordic Council of Ministers, 2014). When evaluating iodine intake, it must be kept in mind that intake below the recommendation does not necessarily imply deficiency, while intake lower than the EAR indicates an increased likelihood of insufficiency.

Different international and Nordic authorities have made recommendations for daily iodine intake in breastfeeding women and children < 2 years (Table 1).

Table 1. Recommended daily iodine intake by different authorities in lactating women and children < 2 years.

Authority	*Lactating women μg/day*	*Child < 2 years' μg /day*
WHO, ICCIDD, UNICEF (RDI) (2007)	250	90
US Institute of Medicine 2001 (EAR) (2001)	209	90-130[1]
European Food Safety Authority (RDI) (2014)	200	70-130
Nordic Nutrition Recommendations (RDI) (2014)	200	50-70

[1]0-6 months: 110 μg/day

During pregnancy and lactation, an extra daily supply is needed to cover the needs of the fetus and newborn, to maintain maternal thyroid gland function, and to provide sufficient iodine in the breast milk. For non-pregnant adults, the recommended dietary intake for iodine is 150 μg/day. For lactating women, the recommendation from World Health Organization (WHO), the International Council for the Control of Iodine Deficiency Disorders (ICCIDD) and the

United Nations Children's Fund (UNICEF) are the same as for pregnant women, 250µg/day (WHO, 2007). However, the Nordic Nutrition recommendation (NNR) and the European Food Safety Authority (EFSA) recommends 200µg for lactating women and 175µg for pregnant (Nordic Council of Ministers, 2014; EFSA, 2014). The Institute of Medicine recommends an Estimated Average Requirement (EAR) of 209 µg during lactation, which is higher than the EAR of 160µg during pregnancy (Institute of Medicine, 2001).

The requirement of iodine in neonates is calculated to be at least 15 µg/kg in full term and 30 µg/kg in preterm infants per day, corresponding to 90 µg/day (Azizi & Smyth, 2009; Andersson et al, 2007; Delange, 2004).

Both too low and too high iodine intakes might have harmful health consequences (Zimmermann, 2009). The lower level for iodine intake is sat to 70µg/day for adults and adolescents, to avoid goiter development (Nordic Council of Ministers, 2014). Insufficient iodine levels during lactation result in neurologic and psychological deficits in children (Leung et al, 2011). The higher iodine intake was established as 200µg for children and 600µg for adults, pregnant and lactating women (Nordic Council of Ministers, 2014). The Institute of Medicine US Food and Nutrition Board has determined the higher iodine intake as 1100µg per day for adults including lactating and pregnant women (Institute of Medicine, 2001). The use of excessive amounts of iodine during breastfeeding (e.g., kelp and seaweed) can increase breastmilk iodine levels and cause transient hypothyroidism in breastfed infants. (Alexander et al., 2017).

2.3 Thyroid metabolism

Iodine plays a vital role in thyroid physiology, being both a major constituent of thyroid hormones (TSH) and a regulator of thyroid gland function (Andersen, 2014). A healthy adult body contains 15-20 mg of iodine, 70-80% of which is stored in the thyroid gland Zimmermann, 2009). Iodine from the diet is rapidly absorbed (>90%) throughout the gastrointestinal tract (Zimmermann, 2009). Dietary iodine is converted into the iodide ion before it is absorbed, then iodine enters the circulation as plasma inorganic iodide, which is cleared from circulation by the thyroid active transport system (sodium-iodide symporter protein-NIS) and kidney (Sharp, 2011). NIS is most highly expressed in the thyroid gland, but low levels are present in the salivary glands, lactating breast, and placenta (Sharp, 2011; Institute of Medicine, 2001). The iodide is used by the thyroid gland for synthesis of thyroid hormones (T3, T4), and the kidney excretes iodine with urine. The physiologic actions of thyroid hormones are growth and development, and control of a range of metabolic processes in the body. These include carbohydrate, fat, protein, vitamin, and mineral metabolism. For example, thyroid hormone increases energy production, increases lipolysis, regulates gluconeogenesis and glycolysis (Hetzer, 1983; Sharp, 2011).

The iodide transport mechanism is highly regulated, allowing adaptation to variations in dietary supply. Thyroid secretion is regulated by the hypophysis through TSH, which operates on a feed-back mechanism tuned to T4 level in blood. TSH stimulates NIS-mediated iodide transport into the thyroid gland (e.g. via regulation of NIS expression) (Dohan et al., 2003). Under low iodine levels and when the iodine stores are exhausted, blood level of T4 starts declining, and the hypophysis increases TSH secretion and the amount of NIS which stimulates the thyroid to increase the uptake of iodide and ensure the release of thyroid hormones in adequate strength (Ahad & Ganie, 2010). However, in the state of deficiency when iodide uptake of the thyroid is seriously inhibited, TSH fails to promote the release of T4 and only ends up with the hyperplasia of follicular cells. In a situation of severe iodine deficiency, while the level of T4 remains low, the level of TSH remains high (Ahad & Ganie, 2010). Under continuing TSH stimulation in endemic areas, the thyroid gland undergoes hypertrophy and hyperplasia of follicular cells and in the process, enlarges in size and appears as a goiter which may in certain cases attain an enormous size (Ahad & Ganie, 2010). The selective expression of NIS in the thyroid allows isotopic scanning, treatment of hyperthyroidism, and ablation of thyroid cancer with radioisotopes of iodine, without significant effects on other organs (Dohan et al., 2003). In chronic iodine deficiency (ID) the uptake of iodine by the thyroid can exceed 80% and the iodine content of the thyroid may fall below 20μg (Zimmermann, 2009).

2.3.1 Iodine metabolism during lactation

During lactation, the mammary gland concentrates iodine and secretes it into breast milk to provide for the newborn (Zimmermann, 2009) (Figure 1). Iodine is secreted into breast milk at a concentration gradient 20 to 50 times that of plasma through increased expression of the NIS present in lactating breast cells (Tazebay, 2000). During breastfeeding, around 40-45% of ingested iodine is excreted into breast milk, and < 90% of ingested iodine is excreted in the urine (Laurberg & Andersen, 2014). NIS is expressed in the lactating mammary gland and mediates the transport of iodide into breast milk (Andersen, 2014). The transport is inhibited by thiocyanate from maternal smoking, but in contrast to transport of iodide in the thyroid gland and the placenta, the transport of iodide into breast milk is not autoregulated (Laurberg et al., 2004; Tazebay, 2000).

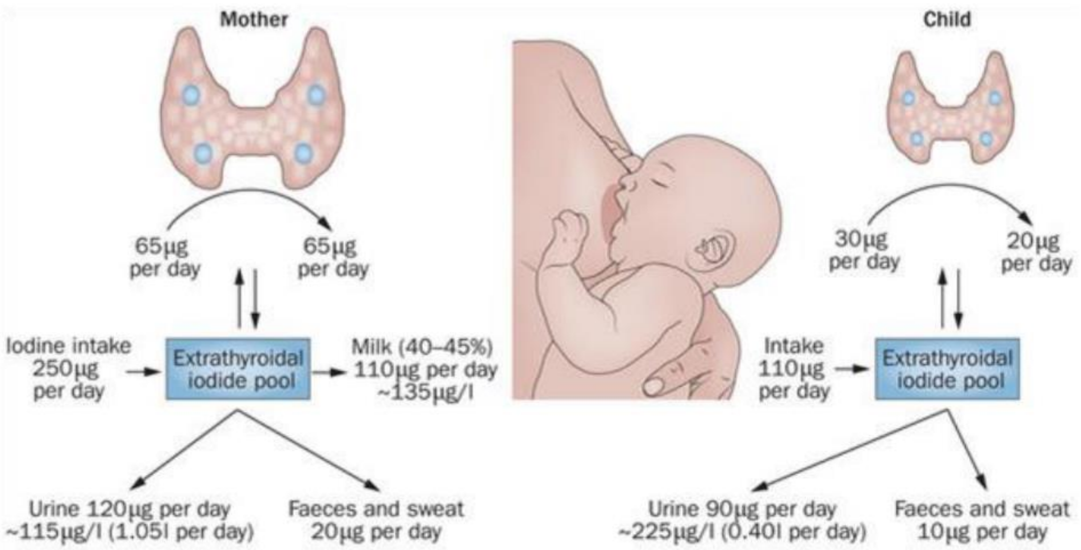

Figure 1. Estimated iodine balance in breastfeeding mother with recommended iodine intake and her child. Recommended iodine intake is set to 250µg per day (WHO, 2007) and to 200 µg by Nordic Nutrition Recommendations (Nordic Council of Ministers, 2014). Reproduced from Laurberg (2014)

2.4 Iodine deficiency disorders

Iodine deficiency disorders (IDD) constitute the single largest cause of preventable brain damage worldwide. Majority of consequences of IDD are invisible and irreversible but at the same time these are preventable (WHO, 2007). The etiology of iodine deficiency is a low dietary supply of iodine, isoflavones and goitrogens (chemicals and dietary substances that affect thyroid metabolism) (Zimmermann, 2009). Competitive inhibitors (goitrogens) are perchlorate, thiocyanate and nitrate some suppress iodide uptake by the thyroid gland (Dohan et al., 2003; Cengiz & Bilgin, 2016). Perchlorate is a toxin found in drinking water, and is widespread in the environment because it is used in rockets, fireworks, fertilizers, moreover, it has also been found in foods such as lettuce, wheat, cows' milk, wine, beer, and multivitamins (Pearce, 2012). Thiocyanate is found in cigarette smoke and plant foods such as cassava, cabbage, turnips, broccoli, brussels sprouts, and cauliflower (Pearce, 2012; Laurberg et al., 2009; Zimmermann, 2009). Isoflavones are found naturally in soy products, peas, beans, nuts, grain products, coffee, and tea (Pearce, 2012). Large doses can decrease thyroid hormone. Infants fed soy formula without enough iodine nutrition may develop low thyroid function (Pearce, 2012).

Populations living in areas where the soil has a low iodine content, and crops grown in this soil, therefore, do not provide adequate amounts of iodine when consumed. If the iodine deficiency occurs, the thyroid gland may no longer be able to synthesize sufficient amounts of thyroid hormones (WHO, 2007). IDD have many negative effects on growth and development in humans as lower intelligence quotient (IQ) in children, lower child learning capacity and economic productively, affects women's health, and cause low level of thyroid hormones in the blood (hypothyroidism) which further can affect the public health status of a community (WHO, 2007). Under iodine deficiency circumstances, thyroid will adjust all the physiological processes of thyroid hormone production in order to maximize the use of iodine, some can lead to an increased thyroidal iodine uptake and to enlargement of the thyroid (goiter) (Zimmermann, 2009). Goiters is not seen in populations with a median iodine intake of over 150 μg/day (WHO, 2007). Depending on the degree of iodine deficiency, iodine supply may be insufficient for thyroid hormone synthesis resulting in maternal and neonatal hypothyroxinemia (low T4, normal TSH) or hypothyroidism (low T4 and high TSH) (Andersen, 2014). Hypothyroidism is the main reason for the harmful effects of IDD, with the most damaging effect being on the developing brain. The thyroid hormones are crucial for myelination of the central nervous system and iodine deficiency during perinatal development can therefore cause mental retardation (WHO, 2007). Mild-to-moderate ID can also increase the risk of nontoxic and toxic goiters, and corresponding hyperthyroidism and subclinical hypothyroidism, as well as an increased risk of aggressive subtypes of thyroid cancer (Zimmermann, 2009).

2.4.1 Iodine and brain development

The most serious and adverse effect of iodine deficiency is developmental brain damage in the prenatal and postpartum period. Brain development is initiated in the very early pregnancy and continues throughout the first years of life (Delange, 2000). The neurological consequences of iodine deficiency in neonates are mediated by thyroid hormone deficiency, varying from minimal brain function to a syndrome of severe intellectual disability (cretinism). Thyroid hormones are essential regulators of brain development and involved in myelination, cell differentiation, migration and selective cell death, some are impaired during period of brain growth (neurogenesis) (Bernal, 2005). Evidence suggests alterations in synaptology, neurons, myelin sheaths, glial cells, and morphology of cerebrum and cerebellum in severe iodine deficiency. Severe iodine deficiency can cause cretinism which is characterized by profound mental and physical disabilities, as irreversible neurological deficits (spasticity and squint), and may develop when iodine intake is <25µg per day (Rasmussen et al., 1996). This is due to iodine deficiency *in utero* resulting in maternal hypothyroxinemia (Rasmussen et al., 1996; Pharoah et al., 2012).

2.4.2 Iodine deficiency prevention

Iodized salt has been used to prevent iodine goiter and cretinism all over the world since the 18th century (Zimmermann, 2008). Universal salt iodization has become the most effective resource to eliminate iodine deficiency around the world (WHO, 2007). However, another way to maintain an adequate iodine supply in vulnerable groups as lactating and pregnant women, is to advice a daily intake of iodine-containing supplements (WHO, 2007; Andersson et al., 2007).

Salt iodization

As recommended by WHO and ICCIDD iodization of salt has been- and still is the preferred strategy to control iodine deficiency (WHO, 2014; Bath et al, 2013). In relation to the Nordic countries, iodized table salt is available in Denmark, Sweden, Finland, and contributes to the iodine intake (Nordic Council of Ministers, 2014). The concentration of iodine present in iodized salt varies from 5 µg/g to 50 µg/g in the Nordic countries (Nordic Council of Ministers, 2014). Since year 2000, Denmark has implemented use of iodine fortified salt in commercial bread, which has resulted in a significantly increase in urine iodine excretion in the population (Andersen et al, 2014). Iodized salt is not commonly used in Iceland. In Norway, the contribution of iodized salt is insignificant because only some brands of table salt are iodized, the concentration is low (5 µg/g) and industrial salt is not iodized. Consequently, in the Norwegian population iodization of cow fodder has been much more important for iodine intake than iodized table salt (Nordic Council of Ministers, 2014). During the 1930s and 1940s, goiter due to iodine deficiency was common in many areas in Norway. However, since iodization of cow fodder was introduced in the 1950s, the Norwegian population has been considered iodine-replete (Brantsæter et al., 2013).

Supplementation

Systematic iodine supplementation during lactation and pregnancy has not become a normal practice around the world during the last years, except USA (The American Thyroid Association, 2006), Australia and New Zealand (NHRMC, 2010). The reason why USA has implemented iodine supplementation, is the small risk of excessive iodine intake compared to the profound consequences of ID, especially during pregnancy (The American Thyroid Association, 2006). Moreover, WHO recommends each country to assess the iodine status in the population every five-year to make sure that women at risk of ID have an adequate intake of iodine during lactation. Today, there is no recommendation for use of iodine supplementation for lactating women in Norway (Norwegian Directorate of Health, 2016). However, The American Thyroid Association recommends that all women who are pregnant, lactating, or planning a pregnancy should ingest dietary supplements containing 150 µg of potassium iodide per day (The American Thyroid Association, 2006). Women with a low intake of iodine-rich food like fish, dairy products and eggs are particularly vulnerable for low iodine intake, and could benefit from iodine-containing supplement (Skeaff, 2011). The National Nutrition Council highlighted in the report published in 2016 that several groups of the Norwegian population are at risk of insufficient iodine intake due to few dietary sources, and also showed that even those who adhere to the food based guidelines for a healthy diet will not reach the recommended intake of iodine. To secure an iodine intake of 200µg per day during lactation, women, would need to drink appx. 0.8 l milk or yogurt daily and consume 300-500g seafood weekly or take an iodine-containing supplement (National Nutrition Council, 2016). The health authorities have decided to evaluate and implement actions to improve iodine nutrition in Norway and the actions include quantifying the amount of daily milk/yoghurt intake and to increase the amount of iodine in iodized salt in Norway (Norwegian Health Authorities, 2017).

2.5 Sources of dietary iodine

Geological and climatic conditions are the most important predictors for iodine content in food and, thus for iodine intake levels, as there is a cycle of iodine in nature. Most iodine is found in the world's oceans. Copious amounts of iodine leach from surface soil by glaciations, snow, and rain and carried by rivers and floods into the sea. Therefore, many mountainous areas, but also lowlands far from the oceans, are depleted of iodine (Hetzel, 1989). Iodine is found naturally in foods and drinking water, artificially in foods fortified with iodine, in iodine-containing dietary supplements, radiographic contrasts agents, and in medicaments (Zimmermann, 2009; National Nutrition Council, 2016). There are relatively few food groups containing iodine, and the main sources of dietary iodine vary between countries and may also vary within the same country (Andersen, 2015). Fish, seafood and seaweed are rich in iodine because marine plants and animals concentrate iodine from seawater. In populations with a high intake of fish, these food items are the major source of iodine (Zimmermann, 2009). However, the iodine content varies greatly between lean and fatty fish with the highest content in lean fish like cod, haddock and saithe (Rasmussen et al., 2009). Drinking water is an important source of iodine in some populations. The content of iodine in drinking water in Norway is generally too low (<2µg/L) to contribute to iodine intake (Dahl et al., 2004). The main source of iodine in Norway today is milk and dairy products, contributing with almost 60% of iodine in the diet (National Nutrition Council, 2016). Seafood and eggs are also important sources of iodine in the Norwegian diet (Dahl et al., 2004; National Nutrition Council, 2016) (Table 2). The mean iodine concentration in other food items, e.g., meat and meat products, bread and cereals, vegetables, potatoes, fruits and berries, fats and oils is assumed to be 2-3 µg/100g and their contribution of iodine to the diet are therefore limited (Dahl et al., 2004; National Nutrition Council, 2016).

Lactating women who have low intake of fish and milk products will have very low levels of iodine in breast milk if they are not taking supplements with iodine (National Nutrition Council, 2016). In master thesis conducted at Oslo University Hospital, Ullevål, iodine concentration in urine among infants whose mothers followed a milk-free diet (n = 57) was examined. The results indicate that infants who were exclusively fed by mothers on milk-free diet, was in danger of getting insufficient iodine, while children who ate iodine-fortified porridge received sufficient iodine (Thomassen, 2015).

Table 2. Overview of iodine-containing foods according to Norwegian Food Table Composition. Adopted from National Nutrition Council (2016)

Food product	***Iodine content appx. µg/100g****	***Portion size****	***Iodine amount per portion size****	***% part of recommended intake[1] NNR (WHO)***
Iodized salt	500	1 gram	5	2.5 (2)
Milk[2]	13	1 glass (2dl)	40	20 (16)
Yogurt	17	1 box (150g)	26	13 (10,4)
Cheese	40	20g	8	4 (3,2)
Brown cheese	140	16g	22	11 (8,8)
Mackerel	60	150g	90	45 (36)
Cod	120	200g	240	120 (96)
Farmed salmon	10	150g	18	6.5 (7,2)
Caviar	85	15g	13	9 (5,2)
Mackerel in tomato	75	40g	30	15 (12)
Egg[2]	30	1egg (56g)	27	13.5 (10,8)
Water	0.2	1 glass (2dl)	0,4	0.2 (0,16)

[1] Recommended iodine amount for lactating women according to NNR (2012) 200µg iodine/day, and WHO 250µg/day
[2] Updated data (2016); iodine content in milk and cheese have been changed last year (The Norwegian Food Safety Authority (2017)
* Measurements and portion size for food products, The Norwegian Food Safety Authority, University of Oslo and the Norwegian Directorate of Health (2015)

2.5.1 Iodine status in Nordic countries

There is a large knowledge gap regarding the iodine situation of lactating mothers in most Nordic countries (Table 3) (Nystrom et al., 2016). The only country with available data is Denmark. Here, the use of multivitamins containing iodine during the lactation period was reported by 47%, in comparison to 83% in pregnant women. Regardless of whether women take supplements containing iodine or not, the Danish women in the study did not attain the WHO recommendations (Andersen, 2014). The situation is further impaired for smokers, as smoking halves the milk iodine concentration (Laurberg et al., 2004). Trials are ongoing in Sweden and Finland, while no data are underway from Iceland (Nystrom et al., 2016). The results presented in this master thesis on iodine during lactation present the latest information about iodine status in lactating women in Norway.

Table 3. Summarized data on current iodine status in the Nordic countries*

Risk groups	Iceland	Norway	Denmark	Sweden	Finland
Pregnant women	Sufficient	Mild ID[1]	Mild ID	Mild ID	Unknown (to be analyzed)
Percentage of pregnant women using iodine-containing multivitamins	Unknown	32%	87%	Unknown (to be analyzed)	Unknown
Lactating women	Unknown	Mild ID[2]	Mild ID	Unknown (to be analyzed)	Unknown (to be analyzed)
Percentage of lactating women using iodine-containing multivitamins	Unknown	29%[2]	47%	Unknown	Unknown
Children <1 year	(to be analyzed)	Unknown	Unknown	Unknown	(to be analyzed)

1 ID=iodine deficiency
2 Data from this master thesis
* Adapted from Nystrom et al. (2016)

Table 3 illustrates the current iodine status in the Nordic countries. There is a general lack of data in all the Nordic countries in both pregnant and lactating women and infants, but data from several ongoing studies will be analyzed.

The five Nordic countries employ different strategies to ensure adequate iodine intake. The iodization of salt is the most commonly used tool for iodine prophylaxis, but the amount of iodine added to table salt varies from country to country (WHO, 2006). Table 4 highlights differences between the Nordic countries' iodization program, regulations, current iodine sources and iodine status, and fortification policies adapted to ensure adequate iodine status in the general population.

Table 4. Comparisons of the Nordic countries regarding iodine levels in water, historical data on iodine intake levels and salt iodization. Adapted from Nystrom et al. (2016)

	Iceland	**Norway**	**Denmark**	**Sweden**	**Finland**
Water iodine level (median)	0.12 µg/L	<2 µg/L	12.2±8.3 µg/L (mean)	3.7 µg/L	Dug wells: mean 6.78±35.1µg/L
Iodine status before iodination	Sufficient	Severe to moderately deficient	Moderate to mildly deficient	Severely deficient	Moderately deficient
Fortification of cow fodder (starting point)	Fish meal used in cow fodder voluntary	Mandatory from 1950, level: 2 µg/g salt.	Voluntary	Voluntary	Voluntary
Start of iodination to the population	-	Late 1930s	2000	1936	1946
Type of iodination	-	Table salt	Table salt and salt for bread production	Table salt	Table salt and cow fodder
Level of iodine added	-	5 µg/g salt	13 µg/g salt	50 µg/g salt	25 µg/g salt
Type of legislation	-	Voluntary	Mandatory	Voluntary	Voluntary
Cow milk iodine concentration (µg/L)	2006: average 145	2000–2012: 100–150 2012–2015: 190 2015: 200	-	2001: 160 2009: 117	2015: 150
Mean amount of fish by adults (g/day/person)	Fish and seafood 46g	Fish 67g Seafood: 52g	Fish 37g	Women 37, Men 43	Fish 40g
Major source for iodine	Fish	Milk	Milk and salt	Salt	Milk

2.6 Iodine in human milk

The iodine concentration in breast milk varies with the iodine intake from the diet (Nordic Council of Ministers, 2014). There is no clear cut-off for BMIC, but several international researchers and WHO have recommended that BMIC is optimal at concentrations of 100–200 µg/L to ensure a sufficient iodine level in infants (90µg/day) (WHO, 2007; Ares et al., 2005; Delange, 2004). A wide range of median or mean BMIC values has been reported in several reviews conducted in areas of varying iodine sufficiency (Azizzi & Smyth, 2009; Dorea, 2002). BMIC typically ranges from <50 µg/L in iodine-deficient areas to 100–150 µg/L in areas of iodine sufficiency and as high as 150–180 µg/L in areas of good iodine supply (Azizzi & Smyth, 2009; Dorea, 2002) (Table 5). A BMIC < 100 µg/L has been identified in studies from Finland, France, Germany, Belgium, Sweden, Spain, Italy, Denmark Azerbaijan and Zaire while studies from USA, China, Iran, Thailand and South Africa have identified >100µg/L (Azizzi & Smyth, 2009; Heynh et al., 2016; Mobasseri et al., 2014; Osei et al., 2016; Mekrungcharas & Kasemsup, 2014). A study in Nepal identified a median BMIC of 250 µg/L, and the estimated iodine intake of the infants involved (0–6 months) was 200 µg/day (Henjum et al., 2016). WHO's recommended maximum iodine intake for infants <2 years old is 180 µg/day (Andersson et al., 2007), therefore some infants in this area may be consuming excessive iodine intakes through breast milk (Henjum et al., 2016). This can result in subclinical hypothyroidism and permanently affect their neurodevelopment (Zimmermann, 2009).

Table 5. BMIC criteria for assessing iodine nutrition based on median BMIC in lactating women (WHO, 2007)

BMIC (µg/L	***Iodine intake***
<100	Insufficient
100-200	Adequate
>200	Above requirements

BMIC is influenced by, and may be an indicator of, maternal iodine status during breastfeeding (Azizi & Smyth, 2009; Dorea, 2002; Zimmermann, 2009). According to the latest research by Dold et al., BMIC is a more accurate biomarker of iodine status than UIC in exclusively breastfeeding women (Dold et al., 2017). In iodine-sufficient mothers when iodine intake is low, there is increased portioning of iodine into breast milk, but at the same time iodine excretion in urine decreases; for this reason, maternal UIC alone may not reflect iodine status, and BMIC should also be measured to assess iodine status in lactating women (Dold et al., 2017).

2.6.1 BMIC status in Nordic countries

Totally 127 breastfeeding women were examined after the introduction of the mandatory iodine fortification of salt in Denmark (Andersen et al., 2014). Reported levels in breast milk from the National research in Denmark, showed that BMIC was 83 µg/L (61–125 µg/L) and were higher in iodine-supplemented mothers; 112 µg/L (80–154 µg/L) versus 72 µg/L (47–87 µg/L), $p<0.001$ (Andersen et al., 2014). Older data from Finland reported average levels of 25 µg/L in breast milk from goitrous areas compared to 53 µg/L in non-goitrous areas (Pirkko & Panu, 1960). Systematic review by Azizi and Smyth presented BMIC of 92µg/L from Sweden. Moreover, a new study in Sweden will provide new data on BMIC among Swedish women (Filipsson, 2016), which is currently recruiting participants. Iceland has in the past been known for its high iodine intake, based on results from studies of iodine intakes from 1939, 1988, and 1998 suggested to be due to high fish consumption (Gunnarsdottir et al., 2009)

In relation to Norway, only few data are available. In master thesis on “Determination of 12 elements in breast milk from Norwegian mothers”, breast milk for iodine analyze was taken from the population based on cohort called Norwegian Human Milk Study (HUMIS) conducted in the period 2002 to 2006. A total of 301 samples were used. Mother collected milk over 8 days on average. BMIC was reported to be 59 µg/L (Vollset, 2015). Only one other study, ‘Fjell studien’, assessed iodine status in lactating women. However, iodine was measured in urine only, not in breast milk (Seldal, 2012).

2.7 Urinary iodine

In 1990, urinary iodine was presented as an effective biochemical indicator to assess recent dietary iodine intake in population (WHO, 2007). For this purpose, the median UIC used to assess iodine status (WHO, 2007). In lactating women, the cut-off for median UIC are like the cut-off for non-pregnant adults and children ≥ 6 years, less and over 100µg/L (Table 6). Sufficient iodine level for lactating women is less than for pregnant (>150µg/L) due to iodine excreted through breast milk (>100µg/L) and less into urine (WHO, 2007). Iodine concentrations measured in spot urine samples collected in the morning, or randomly during the day will not be a precise measure of iodine status in an individual, but is suitable to adequately assess iodine status at the population level if the sample includes at least 500 individuals (WHO, 2007; Vejberg et al., 2009).

Table 6. Epidemiologic criteria for assessing iodine nutrition based on median urinary iodine concentrations in lactating women, according to WHO cut-off

Median UIC (µg/l)	***Iodine intake***	***Iodine status***
< 100	Insufficient	Iodine deficiency
≥ 100	Adequate	Adequate iodine nutrition

Results from the above-mentioned studies and from MoBa study have shown low iodine intake and insufficient iodine status (<70µg/L) in lactating and pregnant women (National Nutrition Council, 2016). Based on results from MoBa, Norway has now been marked as a country with iodine deficiency among pregnant women by WHO (National Nutrition Council, 2016).

2.8 Methods to assess iodine status

Iodine status in a population can be assessed with different methods. However, the methods recommended include UIC, thyroid size by neck inspection and palpation and/or thyroid ultrasonography, serum thyroid stimulating hormone (serum TSH) and serum thyroglobulin (serum Tg). These indicators are complementary (Skeaff, 2011). While UIC show a more recent iodine intake, Tg shows an intermediate response, whereas changes in goitre rate reflects more long-term iodine nutrition (Zimmermann, 2008).

2.8.1 UIC

Because more than 90% of dietary iodine eventually appears in the urine, UIC is an excellent indicator of recent iodine intake (Zimmermann, 2009). UIC can be expressed as a concentration (micrograms per liter), in relationship to creatinine excretion (micrograms iodine per gram creatinine), or as 24-h excretion (micrograms per day). For populations, because it is impractical to collect 24-h samples in field studies, UIC can be measured in spot urine specimens from a representative sample of the target group and expressed as the median, in micrograms per liter (Zimmermann, 2009). The UIC cut-offs value for lactating women are <100µg/L insufficient, >100µg/ adequate (WHO, 2007; Nordic Council of Ministers, 2014). In lactating women, the cut-off for median UIC is lower than that the iodine requirements for pregnant women because of the iodine excreted in breast milk (Zimmermann, 2009). UIC is the concentration of iodine (µg/L) and varies with fluid intake and recent iodine dietary iodine intake (WHO, 2007). Creatinine is a product of muscle metabolism which is excreted in the urine at a relative constant rate, and it has been suggested to use the iodine/creatinine ratio (µg iodine/gram creatinine) to adjust for variation in urine volume (WHO, 2007; Zimmermann, 2009). Another aspect is the variation in UIC during the day. In particular, UIC in a fasting morning spot sample tend to be lower (Zimmermann, 2009). Although the median UIC does not provide direct information on thyroid function, a low value suggests that a population is at higher risk of developing thyroid disorders (Zimmermann, 2009).

2.8.2 BMIC

BMIC analysis is challenging, but latest findings suggest that median UIC is not an accurate biomarker of iodine intake exactly in lactating women with intakes at the lower end of the adequate range because of preferential portioning into breast milk (Dold et al., 2017). Thus, BMIC has been proposed as a more accurate indicator of iodine status than maternal UIC (Dold et al., 2017). There is no established cut-off for BMIC to evaluate iodine sufficiency, but recent studies suggest that BMIC >100µg/L may be considered as adequate, and spot breast milk samples are common measurement method (WHO, 2007; Azizzi & Smyth, 2009; Dorea, 2002). When assessing iodine status in lactating women, median BMIC should be used (WHO, 2007). Because the mammary gland can concentrate iodine, iodine supply to the new born via the breast milk may be maintained even in the face of maternal iodine deficiency (Dold et al., 2017). This may help explain why, in areas of iodine deficiency, BMIC is often higher than expected based on the UIC of the lactating mother (Dold et al., 2017). For example, a recent study in lactating women from United States with a median UIC of 114 µg/L reported a median BMIC of 155 µg/L (Dold et al., 2017).

2.8.3 Other methods

Three other methods for assessment of iodine status in a population are goiter rate, serum TSH and serum thyroglobulin (Tg). Goiter is measuring by neck inspection and palpation, and/or by thyroid ultrasonography (Zimmermann, 2009; Andersen, 2014). By palpation, a thyroid is considered goitrous by size classification system of WHO (WHO, 2007). Goiter surveys are usually done in school-age children. Thyroid size is a long-term indicator of iodine status (months to years) and although thyroid ultrasonography is non-invasive and quickly performed, the method requires training and differences in technique can produce inter observer variation (Andersen, 2014; Zimmermann, 2009). Measurement of serum Tg can be used as an indirect measurement of goiter because of an increase of Tg in the blood when thyroid volume increases (Skeaff, 2012; Zimmermann, 2009). Measurement of serum TSH is a good indicator of iodine status in new-born and is often used in screening to detect congenital hypothyroidism in new-born (Zimmermann, 2009). Serum TSH is, however, an insensitive indicator of iodine status in adults, as well as in moderate-to-mild ID, because the serum TSH is higher in iodine-deficient populations than in iodine-sufficient populations, but the difference is small and overlap in TSH values often occurs (Skeaff, 2012; WHO, 2007).

3. Objectives

The overall objective of this study is to assess iodine status (breast milk iodine, urinary iodine concentration and iodine intake from food and supplements) in lactating women in Norway.

More specific objectives are:

1. To describe iodine concentrations in breast milk (BMIC) and compare them with a suggested WHO cut-off, in addition describe BMIC variation by the child's age
2. To estimate the intake of iodine from food and dietary supplements from 24-hour iodine intake and habitual food frequency questionnaire, and compare the intakes with recommended intakes
3. To assess urine iodine concentrations (UIC) in lactating women and compare with WHO cut-off
4. To assess correlations between BMIC, UIC and iodine intake from habitual and 24-hour iodine intake
5. To identify significant predictors BMIC (μg/L) in multiple regression analysis

4. Material and methods

In this part of the thesis, the study population and the methods will be described in detail.

4.1 Population and sampling

In this cross-sectional study, we randomly selected five out of 18 Mother and Child Health Centers in Oslo to represent all different parts of Oslo, Norway. Study purpose was presented to the first Mother and Child Health Center on 6th October 2016, and recruiting process started next week. In Norway, all mothers who deliver an infant are offered postnatal care visits free of charge. Routine visits for health check-up with a doctor are scheduled when the baby is 6 weeks, 3 months and 6 months, but mothers are free to come whenever they need to weigh the baby or if they would like to talk to a health nurse.

Healthy lactating women from five Mother and Child Health Centers in Oslo who had delivered a baby within the last six months and who were still lactating, either fully or partly were eligible for inclusion. Exclusion criteria were lack of Norwegian language skills and women who were not breastfeeding. All women were given written information on the study purpose on the first visit at the health center. They were informed about the study purpose and that they would have the opportunity to refuse to participate. Women who agreed to participate had filled out an informed consent form. After I had presented the objective of the study and described for each woman what participation in the study would require of her, we individually agreed about timing and delivering of breast milk and urine samples and the questionnaire. In total 254 lactating women between 2nd and 28th weeks postpartum were invited to participate, 193 accepted to participate and 175 fulfilled the study. From the first health center, 38 women participated and appx 7 declined to participate; from the second health center, 30 women participated and appx 20 declined; from the third, 27 women participated and appx 30 declined; from the fourth, 45 women participated and appx 9 declined; from the fifth, 35 women participated and appx 12 declined. In total, appx 78 women declined immediately to participate after study introduction. Main reasons for declining to participate were lack of time, lack of interest, that it is difficult, difficulties with logistic, no desire to press out milk. All necessary equipment, as an informed consent form, questionnaire, bottle for urine collection, were the same as those used in the first part of survey on pregnant women.

The recruitment took place from 6th October to 21th December 2016. Sampling included donating of breast milk (5-10ml) and urine samples, as well as to provide information about demography, health, lifestyle and diet. Background characteristics and dietary habits history of the lactating women were obtained through a short-structured questionnaire administered by self-reported interview. This questionnaire was an adapted version of a questionnaire from the first part of research project for assessment of iodine status in pregnant women, and consisted of three parts: questions about background, questions about iodine knowledge, and questions about food intake for calculating iodine intake from food and supplements. Habitual dietary intake was assessed using a 31-item, semi quantitative food-frequency questionnaire (FFQ), where lactating women were asked how often they consume each food item. Participants who consented to take part were given a plastic bag with two collecting containers (one for breast milk and another for urine), the questionnaire, and a plan with detailed instructions. In addition, oral instructions were provided for better understanding about what women should do, including information that both samples had to be stored in the fridge until delivery. All papers and collecting containers were marked with ID number. Further, date for collecting samples and interview were agreed directly with each woman. It was specified that samples had to be collected on day one, and day two was the interview, due to sample storing requirements and 24-hour iodine intake questions. Because the composition of breastmilk varies during the day and during time when the baby sucks, the instruction for sampling of breastmilk was to express breastmilk manually or using pump into the provided same plastic container four times during a day. Two in the morning and two in the afternoon, to with hind milk and two with foremilk.

In relation to urine sampling, the women provided one non-fasting spot urine taken after breakfast, and mothers were instructed to donate the sample on the same day as collecting breastmilk and close in time to the collection of the first breast milk sample. All women were told to fill out the questionnaire day 2. The women were provided with a separate paper called ‘Notes’ where the different time points of sampling were recorded. All information provided by the participants were kept confidentially.

4.2 Data collection

Delivering of samples took place at the same Mother and Child Health Centers where the woman was recruited, in some days or weeks, however different meeting points occurred during the all recruitment process. Data collection and interview occurred by individual appointment at health centers. The interview included to check the completed questionnaire, especially to find and fill in missing data, and to check timing for sample collection, and to collect breast milk samples and urine sample. Those who had difficulties with the questionnaire, got advices and help. Urine and breast milk samples were stored frozen at –80^{0}C prior to analyze. The samples were sent to Norwegian University of Life Science (NMBU) where breast milk and urine samples were analyzed for iodine between January 2017 and February 2017. Sample size calculations were not performed because there are few studies on BMIC, and no such study in Norway. Therefore, we did not have any estimated prevalence of lactating women with suboptimal BMIC to use in the power calculation. In addition, WHO does not have recommended number of subject required for analyzes of BMIC like for UIC.

4.4 Ethics

The present study was conducted according to the guidelines in the Declaration of Helsinki and was approved by the Regional Committee for Medical and Health Research Ethics Norway (2015/1845) (Appendix 1).

4.5 Determination of iodine in breast milk and spot urine

Deep-frozen samples of breastmilk were thawed and heated to 37 °C in a heating cabinet, subsequently homogenized, and finally aliquoted into 15 mL pp centrifuge tubes (Sarstedt) by means of a 100-5000 µL electronic pipette (Biohit). A conformance test between volume and weight of sample matrices confined concentration of iodine to two significant figures. An aliquot of 1.00 mL of breast milk were diluted to 10,0 mL with an alkaline solution (BENT), containing 4% (w/V) 1-Butanol, 0.1% (w/V) H4EDTA, 5% (w/V) NH4OH, and 0.1 % (w/V) Triton™, X-100, and analysed for iodine concentrations by means of the Agilent 8800

ICPMS-QQQ using oxygen reaction mode. Iodine was determined on mass 127. 129I was used for correction of non-spectral interferences. The quantification of iodine in spot urine followed the same procedure, except that that the urine was thawed, but not heated before the alkaline dilution, and the concentration of NH4OH in BENT was decreased to 2% in order to avoid precipitation of struvite (MgNH4PO4□6H2O) in urine. Reagents of analytical grade or better and deionized water (>18 MΩ) were used throughout. Accuracy was checked by concurrent analysis of standard reference materials (SRM); Institute for Reference Materials and Measurements (IRMM) BCR® – 063R Skimmed milk powder, European Reference Materials ERM® – BD150 and ERM® – BD151 Skimmed milk powders, National Institute of Standards & Technology (NIST) 1549a Whole milk powder, Seronorm™ Trace Elements Urine L-1, Seronorm™ Trace Elements Urine L-2, and NIST 2670a Toxic elements in freeze-dried urine. Allowing for experimental error, our data were within the recommended values issued. Considering breastmilk, the limit of detection was 0.10 µg/L and the limit of quantification was 0.50 µg/L, calculated on replicate measurements of blank samples. Regarding urine, the limit of detection was 0.90 µg/L and the limit of quantification was 3.0 µg/L. Intermediate precision (within-laboratory reproducibility) was < 4%.

4.6 Measurement of iodine status

In this master thesis, BMIC, UIC, and dietary iodine intake was used to assess iodine status in lactating women, and compared with NNR, EAR and WHO recommendations and cut-off values (Nordic Nutrition Recommendations, 2012; Institute of Medicine, 2001; WHO, 2007). The estimated iodine intake among infants 0–6 months was calculated based on a mean estimated consumption of breast-milk of approximately 0.78 L/day (WHO, 2002):

Consumed breast milk (0.78L/day) x BMIC µg/L = estimated daily iodine intake

The median UIC above 100µg/L in lactating women was considered as sufficient (WHO, 2007). UIC was based on one spot urine sample after breakfast collected from the participants and expressed as median and mean µg/L. UIC can be used to estimate daily iodine intake based on the following formula from the Institute of Medicine (Institute of Medicine (US), 2001):

Urinary iodine (µg/L) x 0.0235 x weight (kg) = estimated daily iodine intake

4.7 Calculation of iodine intake from food and supplements

Iodine intake was calculated using two approaches, one focusing on habitual iodine intake and one based on 24-hour iodine intake:

Table 7. Two approaches used in our study

Habitual iodine intake		**24-hour iodine intake**	
Iodine intake from food	Total iodine intake (food and supplement)	Iodine intake from food	Total iodine intake (food and supplement)

The Food Frequency Questionnaire was designed to assess habitual food consumption and a 24-hour dietary intake to assess iodine intake of selected iodine rich food items during the last 24-hour (Appendix 2). Likewise, participants were asked about habitual use of dietary supplements as well as specification of supplements taken the last 24-hour.

The iodine rich food items included in the 24-hour iodine intake questions were 1) milk and yoghurt (number of glasses), 2) all types of cheese (number of slices), 3) eggs (including dishes with eggs) 4) fish (lean and fatty fish for dinner and/or on bread). The habitual food intake assessment included 31 questions about average intake of defined food items. Of these, three questions assessed intake of milk and dairy products, four assessed intakes of fish and fish-dishes, and one assessed intake of egg and egg-dishes. The questions had seven answer alternatives, ranging from rarely/never to 5 times daily or more. The answer alternatives were converted to daily intakes by dividing the times per month and times per week alternatives with 30 or 7 days, respectively. For answer alternatives covering a range, e.g. 4-6 times per week, the middle frequency was used (5 times/week=5/7=0.7 times/day), while the highest alternative frequency, i.e. 5+ times/day, was converted to 5.5 times/day.

Answers to the habitual intake of milk, cheese, fish and egg were assigned a portion size and the amount multiplied with iodine concentrations for each food item/dish. Iodine concentrations given in the Norwegian Food Composition Table (The Norwegian Food Safety Authority, The Norwegian Directorate of Health & University of Oslo, 2015) were used except for the values for milk and egg. Because recent analytical results for iodine concentration in milk and eggs has been lower than the values in the food composition table, 13 µg/100g was used instead of 20 µg/100g for milk and yoghurt (information from producers), and 30 µg/100g instead of 49 µg/100g was used for eggs (Mattilsynet, 2017). We applied recipes for deriving iodine concentrations to use for composite dishes and for averaging concentrations from different fish species. To account for iodine contributed by foods and dishes that were not covered by the food items included in the dietary assessment, 30µg/day from "other food" was added to the estimated total intake for all participants both for habitual and 24-hour iodine intake. The same approach (adding 30 µg/day from "other food") was used when iodine intake was estimated from the amounts of fish, milk and eggs reported in the National dietary survey Norkost-3 (National Nutrition Council, 2016).

All dietary supplements were recorded by name, and the amount of iodine in each supplement was provided by each participant in a separate question. Otherwise, content information available on the label or provided by the producer on internet was used to make list of iodine content per dose of the supplement. This was used for calculating habitual iodine intake contributed by supplements, and with intake specified in the 24-hour for calculating iodine contributed by supplements in the last 24-hour. Total habitual and total 24-hour iodine intakes were calculated by adding together the amounts of iodine coming from food and iodine from supplements.

4.8 Definitions and other variables

In this study two definitions for breastfeeding were used, exclusive and partly breastfeeding. Exclusive breastfeeding means that the infant receives only breast milk (including milk expressed); no other liquids, solids and water are given, except for oral rehydration solution, or drops/syrups of vitamins, minerals or medicines (WHO, 2008). Partly breastfeeding according to WHO could be define as complementary feeding, when infant receives breast milk (including milk expressed) and solid or semi-solid foods (any food or liquid including non-human milk and formula) (WHO, 2008).

Infant's age was divided into three categories (0-10 weeks, 11-19 weeks, 20-28 weeks) to compare BMIC by infants age. Body Mass Index was calculated as weight/(height)^2 (kg/m^2). Maternal weight and height before and after delivery were calculated to body mass index

(BMI, kg/m^2), which was divided into three categories, underweight (<18.5), normal weight (18.5-24.9), and overweight (>25). Breast milk iodine concentration was divided into three categories as low BMIC (<100µg/L), optimal BMIC (100-199µg/L), and high BMIC (>200µg/L). Urinary iodine concentration (UIC) was divided in two categories, low UIC (<100µg/L) and normal UIC (> 100µg/L).

The proportions of infants at 0-3 and at 0–5 months of age who are fed exclusively with breast milk were used as indicators for exclusive breastfeeding by 3 and 6 (WHO, 2008).

$$\frac{\textit{infants 0-3 (0–5) months of age who received only breast milk during the previous day}}{\textit{infants 0-3 (0–5) months of age}}$$

4.9 Statistical methods and data analyses

Analyses were performed with the statistical software SPSS version 23 (SPSS Inc., Chicago, III., USA). Parametric data are presented as means and standard deviation (SD), while non-parametric data are presented as medians with 25th and 75th percentiles. For other descriptive statistics min and max, and percentages were presented as well. Figures and tables were made using SPSS 23 and Microsoft Excel version 17.02 (2016). BMIC, UIC, habitual and 24-hour iodine intake were skewed, thus as for not normally distributed variables, the Mann–Whitney U test was used for two group comparisons and the Kruskal–Wallis test for multiple group comparisons. In addition, the Mann-Whitney U test was used to find associations between BMIC and maternal background characteristics. Two-tailed tests with a 5% significance level were used for all analyses. Spearman's correlation coefficients were used to evaluate the agreement between continuous variables as BMIC and both habitual and 24-hour iodine intake, and UIC.

Multiple linear regression analyses were used to explore whether exclusive breastfeeding, number of children, age of the mother, education, work status, civil status, smoking habits and country of origin were predictors of BMIC (dependent variable) in lactating mothers. Other dietary and maternal factors [thyroid disease] was also tested using a stepwise procedure, but none of those were significant predictors of BMIC and were therefore not included in the final regression models. Due to the skewed distribution, BMIC (dependent variable) was log transformed prior to the regression analysis. All covariates showing a linear association ($p < 0.10$) in the crude regression models were included in a preliminary multiple regression model. Excluded variables were reintroduced and those who were still significantly associated in this model ($p < 0.10$) were retained in the final model. Analysis of the residuals was performed in order to examine the fit of the model.

5. Results

5.1 Study population

Table 8 shows the sociodemographic characteristics of the participants. The mean age of mothers were 32 years (range 23-44), and for infants was 11 weeks (range 2-28 weeks). A total of 69% of women had a normal BMI (18.5-24.9kg/m2) before maternity, after maternity mean BMI was 24 (60%). Exclusive breastfeeding by 3-month-old infants was reported by 80%, and by 6-months-old infants was reported by 26%. Mean duration of exclusive breastfeeding was 11.12 weeks. The majority of participants were born in Norway (65%). In total, 79% women reported use of any kind of dietary supplements habitually, while habitual intake of iodine-containing supplements was reported by 29%, but only 18% reported taking it the last 24-hour. Most participants had delivered their first baby (61%).

Table 8. Sociodemographic characteristics of study population, n=175

Characteristic	*Mean* ± *SD*
Age of mother, years	31.8 ± 4.2
Age of infant, weeks	11.4 ± 6.6
BMI[a] before maternity, kg/m²	23.6 ± 4.6
BMI now, kg/m²	24.6 ± 4.7
	n (%)
Lactation	
Exclusive breastfeeding	140 (80.0)
Partial breastfeeding	35 (20.0)
Origin	
Born in Norway	113 (64.6)
Born outside Norway	62 (35.4)
Marital status	
Cohabiting	83 (47.4)
Married	84 (48.0)
Single	8 (4.6)
Education	
< 12 years	11 (6.3)
12 years' secondary school	21 (12.0)
1 - 4 years high school/university	53 (30.3)
≥ 4 years high school/university	90 (51.4)
Smoking habits	
No	167 (95.4)
smoking now	4 (2.3)
using dry snuff	4 (2.3)
Thyroid disease	
No	164 (93.7)
Yes	11 (6.3)
Iodine supplement use habitually	
No	124 (70.9)
Yes	51 (29.1)
Iodine supplement use last 24hours	
No	144 (82.3)
Yes	31 (17.7)

a BMI = body mass index

5.2 Breast milk iodine concentration (BMIC)

The median (P25, P75) BMIC among lactating women was 68 µg/L (45, 98µg/L) (Table 9 and Figure 2). BMIC was divided in three groups: low (<100µg/L), optimal (100-199µg/L) and high (200µg and above).

Table 9. Distribution of breast milk iodine concentration (n=175)

Measurement	*N (%)*	*Median*	*Min*	*Max*	*P25[a]*	*P75[b]*
BMIC (µg/L)[c]	175 (100)	68	16	600	45	98
Low[d] BMIC	133 (76.0)	55	16	99	42	72
Optimal[d] BMIC	31 (17.7)	140	100	190	120	140
High[d] BMIC	11 (6.3)	260	200	600	210	290

a P25 = 25th percentile
b P75 = 75th percentile
c BMIC=Breast Milk Iodine Concentration
d Low=<100µg/L; Optimal=100-199µg/L; High=200µg/L and over

Totally, 76% women had BMIC lower than 100µg/L, 18% had BMIC between 100 and 199µg/L, and 6% had over 200µg/L, respectively. One woman had an extremely high level of BMIC (600µg/L). Interestingly, this participant reported a relatively high intake of iodine from supplements.

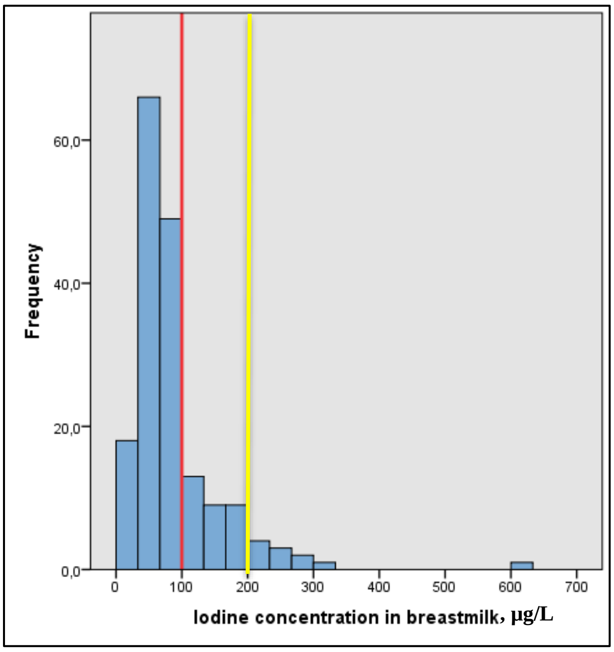

Figure 2. Frequency distribution of breast milk iodine concentration (µg/L) among lactating women (n=175). Red line shows that majority of women had BMIC less than the suggested cut-off level for adequacy of 100 µg/L. Range between red and gold line shows an optimal BMIC level

5.2.1 Breast milk iodine by infant age

BMIC decreased with increasing age of the baby, with ranging median of 70 µg/L at 0-10 weeks until 47.5 µg/L at 20-28 weeks ($p<0.034$).

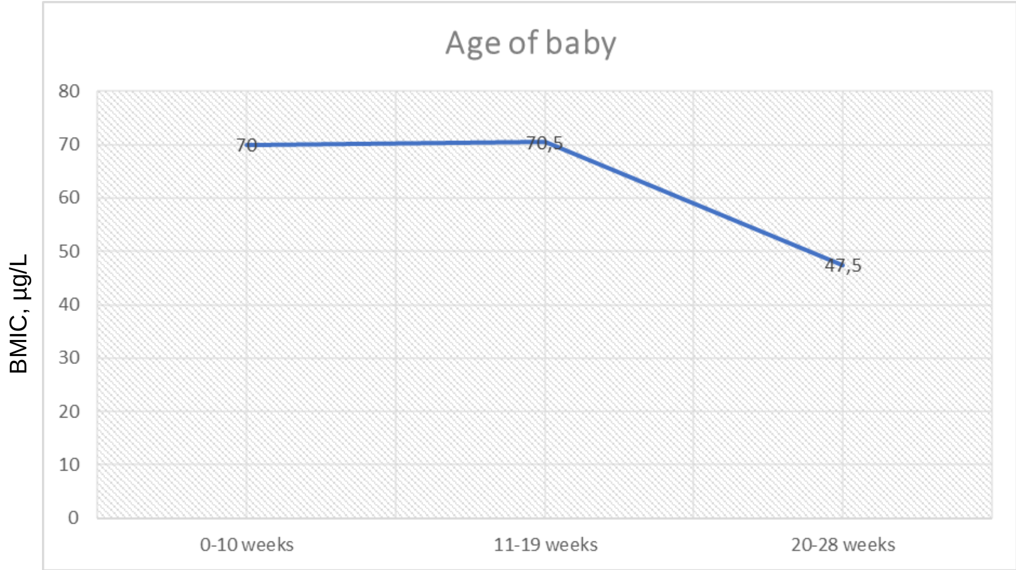

Figure 3. BMIC by infant age, the line diagram represents median BMIC to child's age in weeks.

5.3 Iodine intake from food and iodine-containing supplements: habitual and 24-hour iodine intake.

The median (P25, P75) habitual iodine intake from food in lactating women was 106µg/day (79, 138) (Table 10). When including iodine-containing supplement to iodine intake from food (total iodine intake), the median (P25, P75) total iodine intake increased to 135µg/day (94, 212). In relation to iodine intake from food and total iodine intake, i.e. from food and supplement, last 24-hour, the median (P25, P75) was 121µg/day (82, 162) and 134µg/day (95, 222), respectively.

Iodine intake from food only was significantly lower and iodine from supplement significantly higher for habitual than for 24-hour iodine intake (both $p < 0.05$), while there was no difference in the total iodine intake estimated for habitual and 24-hour iodine intake ($p= 0.39$). The correlation between habitual and 24-hour iodine intake from food was r_s=0.34, for iodine from supplements r_s =0.78, and for total iodine (food and supplement) r_s =0.55 (all p<0.001). One woman had an excessive habitual iodine intake from food and total iodine intake, i.e. 677µg/day and 877µg/day, respectively. Furthermore, iodine intake estimated from UIC and the median was 102µg/day.

Table 10. Calculated iodine intake from food (including food sources), from iodine-containing supplement, total iodine intake (food and supplement) by habitual and 24-hour iodine intake, and estimated iodine intake (n=175).

	Median	*P25*[a]	*P75*[b]	*Mean ± SD*
Habitual iodine intake				
Iodine from food only, µg/day	106	79	138	116 ± 65
- from milk/dairy	42	23	61	49 ± 41
- from fish/fish dishes	15	10	46	31 ± 35
- from eggs and all other food	34	34	41	37 ± 8.0
Iodine from supplements	0	0	86	42 ± 71
Total iodine intake[c], µg/day	135	94	212	158 ± 97
24-hour iodine intake				
Iodine from food only, µg/day	121	82	162	130 ± 64
- from milk/dairy	66	26	108	71 ± 53
- from fish/fish dishes	0	0	6.0	12 ± 29
- from eggs and all other food	45	30	50	47 ± 20
Iodine from supplements	0	0	0	31 ± 68
Total iodine intake, µg/day	134	95	222	160 ± 92
Iodine intake estimated from UIC[d], µg/day	102	58	156	129 ± 117

[a] P25 = 25th percentile
[b] P75 = 75th percentile
[c] Calculated iodine intake from food and supplements
[d] UIC (µg/L) x 0.0235 x weight (kg) = estimated daily iodine intake

5.3.1 Comparison of habitual and 24-hour iodine intake with Nordic and WHO recommendations and with Estimated Average Requirement

According to Nordic Nutrition Recommendations (NNR), lactating women should consume 200µg iodine daily, while the WHO recommendation is 250µg iodine per day. According to IOM, EAR is 209 µg/day. The proportion of lactating mothers categorised by these cut-off values resulted in comparable distribution for habitual and 24-hour iodine intake (Figure 4). Nearly all (94%) of the lactating women had habitual iodine intakes below the NNR recommendation, and 74% had total habitual iodine intakes (food and supplement) below the NNR recommendation. An even higher proportion did not reach the WHO recommendation, and only 17% achieved a total habitual iodine intake of 250µg/day. When comparing habitual total iodine intake with EAR, 75% had intakes below EAR (209 µg/day).

When looking at 24-hour iodine intake, 85% did not reach the recommended intake of iodine from food alone, while the percentage decreased to 70% when iodine from supplements was included (total 24-hour iodine intake). Adequate iodine intake from food and total 24-hour iodine intake was reached by 10% and 11%, respectively, according to NNR. The WHO recommendation was reached by 19% of women looking at total 24-hour iodine intake. When comparing total 24-hour iodine intake with EAR, 73% had intakes below EAR.

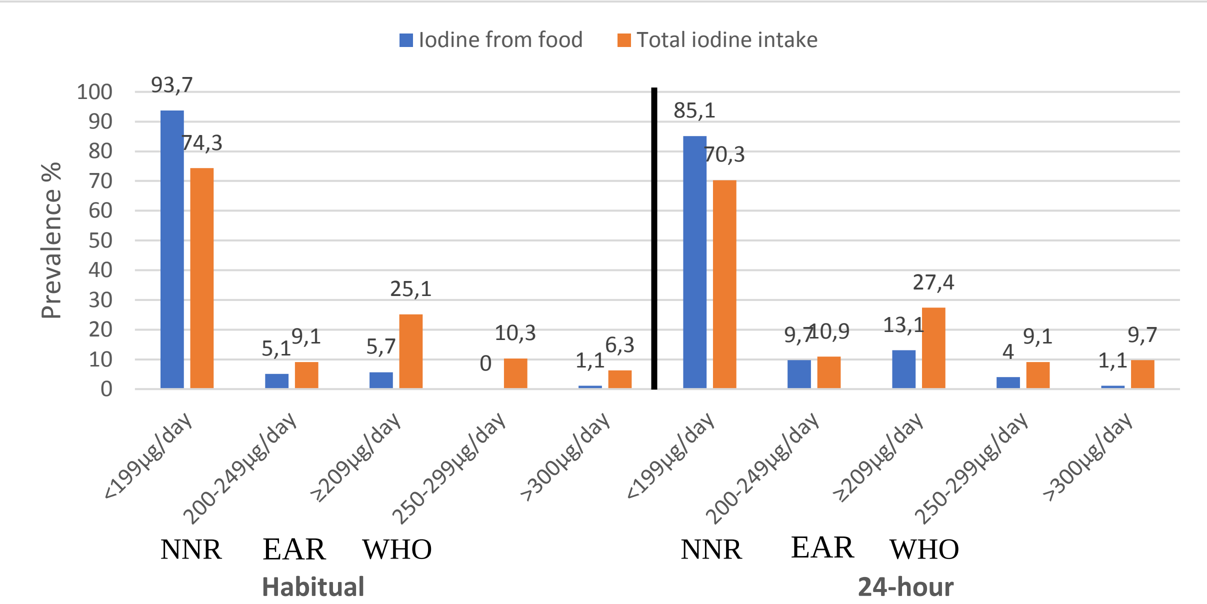

Figure 4. Iodine intake from food and total iodine intake (food and supplements) by two time frames: habitual and 24-hour. Comparison by Nordic Nutrition Recommendations (NNR), Estimated Average Requirement by IOM (EAR), and by WHO recommendations for lactating women (n=175)

5.3.2 Dietary sources of iodine

Iodine from milk and yoghurt was the largest contributor to total iodine intake. This was evident for habitual iodine intake as well as for iodine intake estimated for the last 24-hour, and contributed 42% and 55% of habitual and 24-hour iodine intake from food, respectively. The contribution from milk and dairy was lower and the contribution from fish was higher according to habitual intake than 24-hour intake. For mothers who took iodine-containing supplement, the contribution from supplement was substantial, comprising 26% and 19% to habitual and 24-hour iodine intake, respectively. Fish consumption was lower than milk consumption, and was contributed 26% for habitual iodine intake from food and 9% for 24-hour iodine intake from food. Other food groups contributed 32% and 36% to habitual and 24-hour iodine intake from food (Figure 5).

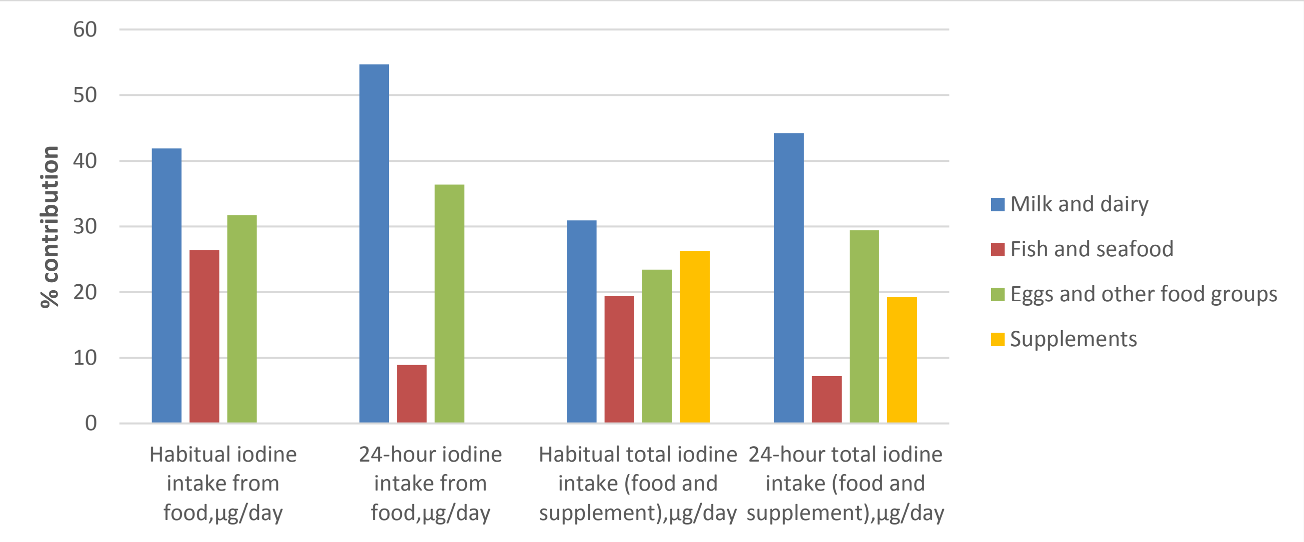

Figure 5. Percentage contribution to iodine intake from food and total iodine intake (food and supplement) estimated habitual and 24-hour iodine intakes

Figure 6 illustrating more detailed contribution (%) to habitual iodine intake from different food groups.

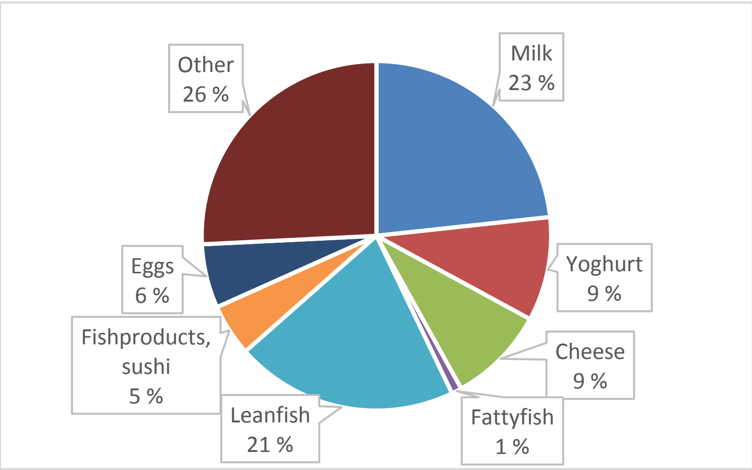

Figure 6. The contribution (%) to iodine intake from different food groups, total overview. For product group 'Other' it is 30µg iodine per day from non-iodine sources

5.4 Urinary iodine concentration (UIC)

The median (P25, P75) UIC of lactating women (n=175) was 64 µg/L (39-95µg/L) (Table 11). The distribution of UIC is shown in Figure 7. A total of 81% women had UIC <100 µg/L, considered as insufficient iodine intake according to the WHO cut-off value. In all, 19% had UIC over 100µg/L, of which three women had more than 400 µg/L

Table 11. Urinary iodine concentration in the lactating women (n=175)

Measurement	*Mean ± SD*	*Median (min,max)*	*P25*[a]	*P75*[b]
Iodine concentration (µg/L)[c]	81.17 ± 75,8	64 (3, 520)	39	95

a P25 = 25th percentile
b P75 = 75th percentile
c One spot urine

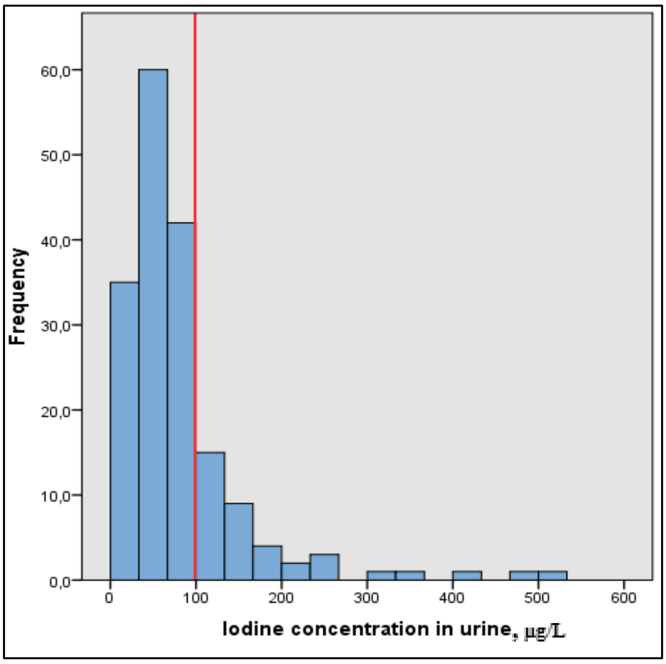

Figure 7. Frequency distribution of maternal spot UIC (n=175). Red line shows WHO cut-off level (<100µg/L)

We found a positive correlation between UIC (µg/L) and BMIC (µg/L). That is, as the UIC increased, the BMIC increased as well. The spearman's rho was 0.27 (p<0.001), indicating a moderate correlation. The diagonal line shows where the perfect correlation between variables should be, i.e. correlation of 1.0 (Figure 8)

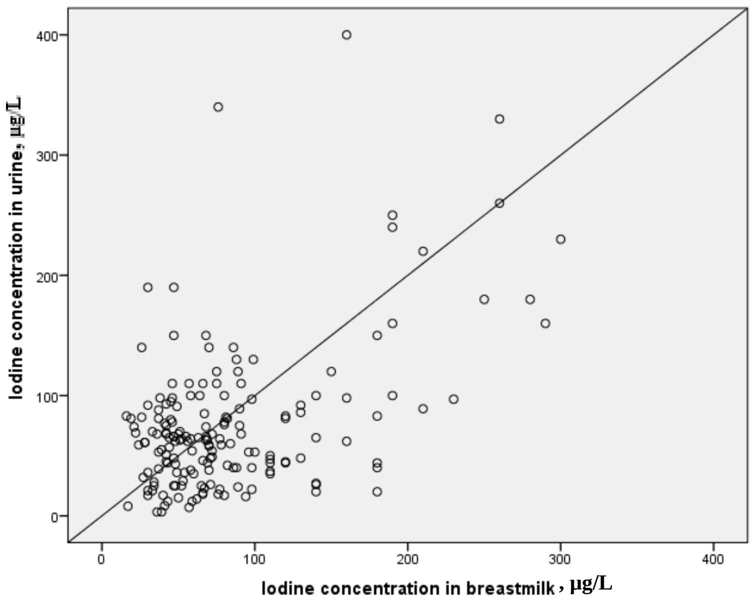

Figure 8. Scatter plot showing the relationship between UIC and BMIC

Contrary to what was found for BMIC, where iodine supplement use reported both as habitual and 24-hour use was significantly higher, UIC was only significantly higher in participants who reported use of iodine containing supplements during the last 24-hour (p<0.001).

5.5 Iodine supplement use by BMIC and UIC

Altogether 29% (n=51) lactating women took iodine-containing supplements habitually and 18% (n=31) took iodine-containing supplement the last 24-hour. The most commonly reported supplements were different types of multivitamins as 'Lifeline care', 'Nycoplus' and 'Vitaminerals'. The iodine amount in one daily dose is between 50µg and 200µg (range 45µg-225µg). Lactating women consuming iodine-containing supplements habitually had a significantly higher (p<0.001) BMIC (99µg/L) than non-iodine supplement users (60µg/L), however UIC was not significantly different between those two groups. Furthermore, there was significantly higher BMIC (140µg/L) and UIC (92µg/L) among women who took iodine-containing supplement in the last 24-hour than in those who did not take an iodine-containing supplement, BMIC 61µg/L and UIC 62µg/L, respectively ($p<0.001$) (Figure 9 and 10).

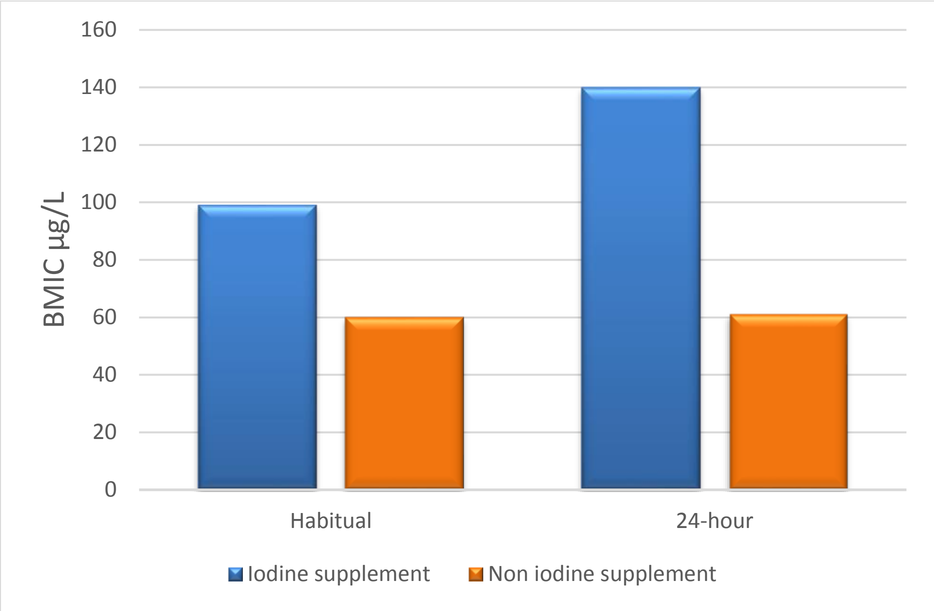

Figure 9. Comparison of median BMIC in two groups: those who use and not use iodine-containing supplements habitually and those who took iodine-containing supplement last 24-hour

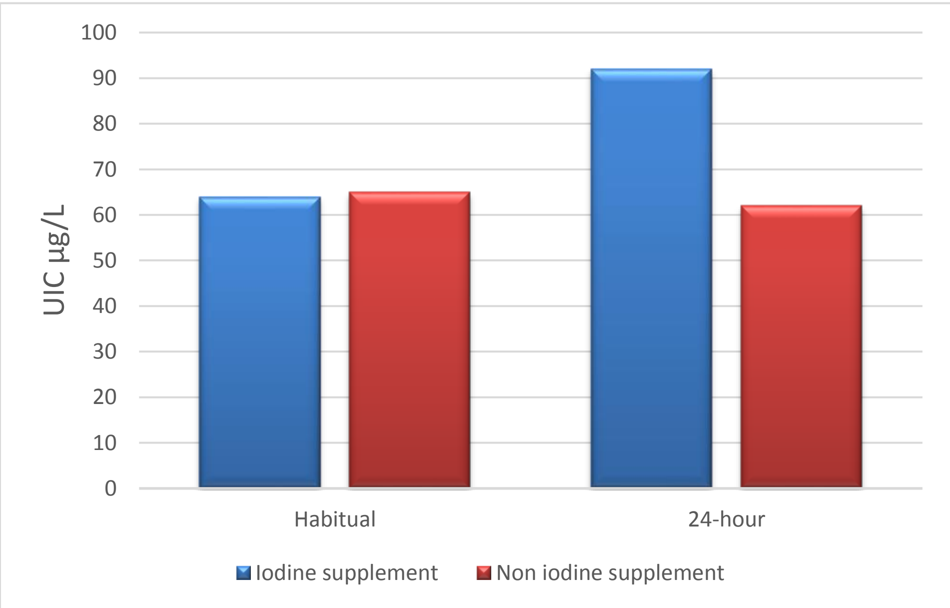

Figure 10. Comparison of median UIC in two groups: those who use and not use iodine-containing supplements habitually and those who took iodine-containing supplement last 24-hour.

5.6 Differences in breast milk iodine concentration by maternal characteristics and urinary iodine concentration

We examined the potential differences in BMIC by maternal characteristics. There was a weak increase in BMIC with increasing maternal age, BMI and partial breastfeeding, but these associations were not significant. Other background variables like country of birth, marital status, education level, smoking and thyroid disorders was not associated with BMIC. However, as reported above, women who used iodine-containing supplements had higher BMIC than non-users, 99µg/L and 60µg/L, respectively (p<0.001). Regarding UIC, women who had low UIC (<100µg/L) had also lower BMIC (<100µg/L) (Table 12).

Table 12. BMIC by the maternal characteristics with significant differences, and by UIC.

Characteristic	*n (%)*	*BMIC µg/L* *Median (P25, P75)*[b]	*P-value*[a]	*BMIC<100 µg/L* *N (%)*
Iodine supplement use habitually				
No	124 (70.9)	60 (42, 84)	<0.001	107 (86.3)
Yes	51 (29.1)	99 (56, 180)		17 (13.7)
Iodine supplement use last 24-hours				
No	144 (82.3)	61 (42, 84)	<0.001	124 (86.1)
Yes	31 (17.7)	140 (90, 190)		20 (13.9)
Urinary iodine concentration, µg/L				
<100 µg/L	142 (81.1)	63 (42, 89)	<0.001	115 (81)
≥100 µg/L	33 (18.9)	91 (69, 205)		18 (55)

[a] *P*-value by Mann-Whitney U-test; [b] p25 = 25th percentile, p75 = 75th percentile

5.7 Correlation between BMIC and UIC with habitual and 24-hour iodine intake

Correlation between BMIC and UIC are presented above in Figure 8. The Spearman's correlation shows the relationship between BMIC and habitual total iodine intake (r_s=0.38, p<0.001), and 24-hour total iodine intake (food and supplements) (r_s=0.37, p<0.001). For UIC, a significant correlation was seen for 24-hour total iodine intake (r_s=0.25, p<0.001) (Figure 11 a, b, c), while no correlation was found for UIC and habitual total iodine intake.

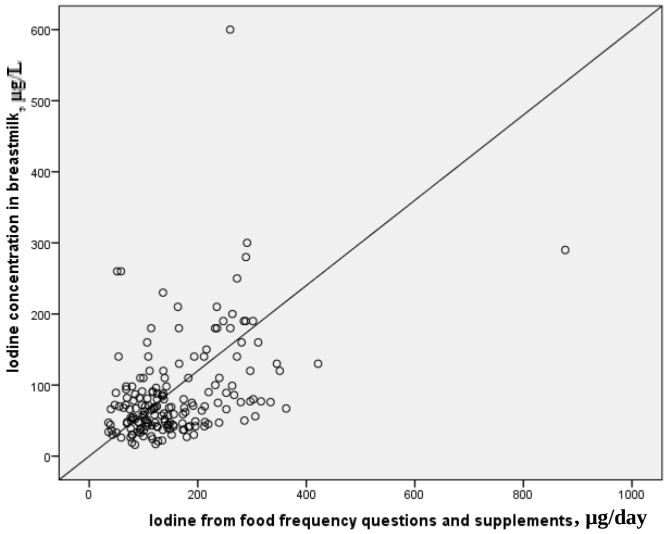

Figure 11a

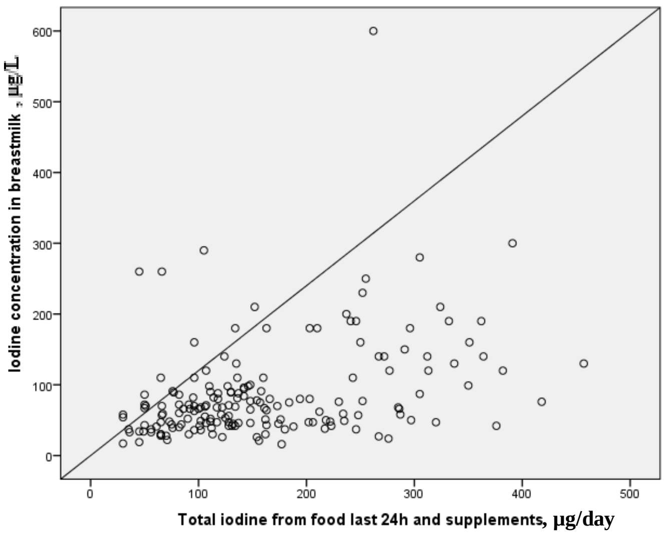

Figure 11b

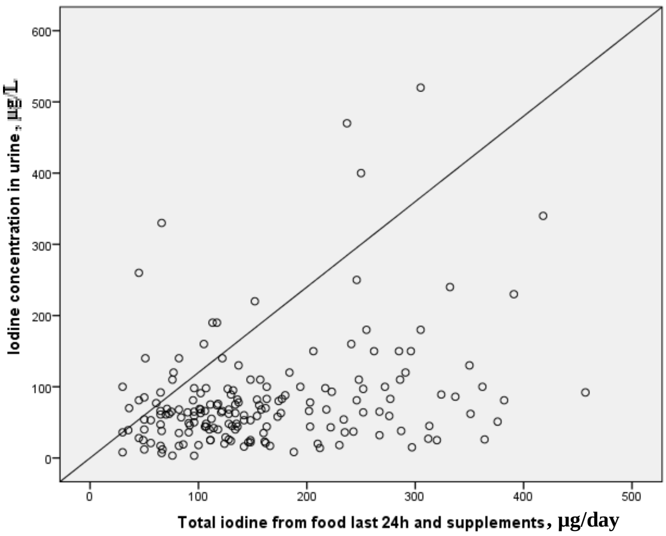

Figure 11c. Scatter plots illustrating the relationship between BMIC and habitual iodine intake (11a), between BMIC and 24-hour total iodine intake (11b), and between UIC and 24-hour total iodine intake (11c).

5.8 Predictors for BMIC

In multiple linear regression models (Table 13), the infant's age, iodine-containing supplement use last 24-hour, smoking status and UIC predicted BMIC, explaining 33% of the variance in BMIC.

Table 13. Predictors of BMIC in lactating mothers from Norway (n=175)

Dependent variables	Predictor variables	Unadjusted coefficient (95% CI)	*p*	Adjusted coefficient (95% CI)	*p*	Stand Beta
BMIC[a], µg/L	Constant			3.3 (2.8, 3.7)	*<0.001*	
	Infant age[b]	-0.02 (-0.03, -0.003)	*0.02*	-0.02 (-0.03, -0.004)	*0.03*	-0.17
	Iodine suppl[c]	0.003 (0.002, 0.004)	*<0.001*	0.002 (0.001, 0.002)	*<0.001*	0.31
	UIC, µg/L	0.003 (0.002, 0.004)	*<0.001*	0.002 (0.001, 0.004)	*<0.001*	0.29
	Smoking[d]	-0.18 (-0.35, -0.01)	*0.042*	-0.18 (-0.32, -0.03)	*0.016*	-0.16
	R^2				**0.33**	

[a] BMIC log transformed
[b] Continues variable of infants in weeks
[c] Iodine intake from supplements calculated from 24-hour iodine intake, continues variable
[d] Number of cigarettes, continues variable

6. Discussion

According to my knowledge, this is one of the first studies in Norway on BMIC. We found that 3/4 lactating women had insufficient BMIC (<100µg/L), which indicates that mild-to moderate iodine deficiency exists among Norwegian lactating women. This was supported by a large proportion of participants having low UIC (81% <100µg/L) and low iodine intake from food and supplements (75% below EAR). Food sources alone did not provide the recommended amount of iodine required during breastfeeding to meet maternal and infant needs.

6.1 Findings

6.1.1 Breast milk iodine concentration

Breast milk is the optimal food exclusively breastfed infants get during the first months of life. Due to high breastfeeding rates among Norwegian women (about 80% women at 6 months, 46% at 12 months), both mothers and children are vulnerable to inadequate iodine intake (Directorate of Health, 2014; Zimmermann, 2009). WHO has proposed a BMIC cut-off of at 100µg/L as indicative of sufficient iodine intake (WHO, 2007). In our study, the median BMIC was 68µg/L, which is below WHO cut-off value (WHO, 2007). Thus, exclusively breastfed infants would get around 53µg iodine per day (68µg/BMIC x 0,78L/breast milk/day) (WHO, 2002), instead of 90µg/day as recommended. Thus, the infants in our study are at risk of insufficient iodine intake (Azizi & Smyth, 2009; Andersson et al, 2007; Delange, 2004). Data regarding BMIC levels in lactating women in Norway are limited to just one master thesis presenting BMIC in Norway (median 59 µg/l), and our finding (median of 68 µg/L) is in accordance with the results (Vollset, 2015). According to existing literature, the lactating women in our study are mild-to moderate iodine deficient, based on median BMIC (Azizi & Smyth, 2009; National Nutrition Council, 2016). Low BMIC in lactating women have been found in other Nordic countries, Denmark (83µg/L) (Andersen, 2015), Sweden (92µg/L) (Azizi & Smyth, 2009) and Finland (53µg/L) (Pirkko & Panu, 1960). In relation to available data from the rest of the world, low BMIC (<100µg/L) was found in France, Germany, Belgium, Spain, Italy, while studies from USA, Australia, Iran, China, Thailand, Nepal and South Africa reported BMIC >100µg/L (Azizzi & Smyth, 2009; Heynh et al., 2016; Osei et al., 2016; Mekrungcharas & Kasemsup, 2014; Henjum, 2016). Mild-to moderate iodine deficiency in prevalent in Europe and in some other countries (WHO, 2007; WHO, 2004). The consequences of insufficient iodine intake during pregnancy and early infancy may be minor brain damage and impaired neurodevelopment of infants (Delange, 2002; Bath et al., 2013). Using data from a prospective cohort in the UK, Bath et al. measured iodine status in pregnant women and found mild-to moderate iodine deficiency in pregnant mothers resulted in lower intelligence quotient (IQ) and reading ability in children at age 8 years. They concluded that even in a country with only mild iodine deficiency during pregnancy and lactating, lower intelligence, reading accuracy and reading comprehension appeared (Bath et al., 2013).

6.1.2 Iodine intake from food and supplements

Dietary iodine requirements are increased during lactation to ensure an adequate supply of iodine to the infant (Nordic Council of Ministers, 2014; WHO, 2007; Institute of Medicine, 2001). In our study iodine intake was calculated by two approaches, one providing habitual iodine intake and another 24-hour iodine intake. The habitual iodine intake, i.e. average intake over a defined time window, provides information on long-term iodine intake, while 24-hour intake reflect the recent (short-time) iodine intake (Ortiz et al., 2009). The median total habitual and 24-hour iodine intakes were almost identical (135µg/day and 134µg/day, respectively). A very low proportion of participants in our study had iodine intake in accordance with NNR and WHO recommendations. This does not necessarily mean that they will be iodine deficient, but the high prevalence of women with intakes lower than EAR (75%) strongly suggest that the probability of adequacy for iodine is low. These results therefore suggest insufficient maternal intakes, and consequently insufficient iodine intake in the exclusively breastfed infants (WHO, 2007; Nordic Council of Ministers, 2014). Iodine-containing supplement users were more likely to reach the NNR recommendation. There is no comparable data on total iodine intake in lactating women in Norway. The 'Fjell studien' which included pregnant and lactating women evaluated seafood and milk consumption, and concluded that iodine intakes from these foods were too low to contribute to the recommended intake of iodine (Seldal, 2012). Milk and dairy products were consumed more regularly (e.g. 73% daily) than seafood (e.g. 20% weekly) (Seldal, 2012). Most studies on iodine status in Norway reported iodine intake or status in pregnant women. Moreover, iodine intake in lactating women in our study were lower than in pregnant women in MoBa, where the habitual median iodine intake was 141 µg/day from food and 166 µg/day from food and supplements (Bransæter et al., 2013). Our findings suggest that for lactating women, food sources alone do not provide the required amounts of iodine during breastfeeding to meet maternal and infant needs.

Dietary sources of iodine

Milk and dairy products were the main contributor of both habitual and 24-hour iodine intake from food, contributed 42% and 55%, respectively. Recent analytical results have shown that iodine concentrations were lower in milk and egg than expected and lower values than those in the Norwegian Food Composition Table. Lower than expected iodine concentration in these food items, and particularly in milk is most probably explained by the presence of goitrogenic substances in cow's fodder (Trøan et al., 2015). Seasonal differences in iodine levels between summer and winter milk has been documented (Dahl et al., 2003), but this is not a likely explanation why the average iodine content in milk has been lower than expected for a prolonged period of time. In addition to reduced iodine concentration in milk, consumption of milk is declining among women, in 2010, 23% reported regularly or occasionally avoidance of milk (Bugge, 2012). Fish contributed with 26% of habitual iodine intake and 9% of 24-hour iodine intake. It is not surprising that habitual fish intake was higher than just one-day fish intake. In comparison, results from MoBa study showed that milk contributed 64% and seafood contributed 15% of habitual iodine intake in pregnant women (Bransæter et al., 2013). Milk/dairy products and lean fish are the major determinants of iodine intake in the Norwegian diet (Dahl et al., 2004), and low consumption of those sources has been shown to be a risk factor for inadequate iodine intake (Bransæter et al., 2013). Our findings that 75% of the lactating women had a total iodine intake lower than EAR is therefore of specially concern. The low intake of milk is in accordance with the latest report from National Nutrition Council (2016) with data on a significant decline in milk consumption last 30 years. Based on results from our study and data from MoBa and the 'Fjell studien' pregnant and lactating women should be encouraged to increase their intake of milk and lean fish.

Supplementation during lactation

In the multiple regression analysis of predictors for BMIC, iodine supplements, but not iodine intake from food was significantly associated with BMIC. Habitual iodine-containing supplement use was reported by 29% women, of which only 18% took this supplement in the last 24-hour. There was a significant difference ($p<0.001$) in BMIC between iodine-supplement users and non-iodine supplement users for both habitual and 24-hour iodine intake. We also observed that BMIC was influenced by time of most recent iodine supplement intake (last 24-hour) with the highest median value when iodine supplement intake was the same day prior to sampling, then in habitual iodine intake time frame. This is in accordance with existing literature that 24-hour approach reflects the recent iodine status (Ortiz et al., 2009). Comparable results were found in Denmark, iodine -containing supplement users had higher median BMIC (112 µg/L) than non-users (72 µg/L) (Andersen et al., 2014). Placebo-controlled trials from New Zealand reported increased BMIC by 31% in women (until 24 week postpartum) who consumed 75 µg I/d and by 69% in women who consumed 150 µg I/d compared with placebo (Mulrine et al., 2010). Dold et al. also reported significant higher BMIC in iodine supplement users than non-supplement users (Dold et al., 2017).

In areas where population are at risk of iodine deficiency, supplemental iodine is recommended by the WHO for all women of childbearing age (WHO, 2007a). However, there is insufficient evidence to support recommending supplemental iodine in areas with mild- to moderate iodine deficiency (Rebagliato et al., 2013; Gunnarsdottir & Dahl, 2012). There are no official recommendations on iodine supplementation in Norway. On the contrary, USA, Australia and New Zealand recommend that all women who are pregnant, breastfeeding or considering pregnancy take an iodine supplement of 150 µg every day (The American Thyroid Association, 2006; NHMRC, 2010). The use of iodine-containing supplements has shown to have a positive effect on median BMIC values, suggesting that supplements as an effective way to increase the iodine content in breast milk, but there is no clear effect on maternal or newborn thyroid hormone levels (Kung, 2007; Zimmermann, 2007). Because the breast milk samples in our study were collected mostly in the early post-partum period and

BMIC of lactating women has been shown to decrease after 20-week postpartum, the use of iodine supplement during lactation is important.

There was a limitation to the interpretation of our study findings, as the impact of time of supplement intake was not examined. Leung et al. reported a rise in BMIC following acute oral ingestion of 600 µg potassium iodide, with peak levels at 6 h post-ingestion, and concluded that recent maternal iodine intake would influence the interpretation of BMIC values (Leung et al., 2012). However, all women were informed to collect both one breast milk sample and the urine sample after breakfast, which would ensure that timing would be consistent within participants given that all take a supplement in the morning.

Iodized salt

According to WHO, the best strategy for preventing iodine deficiency is the iodination of salt, both household salt and salt used in the food industry (WHO, 2014). Iodized salt in Norway contributes negligible to iodine intake (low iodine amount, 5mg/kg salt) (National Nutrition Council, 2016). Consequently, we did not include iodized salt in our FFQ. Contrary, in countries with successful sustained iodized salt programs, pregnant and lactating women and their infants have better iodine status (Zimmerman, 2007). In order for iodized salt to be an effective strategy to increase iodine status in a population, the amount of iodine should be 15 ppm or higher and iodine should be added in industrialized salt (WHO, 2014). Denmark has successfully implemented this strategy by using iodized salt in commercial bread (13mg/kg salt), which resulted in a significantly increase in urine iodine excretion in the population (Rasmussen et al., 2008).

6.1.3 Urinary iodine concentration

The median UIC in lactating women in our study was 64µg/L, which is below the WHO cut-off value (100 ug/L) for adequate iodine status in lactating women. Further, UIC was not significantly higher in iodine-containing supplement users than non-users for habitual iodine intake, while for 24-hour iodine intake, UIC was significantly higher in iodine-containing supplement users than in non-users, 92µg/L versus 62µg/L. This finding differed from what was found for BMIC, where iodine-containing supplement intake reported both as habitual and 24-hour intake was significantly higher. This finding indicate that supplements not used on a daily basis is reflected only in BMIC, not in UIC. Low UIC was associated with low BMIC in our study. We found a positive correlation between UIC and BMIC of 0.27, There are no other data on correlation between UIC and BMIC in Norway. Comparable results were found among Danish lactating women, the correlation was 0.28 (Andersen, 2015); and in the latest study by Dold et al. the correlation between BMIC and UIC was 0.11. There is only one study on urinary iodine assessment in lactating women in Norway, the 'Fjell studien', where low UIC was found as well, with median UIC of 60µg/L (Seldal, 2012). A study from Denmark reported the median UIC of 72µg/L, as well as higher UIC in iodine-supplemented mothers, 83µg/L versus 65µg/L (Andersen, 2015). Study from New Zealand showed that daily supplementation of iodine deficient lactating women increased iodine level in mothers and infants, but the daily consumption of either a 75-µg or 150-µg iodine supplement for 6 month was unable to increase UIC in both groups to 100 µg/L. These findings presumed that the extra iodine consumed by supplemented women was being preferentially taken up by the mammary gland and not excreted in the urine (Mulrine et al., 2010). A systematic review by Nazeri et al. was observed a median or mean UIC <100 µg/L in nearly all lactating mothers residing in countries where implementation of universal salt iodization program was voluntary (Nazeri et al., 2015). Results from above mentioned studies suggest low dietary intake of iodine in lactating women.

6.1.4 Predictors

We investigated predictors for BMIC in multiple regression analyses and found that the infant's age, iodine-containing supplements use last 24-hour, smoking status and UIC predicted BMIC, explaining 33% of the variance in BMIC. Iodine-containing supplements use the last 24-hour has been thoroughly discussed above. In regard to infants age, BMIC decreased with increasing age of the infants with a median of 70 µg/L at 0-10 weeks and 48 µg/L at 20-28 weeks ($p<0.034$), thus BMIC decreased by 32%. The same was found by Mulrine et al., a decrease in BMIC by 40% over 24 weeks (Mulrine et al.,2010).

Four participants in our study reported that they were smoker. In the multiple regression analysis, there was a significant negative impact of smoking on BMIC. This is in accordance with the current knowledge that thiocyanate impairs iodine transport into breast milk, thereby reducing BMIC (Laurberg et al, 2004). A Danish study from 2004, also showed that the level of BMIC among smokers was lower than in non-smokers (Andersen, 2015). The number of smokers was low in our study (2.3%), which is lower than the proportion of self-reported smokers in MoBa, which was 9.3% (Moylan et al., 2015). The low prevalence of smoking in our study could be that these study population had a high proportion of highly educated women and a high proportion of women with another ethnical origin than Norwegian. Infants of smoking mothers are extra prone to insufficient iodine intake (National Nutrition Council, 2016).

6.2 Methodological considerations

6.2.1 Recruitment of study participants

Participants were recruited from five of 18 randomly selected Mother and Child Health Centres in Oslo between October and December 2016, to represent all different parts of Oslo. In each Mother and Child Health Centre, all the lactating women were invited to participate in the iodine study. Exclusion criteria were if a woman did not speak Norwegian and if they did not breastfeed their infant. Original language for questionnaire and the consent form was Norwegian, therefore it was important that all participants could understand and write Norwegian. The recruitment method was convenience sampling, the participants were not randomly selected, and therefore the findings from our study cannot be generalized to whole breastfeeding population in Norway. This is partly due to the risk of sampling bias when using convenience sampling. Sampling bias means that the recruited population sample is selected incorrectly and do not represent the true distribution because of non-random selection, which can reduce the accuracy of a measurement (e.g. mean and median value) (Gibson, 2005). Sampling bias often arises because certain values of the variable are systematically under-represented or over-represented in relation to the true distribution of the variable, as in our study, most participants were high educated, with full time job, married/cohabiting. According to scientific literature, people who voluntarily take part in a study are more likely to differ from the general population by being more health conscious and/or highly educated (Thomson & Subar, 2013). However, our findings in regression analyses showed no maternal characteristics impact on BMIC level. In our study, 30% of the women had 1-4-year higher education, and 51% were highly educated (≥4 year of University). In comparison, in the Norwegian female population, approximately 8 % are highly educated (4 years of University/College), and 27 % have a University/College education (1-4 years) (Statistics Norway, 2015). The number of participants who were born outside of Norway in our study was 35%, and according to Statistics Norway, immigrants account for 14% of the population in Oslo (Statistics Norway, 2017). Thus, we have a sample with relatively highly educated women and a high proportion of women with another ethnical origin than Norwegian. We found no differences in BMIC, UIC, iodine intake related to country of origin. Contrary results were found by Jorgensen et al. that median BMIC was lower for Caucasian than for non-Caucasian population (Jorgensen et al., 2016).

Strengths of our study is a relative large sample size compared to other studies. In addition, the response rate was high (69%). In comparison, participation rate in MoBa study was 39%. Furthermore, the close personal follow up of all participants by a project worker is an important strength, which ensured that there were no missing data in the questionnaire. Missing data is often a problem in surveys relying on self-reported information.

6.2.2 Challenges in assessment of BMIC and UIC.

According to WHO, UIC is the recommended biomarker in evaluating the iodine status in a population, including lactating women (WHO, 2007). Spot urine sample is simple to obtain and was used in our study, expressed as the median (μg/L). However, some factors may challenge the interpretation of the results (Skeaff, 2012). UIC can vary from day-to-day in relation to an individual iodine intake, and spot UIC cannot be used to classify iodine status of individuals because it only reflects short-term iodine intake (Als et al., 2000). According to Ovesen, morning fasting urine samples are not representative of the average iodine intake in an individual or a population. Thus, in our study women were asked to take a spot urine after breakfast, considering that it could be more precise for iodine measurement (Ovesen & Boeing, 2002).

A major strength of our study is that iodine concentration was assessed both in breast milk and urine samples. Breast milk was collected four times per day, as two samples in the morning after breakfast (one before breastfeeding and one after breastfeeding), and two breast milk samples in the afternoon (also before and after breastfeeding). We had a relatively substantial number of breast milk samples (175) in comparison with a study from Denmark with 127 spot samples. Recent maternal iodine intake influence the interpretation of BMIC since BMIC values vary throughout the day, and single breast milk samples provide an imprecise measurement of daily iodine output or maternal iodine sufficiency. A recent study from Switzerland evaluated UIC and BMIC as biomarkers for iodine status in lactating women, and concluded that maternal UIC alone may not reflect iodine status. BMIC should also be measured to access iodine status in lactating women (Dold et al., 2017). Their findings suggest that in lactating women with adequate iodine level there is an increased iodine excretion into breast milk at lower daily iodine intakes, while iodine excretion in urine decreases, indicating primary excretion of iodine into breast milk at lower intakes (Dold et al., 2017). In contrast, lactating women with inadequate iodine intake protective mechanisms preserve a constant iodine supply to the infant even the amount is low. However, in relation to UIC, there is a constant relative iodine excretion in urine in the deficient mothers due to obligatory renal iodine losses, even at very low iodine intakes (Dold et al., 2017). Therefore, BMIC has been proposed as a more accurate biomarker of iodine nutrition in lactating women (Dold et al., 2017). In addition, insufficient iodine intake in our study indicated by BMIC and UIC was clearly supported by calculated iodine intake showing a high proportion (75%) of women having total iodine intake below EAR.

Further research could include investigation of the sampling time of breast milk whether there is significant difference between sampling from one versus both breasts and between sampling before versus after breastfeeding. Findings from such type Danish study showed no difference in BMIC, but individual comparison of BMIC in the subgroup of women who sampled breast milk both before and after breastfeeding suggested that BMIC was slightly higher in samples made before breastfeeding of the child (Andersen, 2015). More data are needed considering the method of breast milk sampling for determination of iodine content.

6.2.3 Iodine intake assessment

The most suitable method to determinate iodine status in Norway is to estimate iodine intake from food, due to few food sources of iodine (milk products and fish) (National Nutrition Council, 2016). However, estimation of iodine intake from the diet is not suitable method in countries where salt contributes significantly to iodine intake because it is difficult to estimate iodized salt intake (Rohner et al., 2014). Moreover, there is no method to accurately quantify dietary intake in free-living individual and all dietary assessment methods have errors that reduce the accuracy and precision of the data (Subar et al., 2015). The accuracy of dietary intake data is defined as the degree to which the estimated intake reflects the actual ("true") intake. Accuracy can be reduced by many factors, such as the ability to recall and report recent as well as average intake, inaccurate recall of amounts, and a desire to please an interviewer. It is known that food items perceived as unhealthy is underreported to a larger degree than food items perceived as healthy. It is also known that food items eaten regularly are easier to report correctly than rarely eaten foods (Shim et al., 2014). The precision of calculated nutrient intakes also relies on the accuracy of the nutrient content value in the Food Composition Table. In our study, lower iodine values than those given in the Norwegian Food Composition Table were used as recent analytical results had consistently lower mean concentrations than those in the Food Composition Table. If the food composition values had been applied, the calculated iodine intakes would have been higher.

FFQ is commonly used in nutritional epidemiology, as it presents considerable advantages in terms of practicality and economy, whereas multiple 24-hour recalls are the most used reference method (Serra-Majem et al., 2009). In our study, we used both methods (habitual iodine intake and 24-hour iodine intake) and this information made it possible to compare iodine intake between long term intake and intake from the same day samples were taken, and to evaluate iodine status not only by UIC and BMIC but also by evaluating iodine intake to recommended intake and EAR. Validation of the MoBa food frequency questionnaire showed that milk intake (and consequently iodine intake) was more accurate than intake of most other foods and nutrients evaluation of urinary iodine excretion as a biomarker for intake of milk and dairy products in pregnant women in MoBa (Brantsæter et al., 2008; Brantsæter et al., 2009). Despite the limitations and uncertainties in dietary assessment, self-report dietary intake data have been shown to be important and useful to inform dietary guidance and public health policy (Subar et al., 2015). Finally, this cross-sectional study included lactating women recruited through the public health care system, and our study provides valuable information about iodine status in lactating women in Norway and raise awareness of the need to secure sufficient iodine nutrition in the population.

7. Conclusion

The findings of the present study indicate mild-to-moderate iodine deficiency in the group of lactating women in Norway, shown through inadequate intake of iodine from food, low median breast milk and urine iodine concentrations. The study confirms previous findings of inadequate iodine intake in pregnant women in Norway. This is one of the first study reporting iodine concentration in breast milk, and is a valuable contribution to raise awareness of the need to secure sufficient iodine nutrition among breastfeeding women.

Regarding the specific objectives:

1. The result showed that 76% of the women had BMIC lower than 100µg/L, which is considered lower than optimal iodine concentration in breast milk. The results indicated lower BMIC with increasing age of the children.
2. The calculated iodine intake from food and supplements in lactating women showed that very few reached the NNR and WHO recommendation, and that 75% had intakes below EAR for lactating women. Milk and dairy products was the main source of iodine from food. Iodine-containing supplement use increased median breast milk concentration by 65% for habitual iodine intake and by 130% for 24-hour iodine intake.
3. The UIC in the lactating women was lower than the WHO cut-off value for adequate UIC in lactating women. The low median UIC further strengthens the findings of inadequate iodine status indicated by low BMIC and low iodine intake from food and supplements, and confirm mild-to-moderate iodine deficiency in the lactating women.
4. A significant correlation was found between BMIC and UIC, and participants with low BMIC had lower UIC. Significant associations with BMIC were found for both habitual and 24-hour total iodine intake, i.e. BMIC increased with increasing total habitual iodine intake. However, for UIC, a significant association was found only for 24-hour total iodine intake.
5. Predictors for BMIC were age of the infant, use of iodine-containing supplement the last 24-hours, smoking status and urinary iodine concentration.

7.1 Future work

The findings from the present study suggest that the Norwegian health authorities should pay more attention to secure iodine status in the lactating women and their infants. One of the suggested actions that could be implemented to increase iodine intake is that Norway follow the WHO guidelines for mandatory salt iodization. This would imply to increase the iodine content in iodized salt and consider use of iodized salt in industrial food products. The WHO recommendation regarding salt iodization is a strong and successful recommendation that have ensured satisfactory and safe iodine intake in populations worldwide. No official recommendation exists on use of iodine-containing dietary supplements in Norway. The recent report from the National Nutrition Council (2016) listed a number of suggestions for how the health authorities could secure sufficient iodine intake in the population. Recommendation of regular and specific amounts of milk and lean fish, and use of iodine-containing supplements are among the suggestions to ensure adequate intake of iodine. This is particularly relevant for lactating women due to the increased iodine requirement during lactation. The health authorities are planning to establish a recommended amount of milk as the current recommendation for a healthy diet only says to include low fat milk but with no specified amount. Lactating women with low intake of milk and lean fish should be recommended to use supplements with iodine. Not least, monitoring of implementation must be followed up by the health authorities, industry and health personnel to ensure successful implementation. Well-designed, randomized, clinical intervention trials are needed to assess the safety and effectiveness of implementation of iodine-containing supplements during lactation, and continuous monitoring of iodine status in the population is needed to avoid iodine deficiency or excess. Future consideration could be to assess infant’s UIC and TSH levels. To measure infant TSH require drawing blood and should only be implemented when strictly needed.

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Appendix 1. REK

REK
REGIONALE KOMITEER FOR MEDISINSK OG HELSEFAGLIG FORSKNINGSETIKK

Region:	Saksbehandler:	Telefon:	Vår dato:	Vår referanse:
REK sør-øst	Tor Even Svanes	22845521	04.07.2016	2015/1845/REK sør-øst C
			Deres dato:	**Deres referanse:**
			30.05.2016	

Vår referanse må oppgis ved alle henvendelser

Sigrun Henjum
HIOA
Postboks 4
0130 Oslo

2015/1845 Jodstatus blant gravide kvinner i Norge

Forskningsansvarlig: Høgskolen i Oslo og Akershus
Prosjektleder: Sigrun Henjum

Vi viser til søknad om prosjektendring datert 30.05.2016 for ovennevnte forskningsprosjekt. Søknaden er behandlet av leder for REK sør-øst C på fullmakt, med hjemmel i helseforskningsloven § 11.

Endringen består i at man også ønsker å undersøke jodstatus hos ammende kvinner i prosjektet. Som en del av utvidelsen vil morsmelk samles inn fra kvinner som fullammer.

Vedtak
Endringssøknaden godkjennes, jf. helseforskningslovens § 11.

Tillatelsen er gitt under forutsetning av at prosjektendringen gjennomføres slik det er beskrevet i prosjektendringsmeldingen og endringsprotokoll, og de bestemmelser som følger av helseforskningsloven med forskrifter.

Forskningsprosjektets data skal oppbevares forsvarlig, se personopplysningsforskriften kapittel 2, og Helsedirektoratets veileder for *Personvern og informasjonssikkerhet i forskningsprosjekter innenfor helseog omsorgssektoren.*

Komiteens vedtak kan påklages til Den nasjonale forskningsetiske komité for medisin og helsefag, jf. Forvaltningslovens § 28 flg. Eventuell klage sendes til REK Sør-Øst. Klagefristen er tre uker fra mottak av dette brevet.

Med vennlig hilsen

Britt-Ingjerd Nesheim
professor dr. med.
leder REK sør-øst C

Tor Even Svanes
seniorrådgiver

Appendix 2. Questionnaire used in the study

SPØRRESKJEMA TIL AMMENDE – JODSTATUS

ID-nummer i prosjektet ☐☐☐☐

Dagens dato: ☐☐ ☐☐ ☐☐☐☐

Postnummer: ☐☐☐☐

Bakgrunnsinformasjon

1. Din alder? ☐☐ år

2. Barnets alder uker? ☐☐ uker

3. Ammer du barnet nå?

☐ Ja helt ☐ Ja delvis ☐ Nei

4. Hvor mange barn har du fra før? ☐
Hvis du har barn fra før, når fødte du ditt forrige barn (dato)
dd mm åååå
☐☐ ☐☐ ☐☐☐☐

5. Høyde og vekt: Hvor mye veide du før svangerskap og hvor mye veier du nå?
Før svangerskapet ☐☐☐ kg

Vekt nå ☐☐☐ kg

Hvor høy er du? ☐☐☐ cm

6. Hva er din sivilstand
☐ Samboer
☐ Gift
☐ Enslig
☐ Annet, forklar ………………………………………

7. Hvilket land er du født i?
☐ Norge
☐ Annet ………………………………………..

8. Hvor mange år har du bodd i Norge?
☐☐ år

9. Hvilket språk snakker du mest hjemme?
☐ Norsk
☐ Annet språk, hvilket:…………………………..

10. Hva er din høyeste fullførte utdannelse:
☐ <12 år (ikke fullført videregående)
☐ 12 år videregående/fagbrev
☐ 1-4 års høgskole/universitet etter videregående
☐ Mer enn 4 år høgskole/universitet

11. Er du yrkesaktiv:
☐ Oppgi prosent stilling: ………………………..
☐ Hjemmeværende
☐ Arbeidsledig
☐ Student
☐ Annet, forklar …………………………………

12. Røykevaner: Røyker du nå?
☐ Nei
☐ Nei, men jeg røkte før
☐ Ja, av og til
☐ Ja, daglig

Hvor mye i gjennomsnitt røyker du per dag? Gi antall:
sigaretter ☐☐ stk

sigarer/cigarillos ☐☐ stk

pipe ☐☐ stk

Snuser du?
☐Nei ☐Ja,
☐Av og til ☐Ja, daglig, gi antall: ☐ stk

13. Har du hatt noen av følgende sykdommer knyttet til skjoldbruskkjertelen?
☐ For høyt stoffskifte
☐ For lavt stoffskifte
Har du hatt brukt medisiner for dette?
☐ Ja ☐Nei
Navn på medisiner:.…………………………………

Kunnskap om jod

1.Vet du hva jod er?
□ Ja
□ Nei
□ Har hørt om det, men husker ikke

2. Hva er de viktigste kilder til jod i kosten? (Du kan sette flere kryss).
□ Kjøtt
□ Melk- og meieriprodukter
□ Frukt og grønnsaker
□ Fisk og sjømat
□ Brød- og kornprodukter
□ Vegetabilske oljer
□ Salt tilsatt jod
□ Kosttilskudd
□ Annet:……………………………………
□ Vet ikke

3. Jod er viktig for? (Du kan sette flere kryss).
□ Normal vekst og utvikling hos barn
□ Forebygge blindhet
□ Normal fosterutvikling
□ Normal styrke i skjelett og tenner
□ Opprettholde normalt stoffskifte
□ Unngå ryggmargsbrokk
□ Vet ikke

4. Jeg tror jeg får nok jod gjennom kosten?
□ Enig □ Uenig □ Vet ikke

5. Jeg har fått informasjon om jod fra helsepersonell
□ Ja □ Nei □ Husker ikke

6. Hva vet du om lavt og høyt inntak av jod blant gravide/ammende i Norge? (Du kan sette flere kryss):
□ For lavt inntak av jod er et problem i Norge i dag
□ For høyt inntak av jod er et problem i Norge i dag
□ For lavt inntak er ikke et problem i dag, men var vanlig før
□ Vet ikke
□ Annet ……………………………………………

Kosthold og kosttilskudd

1. Tar du et eller flere vitamin og mineraltilskudd (for eksempel vitaminer, mineraler, olje, tare-tilskudd)?

☐ Ja ☐ Nei

Skriv navn på tilskudd og hvor mange ganger i uken tar du tilskudd:

1.________________________: ☐ ganger/uke

2.________________________: ☐ ganger/uke

3.________________________: ☐ ganger uke

4.________________________: ☐ ganger/uke

Kan du lese ut fra innholdsdeklarasjonen om noen av disse tilskuddene inneholder jod?

☐ Ja ☐ Nei

Hvis ja, skriv hvilket tilskudd det gjelder og hvor mye jod det er per dose:……………………………………

2. Er du vegetarianer? (dvs spiser ikke kjøtt, fisk og fiskeprodukter):

☐ Ja ☐ Nei

3. Er du veganer? (dvs spiser ikke kjøtt, fisk, fiskeprodukter, melkeprodukter og egg):

☐ Ja ☐ Nei

4. Har du spist/drukket følgende matvarer de siste 24 timer (fra du sto opp i går til du gikk og la deg):

4.1 Kumelk, yoghurt eller annen kumelk basert drikke (inkludert melk via kaffe latte/cappuccino)?

☐ Ja, oppgi mengde i glass (2 dl) siste 24 timer: ☐ ☐Nei

4.2 Ost (brunost, gulost mm)?

☐ Ja, angi hvor mange skiver: ☐ ☐Nei

4.3 Jodert salt?

☐ Ja ☐Nei

4.4 Egg eller produkter med mye egg (e.g. pannekaker, vafler)?

☐Ja, angi antall egg ☐Nei

4.5 Fisk eller fiskeprodukter (inkludert sushi)?

☐ Nei

☐ Ja, utdyp type: ☐ Fet fisk(ørret/laks,sild/makrell)

☐ Mager fisk (hvit fisk):

☐ Tunfisk

Utdyp om det var: ☐ til middag

☐ pålegg

5. Hvor ofte i gjennomsnitt drukket du eller spist disse matvarene etter at barnet ble født:

		Sjelden/ aldri	Sjeldnere enn ukentlig	1-3 ganger per uke	4-6 ganger per uke	1-2 ganger per dag	3-4 ganger per dag	5 + ganger per dag
1.	Brød/knekkebrød, alle typer, (2 skiver)	☐	☐	☐	☐	☐	☐	☐
2.	Frokostblandinger med korn/gryn (usøtet musli, havregrøt) (1 porsjon)	☐	☐	☐	☐	☐	☐	☐
3.	Andre frokostblandinger (corn flakes, honni korn, sjokopuff etc) (1 porsjon)	☐	☐	☐	☐	☐	☐	☐
4.	Ris/pasta kokt (porsjon a 150g)	☐	☐	☐	☐	☐	☐	☐
5.	Kumelk, alle typer gitt i antall glass (ca 2 dl) (og inkludert kaffe latte/cappuccino)	☐	☐	☐	☐	☐	☐	☐
6.	Alternativ melk (fra havre, ris, mandel, soya)	☐	☐	☐	☐	☐	☐	☐
7.	Yoghurt/surmelk, all typer gitt i antall beger (ca2dl)	☐	☐	☐	☐	☐	☐	☐
8.	Rød fisk både til middag og som pålegg (laks, makrell, ørret, tunfisk) (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
9.	Hvit fisk både til middag og som pålegg (torsk, sei, hyse, etc) (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
10.	Fiskekaker, fiske- boller, pudding og pinner, (1 porsjon)	☐	☐	☐	☐	☐	☐	☐
11.	Sushi med fisk/skalldyr (porsjon á ca 10 biter)	☐	☐	☐	☐	☐	☐	☐
12.	Rent kjøtt av okse, gris og lam (steik, koteletter, filet, biff), (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
13.	Bearbeidede kjøttprodukter (pølser, hamburger, kjøttkaker o.l.) (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
14.	Vilt (elg, hjort, rådyr, villfugl, hære o.l.) (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
15.	Kylling og kalkun, (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
16.	Innmat (lever, nyrer, innmatpudding o.l.), (Porsjon á ca 100 g)	☐	☐	☐	☐	☐	☐	☐
17.	Linser, bønner, kikerter	☐	☐	☐	☐	☐	☐	☐
18.	Olivenolje/rapsolje (til salat og matlaging)	☐	☐	☐	☐	☐	☐	☐
19.	Ost, alle typer, (2 skiver)	☐	☐	☐	☐	☐	☐	☐
20.	Egg hele (kokt, stekt) og i matlaging (pannekaker/vafler)	☐	☐	☐	☐	☐	☐	☐
21.	Kaker, sjokolade, iskrem, smågodt	☐	☐	☐	☐	☐	☐	☐
22.	Saltet snacks (f.eks. potetchips, peanøtter)	☐	☐	☐	☐	☐	☐	☐
23.	Søte drikker (som saft, Cola, Fanta, nektar, juice, smoothie)	☐	☐	☐	☐	☐	☐	☐
24.	Kunstig søte drikker (Cola Zero, Pepsi Zero osv)	☐	☐	☐	☐	☐	☐	☐
25.	Vann	☐	☐	☐	☐	☐	☐	☐
26.	Kaffe	☐	☐	☐	☐	☐	☐	☐
27.	Te	☐	☐	☐	☐	☐	☐	☐
28.	Grønnsaker alle typer (f.eks. gulrot, kål, brokkoli, løk, erter, tomat, salat, agurk)	☐	☐	☐	☐	☐	☐	☐
29.	Frukt og bær alle typer (f.eks. epler, pærer, banan, jordbær, druer, appelsin)	☐	☐	☐	☐	☐	☐	☐
30.	Poteter	☐	☐	☐	☐	☐	☐	☐
31.	Nøtter (valnøtter, hasselnøtter, mandler o.l.)	☐	☐	☐	☐	☐	☐	☐

Takk for at du deltok i dette forskningsprosjektet om jod!