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The impact of mandatory iodine fortification and supplementation on pregnant and lactating women in Australia

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Title: The impact of mandatory iodine fortification and supplementation on pregnant and lactating women in Australia.

Short title: Iodine fortification and supplementation in Australia

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Author's contribution

All authors were involved in the conception and design of the study. SH collected and analysed the data. All others were involved in the interpretation and drafting of the manuscript.

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Abstract

Background and Objectives: In Australia, two public health measures were introduced between 2009 and 2010 to reduce iodine deficiency. However there has been a shortage of information regarding their effectiveness and the ongoing prevalence of iodine deficiency in Australia. The primary aim of this study was to assess the extent to which these public health measures have reduced rates of iodine deficiency among pregnant and lactating women. **Methods and Study Design:** A review was conducted to identify all studies published since January 2010 that quantitatively measured the iodine status of pregnant and/or lactating women in Australia. **Results:** We found 25 publications, of which seven were included in this review after our exclusion criteria were applied. Of the seven included publications, three demonstrated the pregnant and lactating women in their studies to be iodine replete (median urinary iodine concentrations (MUIC) greater than 150 μg/L, or a breast milk iodine concentration (BMIC) of greater than 100 μg/L). The remaining four publications found MUIC of pregnant and lactating women to be below the 150 μg/L threshold, in the mild-to-moderate iodine deficiency category. Only two studies, documented iodine sufficiency among pregnant and lactating women in the absence of iodine supplementation. **Conclusions:** Many pregnant and lactating women in Australia remain at least mildly iodine deficient. Antenatal iodine supplementation was the factor most consistently associated with an adequate iodine status. Larger, more representative studies or sentinel studies with a National coordination are needed to understand the differences in iodine status that exist across the country.

Keywords: Iodine; fortification; supplementation; pregnancy; Australia.

Background

Iodine is a trace element essential for the synthesis of thyroid hormones, which are in turn essential for normal human growth and mental development. An inadequate dietary intake of iodine can impair thyroid function and lead to a spectrum of disorders known as the iodine deficiency disorders (IDD). Depending on the severity of the iodine deficiency, and the time in the human lifecycle at which it occurs, these disorders may include miscarriage, mental and physical retardation, thyroid dysfunction or cretinism.[1] A maternal diet sufficiently rich in iodine is critical throughout pregnancy to ensure an adequate delivery of iodine to the foetus. Even subclinical hypothyroidism in the mother, occurring as a consequence of iodine deficiency, can cause irreversible brain damage in the foetus.[1,2] The importance of maternal iodine intake continues throughout breastfeeding as the newborn's brain continues to develop, with breast milk providing its sole source of iodine.[3]

Determinations of iodine status are typically made with reference to epidemiological criteria developed by WHO for assessing iodine nutrition, which are based on median urinary iodine concentrations (MUIC). The values for pregnant women are provided in the Table 1. In lactating women, breast milk iodine concentration (BMIC) can be used as an alternative measure of iodine status. In such cases, a minimum BMIC value of 100 μg/L is typically used as the threshold to determine maternal iodine adequacy.[4]

Research has previously confirmed that the majority of Australian children and pregnant women are mildly-to-moderately iodine deficient.[6] Table 2 sumarises MUIC in pregnant and lactating women in Australia prior to the implementation of fortification and supplementation which ranged from 81[7] to 109 μg/L.[8] The consequences of moderate-to-severe iodine deficiency during pregnancy on the cognitive outcomes of offspring are well established. Two meta-analyses indicate that this level of iodine deficiency can result in a population wide loss of intelligence in children of around 10-13.5 intelligence quotient (IQ) points.[9,10] However evidence supporting a link between mild-to-moderate iodine deficiency during pregnancy, such as that documented in Australia, and detrimental cognitive outcomes in children has only emerged more recently.[8]

In a 2013 longitudinal follow up of a Tasmanian cohort study, the authors found that children whose mothers were iodine deficient during pregnancy had reductions of 10.0% in spelling, 7.6% in grammar, and 5.7% in English performance compared with children whose mothers were iodine sufficient. These associations remained significant after adjustment for a range of potential confounders including gestational and maternal age, gender, birth weight, and maternal occupation and education.[14] These results are consistent with the findings of a larger cohort study undertaken recently in the United Kingdom, which documented progressively worsening child IQ scores with worsening degrees of maternal iodine deficiency during pregnancy.[15]

Because of this, Food Standards Australia and New Zealand (FSANZ) instituted a mandatory food fortification program in October 2009 that requires all salt used in bread making in Australia to be fortified with iodine in the range of 25-65 milligrams of iodine per kilogram of salt[16]. Similarly, in recognition of the increased iodine requirements associated with pregnancy, the National Health and Medical Research Council (NHMRC) released a public statement in 2010 recommending that all women who are pregnant, breastfeeding or considering pregnancy, take an iodine supplement of 150 μg each day.[17]

Following the introduction of these public health measures, there has been a shortage of information regarding their effectiveness and the ongoing prevalence of iodine deficiency in Australia. Considering the importance of an iodine replete diet, and the long-term impact of IDD, this study was undertaken to explore the extent to which the FSANZ fortification program and NHMRC antenatal supplementation recommendation have been effective in addressing rates of iodine deficiency among pregnant and lactating women in Australia. In particular, it asks: are pregnant and lactating women in Australia iodine deficient?

Methods

Identification of studies

The database of peer-reviewed literature, PubMed/MEDLINE, was searched to identify studies and reports published between January 2010 and Jan 2017. Web-based searches, using the internet search engines Google and Google Scholar were also conducted to identify any reports and grey literature (i.e. literature that has not been formally published) that met the inclusion criteria. The references of all retrieved publications were hand searched for any relevant references missing from the database searches.

Search strategy

The search terms that were used are provided in Appendix 1. The objective of the search was to identify all publications in the post-fortification period that quantitatively measured the iodine status of pregnant and/or lactating women. The inclusion criteria for the review required that a publication had:

1. Quantitatively measured the iodine status of pregnant and/or lactating Australian women using urinary or breast-milk iodine concentrations.
2. Based the above measurement on data collected after October 2009 (the post-fortification period).
3. Been published between January 2010 and December 2016.

Data extraction

Data were extracted from the included studies according to the headings listed in Table 3.

Results

A total of 25 publications were retrieved from the literature search including 24 articles and a government report prepared by the Australian Institute of Health and Welfare (AIHW).[18] Thirteen articles were excluded on the basis that they did not report a quantitative measure of the iodine status of pregnant or lactating women. A further five articles were also excluded, three because the data collection occurred prior to October 2009, one because its data were collected outside of Australia, and one because it was a duplicate of another included study.[19] Details of the excluded articles are in Appendix 2. After applying the exclusion criteria, seven publications were included in this review[3,18-23] (see Figure 1).

Study characteristics

The number of participants in the included studies ranged from 60[21] to 783.[19] The data used by the AIHW was drawn from the Australian Bureau of Statistics 2011-2012 National Health Measures Survey (NHMS), which comprised blood and urine tests from over 11,000 participants aged five and over. However, the number of pregnant and breastfeeding women within this data set was not specified.

The data used among the publications were collected between 2009 and 2013. Two of the included studies used data that was at least partially collected in the pre-fortification period, prior to October 2009.[20,23] Four of the included articles were cross-sectional studies[3,20-22] and the remaining two were prospective cohort studies.[19,23] Charlton's cross-sectional study reported data for two separate samples of pregnant women, one collected in 2011 and the other in 2012. The AIHW report is based on a cross-sectional analysis.

Demographic characteristics

Three of the studies were conducted in Adelaide, South Australia,[3,19,23] two in the Illawarra region of New South Wales[21,22] and one in Gippsland in Victoria.[20] The AIHW report was the only publication included in the review which was based on a national data set, and women aged 16 – 44 .[18]

Women who spoke a language other than English at home were excluded from all three of the studies that found pregnant or breastfeeding women to be iodine replete.[3,19,22] The other studies did not report on the inclusion or exclusion of participants based on their language status, although 94% of participants in Rahman's study identified as white.[20]

Other demographic characteristics assessed for association with iodine status varied across the seven publications. Charlton found no difference in MUIC across age, level of education or number of previous pregnancies,[22] while Huynh found positive associations between iodine status and multiparity, alcohol consumption and non-Caucasian ethnicity.[3]

Iodine status

Iodine status was assessed according to MUIC in all of the included publications with the exception of Huynh and colleagues, who measured iodine status according to median BMIC.[3] In this study, a BMIC of more than 100 μg/L was considered sufficient to provide adequate iodine to meet the needs of breast-fed term infants.

Of the seven included publications, three demonstrated pregnant and lactating women in their studies to be iodine replete according to either the WHO criteria of a MUIC greater than 150 μg/L, or a BMIC of greater than 100 μg/L.[3,19,22] The remaining four publications found MUIC of pregnant and lactating women to be below the 150 μg/L threshold, in the insufficient range.[18,20,21,23] Table 3 summarises these results.

Supplement use

Perinatal iodine supplementation was the factor most consistently associated with an adequate iodine status. Only two studies, both from Adelaide, documented iodine sufficiency among pregnant and lactating women in the absence of iodine supplementation.[3,19] No comparisons were made between the iodine status of pregnant and breastfeeding women on the basis of iodine supplementation within the AIHW report as the consumption of iodine supplements was not measured directly as part of the NHMS.[18]

Only one of the included studies assessed changes in iodine status between the pre and post-fortification periods after controlling for supplement use, and both noted improvements in iodine status. Huynh et al estimated the mean BMIC of women not taking iodine supplements to be 1.2 times greater in the post-fortification period than it was prior to fortification.[3] Clifton found that the MUIC of pregnant women not taking an iodine supplement before fortification was 84 µg/L (range 83.4 – 393 µg/L, n = 94).[23] However data post-fortification is not available.

Importantly, all three of the studies that found their sample populations to be iodine replete noted that iodine adequacy was unlikely to be achieved without antenatal supplementation.[3,19,22] Iodine status according to supplement use is described in Table 3.

Data collection during pregnancy and breastfeeding

The MUIC's and BMIC's reported in the included studies were captured at different stages of pregnancy and breastfeeding. These results are described in Table 3.

Discussion

The findings of this review describe a mixed picture of the iodine status of pregnant and lactating women in Australia since the introduction of public health measures to reduce rates of iodine deficiency. On face value, there appears to be a generally upward trend in the iodine status of these women, as seen by the increase in MUIC from 79 µg/L in 2009-10,[23] to 189 µg/L in 2011-12.[19] However these figures belie the differences that exist between the included studies.

Geographical variation

Of the three studies that found the iodine status of their sample population to be adequate, the largest two were both conducted in Adelaide, the capital city of South Australia.[3,19] These results therefore need to be considered in light of the AIHW finding that iodine status varies across Australia, and is highest in certain states, including South Australia, as well as in major cities, such as Adelaide.[18] Furthermore, both of the Adelaide studies drew their sample populations from pregnant or lactating women participating in the same prospective cohort study – Pregnancy Iodine and Neurodevelopment in Kids (PINK).[24] Therefore while these studies report different outputs (MUIC v BMIC) measured at different stages (pregnancy v lactation), they are actually reporting on the same data set and hence largely duplicate their respective results.

The only other study to find an adequate iodine status among its population was conducted in a small geographical area south of Sydney and was considerably underpowered, having a sample size of just 114.[22] Andersen et al, [25] have described that a sample size of 125 will give a precision of ±10% using spot urines for a population estimate. It is important to realise that precision alone should not determine the sample size needed to estimate a population MUIC. External validity is also important. For the results to be generalised to a wider population the sample has to be representative of this population.

Gestational age and urinary iodine excretion

Research has demonstrated that urinary iodine excretion is elevated in early pregnancy, and decreases with advancing gestational age.[26] Studies have shown that early pregnancy MUIC (<16 weeks) can be elevated to such an extent that it significantly exceeds population level controls, thereby giving a false indication of iodine adequacy in the developing foetus.[26-28] In light of these findings, it is noteworthy that the highest MUIC recorded in this review (189 μg/L) was obtained by Condo et al,[19] from a population of pregnant women sampled at a mean gestation age of 16.3 weeks (± 2 weeks). The other studies that reported MUIC values and gestational age at collection primarily obtained their samples in the third trimester of pregnancy, which is likely to account for some of the variation in results.[20,22,23] While Condo's study also reported MUIC at 28 weeks gestation and again found its population to be iodine sufficient (172 μg/L), this discussion illustrates the importance of accounting for gestational age at the time of urinary iodine collection. Unfortunately, the AIHW report did not report the gestational ages of the women in its sample.[18]

Public awareness

As noted above, three of the seven publications included in this review found that pregnant and lactating women in Australia remain iodine deficient despite public health measures to address this issue. This raises questions about the reasons for this ongoing deficiency.

One likely contributing factor is a low level of awareness within the Australian population regarding dietary sources of iodine, its importance, and the potential implications of iodine deficiency during pregnancy and lactation. Of the three articles in this review that assessed these factors, all three concluded that their study participants were poorly informed in relation to dietary sources of iodine and its importance during pregnancy.[3,20,22]

Role of the health provider

While women have consistently identified health providers as their major source of nutritional advice during pregnancy,[29-31] recent studies have shown that providers' knowledge of iodine requirements in the perinatal period is not adequate. In a survey of 396 healthcare providers, Guess and colleagues found that only 73% of respondents reported recommending iodine supplements in pregnancy, which dropped to 56% when planning pregnancy and 52% during lactation.[30] In a similar study, albeit from a different perspective, Martin reported that in a sample of 200 pregnant women in Gippsland Victoria, only 34.5% indicated being made aware of the importance of increasing iodine intake during pregnancy by their medical practitioner.[31]

The studies included in this review had a number of limitations. First, they all relied on a single-spot urine or breast milk sample to determine iodine status. This is problematic because the rate of iodine excretion reflects iodine intake over a short period of time, leading to significant variability in day-to-day samples, reducing the reliability of iodine status estimates.[32] Twenty four hour urinary collections may provide a more accurate estimate of iodine status but are not practical.[19]

Secondly, the majority of the studies were underpowered, with only Condo et al,[19] and Huynh et al,[3] utilising a sample size greater than 300, the minimum required by the WHO to reliably determine the iodine status of a population. While it is likely the AIHW also exceeded this minimum, it did not report the number of pregnant women in its sample.[18] Furthermore, women who spoke a language other than English at home were excluded from all three of the studies that reported a finding of iodine sufficiency, and their involvement in the other studies was not specified. According to the 2016 Australian census 22% of households speak a language other than English at home.[33]

In relation to the AIHW report, despite being a national survey, it did not report gestational age at the time of urinary collection, or report data for supplement and non-supplement users separately. Given the influence of antenatal iodine supplementation on iodine status, it was important to report the results of these two groups separately.

Finally, all of the studies included in this review used a median figure to report the urinary iodine status of their respective study populations. Given the differences in iodine status between the supplement-taking and non-supplement taking cohorts, the median value may overstate the population's urinary iodine concentration.

Conclusion and future directions

The findings of this review demonstrate that despite public health measures to address rates of iodine deficiency in Australia, many pregnant women remain mildly iodine deficient. While recent studies out of Adelaide provide grounds for optimism, these results are yet to be replicated across the country. Antenatal iodine supplementation in accordance with NHMRC guidelines continues to be necessary, as fortification alone does not deliver sufficient iodine to meet the increased requirements associated with pregnancy and breastfeeding.

Given the shortcomings of the studies considered in this review, larger, more representative studies are needed to better understand the iodine status of women across the country. Future studies would benefit from multi-centre, interstate involvement, to better illustrate the influence of geographical, socioeconomic, ethnic and cultural factors that have previously been demonstrated to influence nutritional iodine status.[34] Cross-sectional study designs such as that employed by Charlton could readily be adapted to this purpose. Consideration should also be given to using multiple spot-urine samples to provide a better estimate of iodine status.

Finally, there is a clear need for public health information campaigns and professional education initiatives to better inform the public and healthcare providers about the importance of an adequate iodine intake. As the nutritional choices of pregnant women are shaped by their knowledge of what's important for a healthy pregnancy, improving knowledge about the importance of iodine is a key step in promoting lasting behavioural change that will lead to reductions in the rate of iodine deficiency in Australia.

Disclosure statement

The authors have no conflicts of interest to declare

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Table 1. WHO epidemiological criteria for assessing iodine nutrition based on the median urinary iodine concentrations of pregnant women.[5]

POPULATION GROUP	MEDIAN URINARY IODINE CONCENTRATION (µg/L)	IODINE INTAKE
Pregnant women	< 150	Insufficient
	150 - 249	Adequate
	250 - 499	Above requirements
	≥ 500	Excessive†
Lactating women†	<100	Insufficient
	≥ 100	Adequate

†Iodine intake is excessive if it is more than the amount required to prevent and control iodine deficiency. UICs for lactating women are lower than those for pregnant women because of the iodine excreted in breast milk.

Table 2. Summary of results for urinary iodine excretion in Australian pregnant and breastfeeding women before fortification and supplementation

Population	Year	Number	Median	Reference
Pregnant women in Sydney North	1998-99	81	104	Gunton et al, 1999[11]
Pregnant women in Western Sydney	1998-99	101	88	Li et al, 2001[12]
Pregnant women in Sydney North	2000	84	109	McElduff et al, 2002[8]
Pregnant women in Tasmania	2000-01	285	76	Burgess et al, 2007[7]
Pregnant women NSW Central Coast	2004	796	85	Travers et al, 2006[13]
Pregnant women in Tasmania†	2003-06	288	81	Burgess et al, 2007[7]
Pregnant women in Tasmania	2006	229	86	Burgess et al, 2007 [7]

†24 h urine collection

Table 3: Overview of studies included in the review

Reference	Data collection period	Location	Sample size	Status/period of data collection	Outcome measure
Clifton et al, 2013[23]	2009 – 2010	Adelaide, SA	196	Pregnant 12, 18, 30 & 36 weeks gestation	MUIC Non-supplement: 84 µg/L
Rahman et al, 2011[20]	2009 – 2010	Gippsland, VIC	62	Pregnant ≥28 weeks gestation	MUIC 95.5 µg/L
Axford et al, 2011[21]	2010	Illawarra, NSW	60	Breastfeeding Mean age 2.6 months (SD: 1.0)	MUIC 123 µg/L Non-supplement: 97 µg/L Supplement: 206 µg/L
Charlton et al, 2013[22]	2011 2012	Illawarra, NSW	147 114	Pregnant 2011: 13-24 weeks (37%) & ≥ 25 weeks (61%) 2012: 13-24 weeks (29%) & ≥ 25 weeks (71%)	MUIC 2011: 145.5 µg/L Non supplement: 109 µg/L Supplement: 178 µg/L 2012: 166 µg/L Non supplement: 124 µg/L Supplement:202 µg/L
AIHW, 2016[18]	2011 – 2012	Australia wide	Not	Pregnant & Breast-feeding	MUIC†

			Specified	Not specified	Pregnant: 116 µg/L Breast-feeding: 103 µg/L
Condo et al, 2016[19]	2011 – 2012	Adelaide, SA	783	Pregnant <20 weeks gestation (median 16.3 weeks) 28 weeks gestation	MUIC < 20 weeks: 189 µg/L 28 weeks: 172 µg/L Non supplement: 159 µg/L (MUIC) at < 20 weeks 141 µg/L (MUIC) at 28 weeks Supplement: 221 µg/L (MUIC) at < 20 weeks 187 µg/L (MUIC) at 28 weeks
Huynh et al, 2017[3]	2012 – 2013	Adelaide, SA	653	Breastfeeding Within 7 days of delivery	BMIC 187 µg/L Non-supplement: 137 µg/L Supplement: 195 µg/L

†Intakes for pregnant women aged 16–44 this sample of women, delineated by State, includes women who were pregnant and breastfeeding, as well as women who were not.

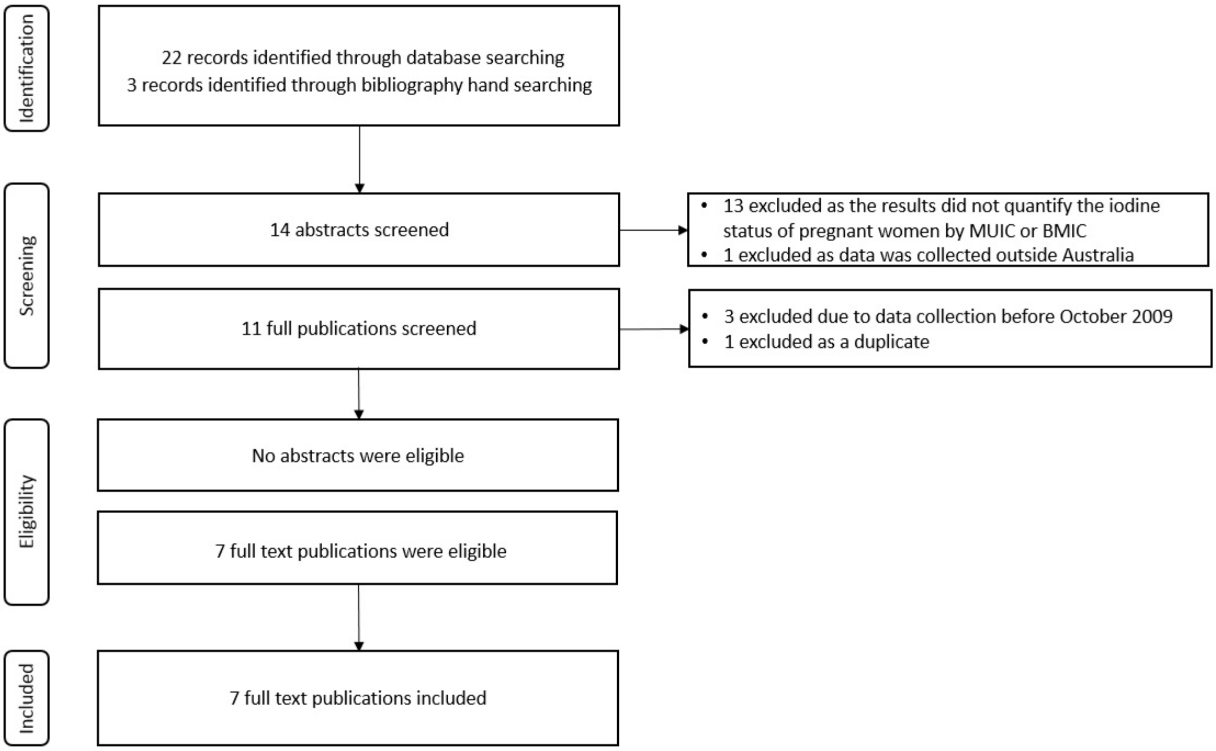

Figure 1. Flow chart showing identification of individual studies for inclusion.