Investigating the Relationship between Maternal Iodine Intake in Pregnancy and Iodine Status or Thyroid Function of Mothers and Infants

A Prospective Cohort Study

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Abstract

Iodine is crucial for thyroid hormone production which is essential for growth and development. Iodine deficiency in pregnancy can lead to cognitive impairment, poor growth, congenital abnormalities and in severe situations cretinism. Mild iodine deficiency re-emerged in Australia in the last decade. To address this issue, in 2009 mandatory iodine fortification of bread was implemented and in 2010 routine iodine supplementation in pregnancy was recommended. Since mandatory iodine fortification there has been limited data on the iodine intake and iodine status of Australians, including pregnant women.

Intervention trials in iodine deficient populations have shown a higher maternal and infant urine iodine concentration (UIC) in iodine supplemented groups compared to controls, with the effect on thyroid function being less clear. However, no studies have assessed the relationships between maternal iodine intake from food and supplements in pregnancy and maternal or infant iodine status and thyroid function in mildly iodine deficient or sufficient populations.

The primary aims of the thesis were to examine the associations between maternal iodine intake/iodine status/thyroid function in pregnancy and markers of maternal and infant iodine status/thyroid function. The secondary aims were to examine the associations between maternal iodine intake/thyroid function in pregnancy and pregnancy/birth outcomes, infant growth and the general health of pregnant and postnatal women.

783 pregnant women in South Australia participated in the study. An iodine specific food frequency questionnaire (I-FFQ) was developed and validated to assess dietary iodine intake at baseline (<20 weeks' gestation) and 28 weeks' gestation. Maternal UIC, maternal thyroid

function and the general health and wellbeing of pregnant and postpartum women was assessed at baseline, 28 weeks' gestation and 3 months postpartum. Breast milk iodine concentration (BMIC) was assessed at birth and 3 months postpartum. Thyroid stimulating hormone (TSH) was collected from newborn screening at birth. Pregnancy/birth outcome data and infant anthropometrics at birth were collected from the women's and infant's medical records and infant UIC, infant thyroid function and infant growth was measured at 3 months of age.

Based on the median UIC, pregnant women in this study were classified as iodine sufficient, both with or without the use of iodine supplements during pregnancy. Maternal iodine intake in pregnancy was positively associated with maternal UIC and BMIC (**Chapter 4**), while no association was found with maternal thyroid function (**Chapter 4**), infant UIC, infant thyroid function (**Chapter 5**) or clinical outcomes (**Chapter 6**). At 28 weeks' gestation maternal free triiodothyronine (fT3) was positively associated with infant fT3 at 3 months of age, while maternal fT3 and thyroglobulin (Tg) was inversely associated with infant TSH at 3 months of age (**Chapter 5**). Furthermore, markers of maternal thyroid function at 28 weeks gestation was associated with the mental and physical health of women at 3 months postpartum as well as the severity of stress at 28 weeks gestation (**Chapter 6**).

In summary, maternal iodine intake in pregnancy is not associated with maternal or infant thyroid function in an iodine sufficient population, although maternal thyroid function at 28 weeks' gestation is associated with infant thyroid function at 3 months of age and with aspects of the general health and wellbeing of pregnant and postnatal women. Further research is needed to better understand these relationships in populations with various iodine status and their impact on infant development.

Declaration

I certify that this work contains no material which has been accepted for the award of any other degree or diploma in any university or other tertiary institution and, to the best of my knowledge and belief, contains no material previously published or written by another person, except where due reference has been made in the text. In addition, I certify that no part of this work will, in the future, be used in a submission for any other degree or diploma in any university or other tertiary institution without the prior approval of the University of Adelaide and where applicable, any partner institution responsible for the joint-award of this degree.

My PhD project is a component of a larger project titled 'The PINK cohort study'. Due to this the study concept and design had been developed and research staff assisted in the recruitment and with aspects of data collection. In addition, data entry and cleaning was performed by data analysts and statisticians assisted with complex data analysis. I certify that I was involved in all aspects of my PhD, including the recruitment of women and data collection at all time points from August 2011-December 2013. I developed an extensive data analysis plan and made decisions regarding the statistical analysis as well as performing all descriptive analysis. I provided intellectual input throughout the study and interpreted all of the results. In addition, I performed an iodine food frequency questionnaire validation study in which I was involved in all aspects including the conception and design, data collection, data entry and the analysis and interpretation of the results.

I give consent to this copy of my thesis when deposited in the University Library, being made available for loan and photocopying, subject to the provisions of the Copyright Act 1968.

Signed:

Date:

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I would like to take this opportunity to thank many people that supported me and assisted with the completion of my PhD. Firstly I would like to thank the women who agreed to participate in the study and involve their babies in research. Your time and dedication to research is extremely appreciated and without you this work would not have been possible.

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List of Abbreviations

AI	Adequate Intake
ATA	American Thyroid Association
b	Coefficient
BMI	Body Mass Index
BMIC	Breast Milk Iodine Concentration
CDC	Centres for Disease Control and Prevention
CH	Congenital Hypothyroidism
CI	Confidence Interval
CRF	Clinical Report Form
DASS	Depression and Anxiety Stress Scale
DMAC	Data Management and Analysis Centre
EAR	Estimated Average Intake
EPDS	Edinburgh Postnatal Depression Scale;
EQUIP	Ensuring the Quality of Iodine Procedures
FFQ	Food Frequency Questionnaire
FMC	Flinders Medical Centre
FSANZ	Food Standards Australia and New Zealand
fT3	Free Triiodothyronine
fT4	Free Thyroxine
fTI	Free Thyroid Index
hCG	Human Chorionic Gonodotrophin
I^-	Iodide ion
ICCIDD	International Committee for the Control of Iodine Deficiency Disorders

IDD	Iodine Deficiency Disorder
I-FFQ	Iodine Food Frequency Questionnaire
KI	Potassium Iodide
LT4	Levothyroxine
MIS	Management Information System
NATA	National Association of Testing Authorities
NHMRC	National Health and Medical Research Council
NINS	National Iodine Nutrition Survey
NIS	Sodium (Na) /iodine (I) symporter
NR	Not Reported
NS	Not Significant
OR	Odds Ratio
PINK	Pregnancy Iodine and Neurodevelopment in Kids
PPT	Postpartum Thyroiditis
RCT	Randomised Controlled Trial
RCTs	Randomised Controlled Trials
RDI	Recommended Dietary Intake
RR	Relative Risk
rT3	Reverse Triiodothyronine
SAS	Statistical Analysis System
SAC	Southern Adelaide Clinical
SD	Standard Deviation
SDS	Self-Rating depression scale
SE	Standard Error
SEM	Standard Error of the Mean
SES	Socio-Economic Status

SF-36	Short-Form 36
SGA	Small for Gestational Age
SPSS	Statistical Package for the Social Sciences
T3	Triiodothyronine
T4	Thyroxine
TBA	Thyroxine Binding Albumin
TBG	Thyroxine Binding Globulin
TBPA	Thyroxine Binding Prealbumin
Tg	Thyroglobulin
TMAH	Tetramethvl Ammonium Hydroxide
TPO	Thyroid Peroxidase
TRH	Thyroid Releasing Hormone
TSH	Thyroid Stimulating Hormone
TT4	Total Thyroxine
UIC	Urine Iodine Concentration
UIE	Urine Iodine Excretion
WAS	Waite Analytical Services
WCH	Women's and Children's Hospital
WCHN	Women’s and Children’s Health Network
Weeks’	Weeks of
WHO	World Health Organisation