Original Article

The influence of mandatory iodine fortification on the iodine status of Australian school children residing in an iodine sufficient region

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Background and Objectives: To counter emerging iodine deficiency mandatory iodine fortification of bread was introduced throughout Australia in 2009. This study investigated the impact of iodine fortification on the iodine status of school aged children living in the iodine replete state of Queensland, and investigated which foods had greatest influence on overall iodine status. **Methods and Study Design:** A convenience sample of 30 children aged 8.0-10.9 years living in south east Queensland, Australia, provided spot morning and afternoon urine samples on two consecutive days. Iodine status was categorised by the World Health Organization criterion. Semi-quantitative food questionnaires (FFQ) completed by carers were used to investigate which foods were having the greatest influence on UIC. Analysis of variance was used to reduce the within person variation observed in urinary iodine concentrations (UIC) and the data were log transformed before statistical analysis. **Results:** Adjusted median UIC was 144 ug/L (IQR 120-210 ug/L) indicating iodine sufficient status. No samples were above the cut off for excessive UIC. Bread was the only statistically significant contributor to UIC (standardized β=0.37, p=0.04) with 14% of variation in UIC explained by bread consumption. UIC increased by 8.7% for each additional serve of bread. **Conclusions:** Iodine fortification of bread has increased the iodine status of school aged children in this Queensland cohort. Despite the small sample size in this study, improvements in methodology allowed its findings to be comparable to other, larger surveys.

Key Words: iodine, school children, iodine fortification, bread fortification, urinary iodine concentration

INTRODUCTION

Iodine is an essential micronutrient required for normal growth and development.[1] Iodine status can influence an individual's mental development, motor function, somatic growth and thyroid function.[2] Monitoring iodine status of populations is considered an important part of preventative medicine.[3] Children are particularly vulnerable to inappropriate dietary iodine intake, with impaired cognitive function and thyroid dysfunction being documented amongst both iodine deficient and iodine excessive populations.[4-6]

The irreversible consequences experienced by iodine deficient populations have generated global attention[7] and are key motivators in the development of iodine prophylaxis programs with the aim being to improve the iodine status of at risk populations.[1,3] The World Health Organization (WHO) and International Council for Control of Iodine Deficiency Disorders (ICCIDD) established criteria (Table 1) to assist with the assessment and definition of iodine status using median urinary iodine concentration (UIC) of a population as a determinant.[1] As 90% of consumed iodine appears in the urine mostly after 4-5 hours of ingestion, UIC is considered the most immediate reflection of iodine nutrition intake.[1,8] The criteria identifies iodine sufficient populations as not only having a median UIC between 100 ug/L-199 ug/L but also no more than 20% of its samples should be below 50 ug/L.[1] Thus not only is the central tendency of a populations' UIC important, but also its spread.

Globally, 130 counties have implemented iodine nutrition monitoring.1 In 2003-2004 Australia conducted its first National Iodine Nutrition Survey (NINS).9 Mild to moderate iodine deficiency was observed in almost 50% of school-aged children.9 Investigators reported a national median UIC of 96 ug/L, below the lower limit of ade-

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Table 1. The proportion of Queensland school aged children falling within each category of the World Health Organization criterion of iodine status

Median urinary iodine concentration range (ug/L)	Iodine status according to WHO and ICCIDD criteria	Proportion of children aged 8-10 years with iodine status	n
<20	Severe iodine deficiency	0% (95% CI 0%-12%)	0
20-49	Moderate iodine deficiency	0% (95% CI 0%-12%)	0
50-99	Mild iodine deficiency	7% (95% CI 1%-22%)	2
100-199	Adequate iodine intake	67% (95% CI 47%-83%)	20
200-299	More than adequate iodine intake	27% (95% CI 12%-46%)	8
≥300	Excessive iodine intake	0% (95% CI 0%-12%)	0

quate iodine intake of 100 ug/L.1,9 However, iodine levels varied across Australia, with some states such as Queensland (QLD) and Western Australia (WA) having adequate iodine status with median UIC's of 136.5 ug/L and 142.5 ug/L, respectively.9 Subsequent Australian surveys10,11 reinforced the inadequate iodine status of some Australian school-aged children and consequently prompted Food Standards Australia and New Zealand (FSANZ) to introduce the mandatory use of iodised salt in all bread manufacturing (except organic) from late 2009.[12] Bread was chosen by FSANZ as the most suitable vehicle to increase the dietary iodine intake because the 1995 National Nutrition Survey (NNS) reported that Australians consume approximately 75-85% of their salt via processed foods, and of that percentage, 50% of salt is consumed via bread and cereal products.[13]

Whilst deliberating on the mandatory use of iodised salt in bread manufacturing, concerns were raised that a blanket fortification program could cause iodine sufficient regions to attain more than adequate or excessive iodine intakes.[14] Previous attempts of iodine fortification in Tasmania, Australia in the mid 1960's resulted in a rise of thyrotoxicosis.[15] FSANZ, however, predicted that the amount of iodine fortification required to improve the Australian iodine status would not cause iodine sufficient regions, WA and QLD, to exceed the optimal range for iodine.[13] Thus the risk of adverse effects as a result of mandatory iodine fortification was considered low.[14]

It was estimated that iodine fortification in bread would increase the dietary iodine intake of children over the age of 2 years by approximately 54 ug/day.[12] Taking into account the bioavailability of dietary iodine,[8] it could be assumed that as a result of iodine fortification, the median UIC of QLD school aged children would increase by approximately 48 ug/L, suggesting that the population median UIC would rise to be within the range of 180-185 ug/L. Although this median level is not considered excessive, due to large variations in UIC, the proportion of samples within the distribution that could reach beyond the excessive bounds needs to be considered also.

Speculation that excessive iodine intakes may occur due to iodine fortification programs can hinder the success of much needed iodine fortification programs amongst iodine deficient regions.[16] Documenting changes in iodine status within a population exposed to an acute rise in dietary iodine provides an important insight into the merit of objecting concerns and improves the implementation of existing fortification programs to benefit the majority.[16]

This study investigated the iodine status of school aged children residing in the iodine sufficient region of Queensland, three years after iodine fortification was introduced to Australian bread manufacturing. The study aimed to identify the proportion of childrens' UIC samples at the lower and upper extremes of the population's UIC distribution, and investigate associations between dietary sources of iodine, in particular bread consumption and iodine status.

MATERIALS AND METHODS

Recruitment

Children aged 8.0-10.9 years residing in south east Queensland, Australia, were eligible to participate. A convenience sample of participants was recruited via various advertisement media including newspaper, television, radio, posters and social media between November 2011 and March 2013. This approach has been shown to attain representative samples in other public health surveys.[17,18] Informed written consent was attained from carers of the participating children. The study was approved by the Medical Research Ethics Committee, The University of Queensland (#2001000125).

Sample collection

Carers supervised the collection of four urine samples from each child over two consecutive days (first morning urine void, and first urine after midday meal).

Semi-quantitative food frequency questionnaire's (FFQ) adapted from the Healthy Kids Queensland survey (Abbott et al) were completed by carers. Foods included in the FFQ were those identified by the 22nd Total Diet Study[19] and FSANZ[12] as notable sources of dietary iodine. Each food was described as a serve with a specified quantity ie. 1 serve of bread = 2 slices or 1 medium roll or 1 flat bread. There were 5 daily frequency options for milk, bread, egg, yogurt, sushi, nori, brassica vegetables and salt water fish ie. never eats, 1 serve, 2 serves, 3 serves or 4 or more serves per day. Brassica vegetables were also included because of their known goitrogenic affect to impair iodine uptake. For sub-categories of food, there were 10 frequency options; never, less than 1 serve per day, one per day, 2 per day, 3 or more per day, once weekly, 2-4 weekly, 5-6 serves weekly, less than 1 serve per month, 1-3 serves per month. For example, bread was split in the sub-categories of 'roll, flat, slice, bagel, turkish, crumbs, fruit bread' 'organic bread' or 'homemade bread', each with corresponding serving sizes. The questionnaire recorded demographic and clinical characteristics, including postcode of residence. Height and weight of the children were measured using standard anthropometric techniques. Body Mass Index (BMI) was calculated using standard formula. Socio-economic status (SES) was measured at the postcode level using the Socio-Economic Indexes for Areas (SEIFA) Index of Relative Disadvantage. This index was developed by the Australian Bureau of Statistics.[20] Participants were categorised into thirds using the Queensland population as the reference.

Sample analysis

All urine samples were stored at -18°C until transported on ice to Westmead Hospital, Sydney for analysis by the same laboratory used by the NINS. UIC was established using ammonium persulfate digestion before a Sandell-Kolthoff[21] reaction. Iodine status was categorised using the WHO criterion[1] for assessing iodine nutrition based on median UIC.

Statistical analysis

Using the mean 152.9 ug/L, and standard deviation 80.1, of UIC in 8.0-10.9 year olds from Queensland school aged children included in the NINS (Eastman C personal communication), and after adjusting for non-normality of the data, it was calculated that a sample size of 57 was required to detect the 48 ug/L increase in UIC predicted by FSANZ.

Stata statistical software (StataCorp, College Station, TX, USA), SPSS (IBM, Armonk, NY, USA) and Microsoft Excel (Microsoft, Redmond, WA, USA) were used for statistical analysis. Analyses of variance was used to reduce the within person variation observed in UIC before statistical analysis using the following formula: Adjusted UIC = [(person's UIC – group mean) × ($s_b \div s_{obs}$)] + group mean.[22] All four UIC samples were used to obtain an overall adjusted UIC, which was used in subsequent calculations. Descriptive statistics were calculated for UIC.

The percentage of individuals in each WHO iodine category was calculated, along with exact binomial 95% confidence intervals. Paired *t*-tests were used to determine the difference between morning and afternoon UIC, and also the difference between the UIC of school children pre-fortification and post-fortification. Univariate linear regression was performed for each identified food to determine the association between dietary iodine contribution and iodine status. Standardised beta coefficients, which indicate how many standard deviations the outcome variable will change per standard deviation increase in the predictor variable, were calculated. For univariate regression, the absolute value of the standardised coefficient equals the correlation coefficient. Foods that had a correlation of greater than 0.32 (ie. R^2>10%) were considered to be important.

RESULTS

Participants

Thirty children aged 8.0-10.9 years (18 males, 12 females) completed the survey. Basic demographics are shown in Table 2.

Urine iodine concentration

The adjusted median UIC for children aged 8.0-10.9 years was 144 ug/L (CV 32.3%, IQR 120-210), with no samples above the cut off for excessive UIC (>299 ug/L), indicating adequate iodine status according to WHO criterion (Table 1). The mean difference between morning and afternoon UIC samples was 44.8 ug/L (95% CI 25.7-64.1), with UIC being highest in the afternoon (p=0.001). No significant difference was detected between the UIC of 8.0-10.9 year olds prior to iodine fortification and the UIC of children included in the current study (p=0.38).

Food frequency questionnaire

The median number of serves of bread consumed was 2 per day, which was calculated to equate to 65.0 grams as shown in Table 3 (based on average weight (g) of 2 slices of bread, 1 median roll or 1 flat bread as defined by AUS NUT 2011-2013[23]). Bread consumption was significantly associated with UIC (β=0.37, p=0.04) with 14% of variation in UIC explained by bread consumption. UIC increased by 8.7% for each additional serve of bread. No other examined food type was significantly associated with UIC as shown in Table 4. No participants consumed 'organic' or 'home made' varieties of bread.

Table 2. Comparisons of characteristics of school aged (8-10 years) participants in iodine nutrition surveys conducted in Queensland

	Current study	2011-12 National Health Measures Survey[24,25]	2003-04 Australian National Iodine Nutrition Study[9]
Median UIC, ug/L (IQR)	144 (120-210)	165.9 (not reported)	136.5 (104.3-183.8)
Age, mean±SD	9.4±0.8	Not reported	9.1±0.4
Sex ratio (F:M)	1:1.5	Not reported	1.3:1
BMI, mean±SD	17.0±2.8	Not reported	17.0
Sample size	30	Not reported	294
Urine collection	Total of 4 samples (2 morning and 2 afternoon)	One spot morning sample	One spot morning sample
Dietary assessment	Food Frequency Questionnaire	24 Food Recall	Not preformed
Methodology to determine UIC	Sandell-Kolthoff spectrophotometric	Plasma-mass spectrometry	Sandell-Kolthoff spectrophotometric
Social economic status, %		Not reported	Not reported
Lower third	7%		
Middle third	10%		
Upper third	83%		

UIC: urinary iodine concentration.

Table 3. Median intake of foods consumed by school aged children considered to be main sources of dietary iodine

Survey	Current survey	National Health Measures Survey 2011-2012[25]	National Nutrition Survey 1995[9]
Age of children (years)	8.0-10.9	9-12	8-11
Bread (g) ± SE	65.0±6.7	76.0±6.0	91.0±NA

DISCUSSION

This is the first mainland Australian study to report iodine fortified bread as statistically significant predictor of UIC since the iodine prophylaxis program began. The samples from school aged children within this cohort were classified as iodine sufficient, with a median UIC of 143.8 ug/L with no samples being above the cut off for excessive UIC. Surprisingly, the median UIC of this cohort was only 6.5 ug/L greater than the median UIC of QLD school aged children prior to iodine fortification, and was substantially lower than the expected increase of 45.9 ug/L. Nevertheless, bread consumption was the only food identified to have a significant, positive, influence on UIC and thus the iodine fortification of bread has had a considerable impact on the iodine status of these children.

This study is greatly limited by its small sample size, however, by collecting multiple spot samples from each participant, the large variance typically affecting the distribution of UIC samples within a group was reduced. As described elsewhere,[24] the adjustment for inter and intra variability in UIC reduced the coefficient of variance by 34.7%. This reduction is comparable to larger iodine surveys where the same adjustment was performed using larger sample sizes.[22,25] Furthermore, the total number of spot UIC samples used in this adjustment (n=120) exceeded the recommendation of 86 spot samples required for ±10% precision range with 90% CI.[26]

In this circumstance, the sample size was adequate to detect the significance of bread consumption but not the difference in UIC between pre and post iodine fortification cohorts. Although the method of recruitment may have impacted on the length of the recruitment process, participant demographic profiles enrolled in the current survey were comparable to larger nutrition surveys (Table 2). As previously mentioned, the statistical adjustment performed by the current study to reduce the impact of variability, in the addition to including an afternoon sample in the analysis improved the accuracy of the sample interpretation.[27]

Recently, the Australian Government released data from the 2011-2012 National Health Measures Survey (NHMS). It reported a median UIC of 165.9 ug/L for QLD school aged children (aged 8.0-10.9 years)[28] also indicating a iodine sufficient status after iodine fortification. The median UIC reported by the NHMS is 22.1 ug/L greater than the current studies median UIC and 29.4 ug/L greater than the UIC of children prior to iodine fortification. Neither of these studies conducted post iodine fortification, reached the estimated UIC of 180-185 ug/L. Children in both the current study and the NHMS survey consumed less bread than that reported by the National Nutrition Survey (Table 3) used by FSANZ to estimate expected changes in dietary iodine, and this could explain why the expected median UIC was not reached. Bread products were reported by the NHMS to be a significant contributor to UIC for the general population, however, the level of this significance was not identified for children 8.0-10.9 years.[29] Although there were differences in sample size, methodology and geography, the results of both of these surveys were comparable reaffirming that the iodine fortification of bread significantly impacted the iodine status of school aged children.

Following mandatory iodine fortification in New Zealand, the median UIC of New Zealand school children aged 8-10 years increased from 68 ug/L to 113 ug/L after iodine fortification was introduced to bread. As observed in the current study the consumption of bread was significantly (p=0.017) associated with increasing UIC.[30] Likewise bread was the main contributor to iodine status within the New Zealand cohort. Although prior to fortification, dietary modelling to predict the outcome of iodine fortification in bread was not available for this age group, in other groups the observed increase in UIC also did not reach expected levels.[31] As with the Australian experience, it could be hypothesised that the assessments made by FSANZ to predict the outcome of iodine fortification were also over estimated.

Typically dairy products, particularly milk, have been described as important contributors to iodine status in other populations.[32] The current study found no significant impact of milk consumption on iodine status, which was also consistent with New Zealand's findings.[30] The National Total Diet Study reported the mean iodine concentration of Australian milk to be 133-159 ug/L,[23] and New Zealand milk to be 94-102 ug/L.[33] These concentrations were remarkably lower than countries where milk is a significant contributor, such as the United Kingdom (UK), where the average milk concentration of iodine is 300 ug/L.[32] Furthermore, the practice of using iodophors in at least one milk sanitation procedure is adopted by

Table 4. Predictors of urinary iodine concentration in univariate linear regression analyses

Predictor	Standardised coefficient (β)	t	p
Bread	0.37	2.10	0.04
Milk	0.10	0.54	0.58
Egg	0.30	1.70	0.09
Yoghurt	0.01	0.02	0.98
Sushi	0.09	0.50	0.62
Nori	0.11	0.61	0.54
Saltwater fish	0.09	0.52	0.60

only half of Australian dairy farmers,[33] whist the use of iodophors is routinely recommended in the UK.[34] As the use of iodophers has been shown to directly impact the iodine concentration of corresponding milk,[35] its limited use may explain why milk may not be a major contributor of dietary iodine in this Australian cohort.

International bodies advise that iodine fortification should be monitored following implementation to evaluate the effectiveness of iodine fortification, and thus maintain its purpose.[1,7] Importantly this study confirmed that the objective to positively influence the iodine status of school aged children through the means of iodine fortification using bread was successful although not to the expected level. The iodine status of school aged children in this cohort was greater than that of Queensland school aged children prior to iodine fortification, however, there was no indication of excessive iodine status. Therefore concerns of iodine excess as result of iodine fortification are not applicable to this group of children. Further investigations are required to determine the level of significance iodine fortification of bread has had in other regions of Australia and whether its impact has been successful in alleviating iodine deficiency in vulnerable groups.

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AUTHOR DISCLOSURES
The authors have nothing to disclose.

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