Factors associated with inadequate urinary iodine concentration among pregnant women in Mbeya region, Tanzania.

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Abstract

Background

Insufficient and above WHO-recommended levels of iodine intake during pregnancy can lead to serious health outcomes. This study aimed to assess median urine iodine concentration and its associated risk factors among pregnant women in the Mbeya region, Tanzania.

Method

A cross sectional survey involving 420 pregnant women (n=420) aged...
15-49, registered in Reproductive and Child Health Clinics was conducted. Socio-demographic and dietary factors were assessed by structured questionnaire and the urine samples were analyzed using the ammonium persulfate digestion method.

**Results**

Median urinary iodine concentration (mUIC) was 279.4 μg/L and it ranged from 26.1 to 1915 μg/L. Insufficient mUIC (below 150 μg/L) was observed in 17.14% of participants, sufficient mUIC was 24.29% and 58.57% had mUIC above the recommended level (>250 μg/L). Sample women who reported consuming fish in the last 24 hours had an increased risk of insufficient mUIC [Adjusted OR= 2.60 (95%CI 1.31-5.15)] while the risk was lower for those who attended at least primary education [AOR= 0.29 (CI 0.08-0.99)]. Further, sample women resident in Mbarali district, in the oldest age group (35-49) and having a higher socio-economic status were associated with an increased risk of having MUIC above recommended level [AOR=4.09 (CI 1.85-9.01)], [AOR=2.51 (CI 0.99-6.33)] and, [AOR=2.08 (CI 0.91-4.71)] respectively.

**Conclusion**

This study demonstrated a significant association between geographical, age and socio-economic factors and median urine iodine concentration above the WHO-recommended level. Further, this study found association between inadequate iodine in diet and insufficient median urine iodine concentration. Therefore, educational programs on iodine intake should be strengthened.

**Keywords**

Iodine deficiency, medium urine iodine concentration; pregnant women; socio-demographic and dietary risk factors
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Introduction

Iodine insufficiency is a significant global public health concern. This element is a constituent of hormones produced by the thyroid gland namely, triiodothyronine (T3) and thyroxine (T4), and must be consumed in the diet as it cannot be made naturally in the body. A diet low in iodine results in insufficiency that can occur at any age. If iodine requirements are not met, the thyroid is unable to produce thyroid hormone in sufficient quantities, leading to iodine deficiency disorders (IDD) with associated dysfunctional and developmental abnormalities.

The daily iodine intake recommended by the World Health Organization (WHO) is 90 μg for children aged 0-5 years; 120 μg for children aged 6-12 year; and 150 μg for those over 12 years. Pregnant and lactating women the recommended iodine intake is 250 μg daily. Although cretinism is the most severe form of iodine insufficiency, minor iodine deficiency can also result in reduced intellectual ability, limited work capacity due to mental and neurological impairment. In 1994, about 1.6 billion people globally (28.9% of global populations) were suffering from iodine deficiency, 11.2 million were affected by overt cretinism, and 43 million people had at least some degree of intellectual impairment.

In Tanzania, the most recent figures indicate that more than 40% of the populations live in geographical regions prone to iodine deficiency. Previous studies have reported that the southern highlands of Tanzania were areas with a high prevalence of endemic goiter. In 1986, Wachter and colleagues investigated the prevalence of goiter before iodine supplementation program in the Southern highlands of Tanzania among 560 schoolchildren aged between 6 to 19 years old and found that 512 children had goitre (a prevalence of 90%). Goitre decreased to 60% by 1995 and further to 17% in 2004. In the 1990s there was a worldwide progress in reducing IDD through universal salt iodization (USI) legislation passed in Tanzania and many other countries. In 2000, more than 28 counties reduced goiter by more than 20% through USI. The Tanzania Demographic and Health Survey (TDHS) indicates that such IDD variations occur largely because of differences in the use of adequately iodised salt (15+ ppm), with households in urban areas more likely to use adequately iodised salt (81%) than those in rural areas (51%) such as the highlands. As recommended by WHO, Iodine Global Network (IGN) and United Nations Children’s Fund (UNICEF), median Urinary Iodine Concentration (mUIC) is considered the most practical biomarker for the assessment and monitoring of iodine nutrition status in the population.

For USI, where all the salt meant for human consumption is iodized, is the most practical intervention strategy to increase iodine intake. Evidence from multiple sources indicates widespread of USI, as 68% of households have access to iodized salt. USI is an effective way of delivering iodine to individuals and in term, improving cognition in populations exposed to iodine deficiency. USI is also affordable, with annual costs of salt iodization estimated at USD 0.02-0.05 per child, while the costs to prevent child death are estimated at USD 1000. There are also large gains in per Disability-Adjusted Life Years (DALYs), at USD 34-36. Before USI, it was estimated that iodine deficiency leads to losses of USD 35.7 billion in the countries affected, which is significant when compared with an estimated cost of USD 0.5 billion for USI, representing a cost benefit ratio of over 70:1.

Tanzanian legislation on USI was enacted in 1995. This was later revised in 2010, and now, all salt consumed by animals and humans in the country is fortified with iodine. Enforcement of this legislation is challenging in Tanzania, especially in areas where small-scale salt producers operate. As a result, iodized salt is not widely available. Further, although household coverage with iodized salt is above 80% nationally, the coverage of adequately iodized salt is at 47% across Tanzania.
Although USI is arguably the successful health intervention in global history, legal regulations on salt production are rarely sufficient to guarantee dietary change among rural populations that consume mainly subsistence food products. In 2005 UNICEF documented that in many African countries less than thirty per cent of households consume iodized salt despite universal legislation, and even iodized salt may be insufficient to reduce IDD in populations whose diets contain substantial amounts of iodine-depleting foods. With the respect to the estimated more than 10% of Tanzania households which remain at risk in spite of salt iodization legislation, the magnitudes of micronutrients deficiencies among pregnant women in Tanzania, particularly, in rural areas and low socioeconomic status justify more research. There is a dearth of information regarding the burden of, and factors associated with iodine deficiency among pregnant women. In 2010 and 2015, the TDHS reported that the prevalence of iodine deficiency amongst pregnant women was 54%, however, the results of the TDHS were heterogeneous across the regions. There are also concerns relating to excessive iodine intake in pregnancy, because although high iodine intakes are well tolerated by most healthy individuals, in some, excess intake can lead to thyroid conditions such as hyperthyroidism, hypothyroidism, and/or thyroid autoimmunity. As insufficient and excessive iodine consumption in pregnancy can result in negative health impacts, it is imperative to investigate current iodine levels and to assess how current USI interventions affect iodine intake, especially in highland areas of Tanzania. The findings of the present study could be useful especially at regional or local salt facility levels for the future decision making on whether levels of iodine added to fortified salt should be increased or decreased. Given the above, this study aimed to firstly, determine the likelihood of iodine levels being above or at recommended levels in the urine (μg/L) of pregnant women in their second trimester. Secondly, assess the likelihood of IDD or otherwise, differing across socioeconomic groups and locations in Tanzania.

Methods

Study site

Mbeya Region is located in the south-western corner of the southern highlands of Tanzania (Figure 1). The Region lies between latitude 7° and 9° 31’ south of the Equator and between longitude 32° and 35° east of Greenwich. The economy of Mbeya is based mainly on agriculture. Agriculture contributes most of the Region’s cash income mainly from maize, sorghum, cassava, beans and pigeon peas’ production. Generally, annual rainfall varies from 650 mm in Usangu plains and Chunya to 2600 mm on the Northern shores of Lake Nyasa and in the highlands. The Mbeya region has a population of 2,707,410 and, in 2020 the region had 318 health facilities of which 17 were hospitals, 23 health centers, and 278 dispensaries, with 251 of the health facilities (both government, private and faith-based organizations) providing reproductive and child health services.
Study design
A cross-sectional survey of 420 pregnant women (gestation age below 28 weeks) registered at the Reproductive and Child Health Clinics (RCH) from the seven districts of the Mbeya Region. This manuscript is part of the project on improving maternal and adolescent nutrition (IMAN) in Mbeya supported by the UNICEF-Tanzania and the Ministry of Health-Tanzania. The study was carried out from September 2020 to October 2020. This study was conducted in 42 RCH across the seven districts of Mbeya region. The allocation of RCH per district for was based to probability proportional to size: Mbeya District Council (n = 11); Chunya District Council (n = 4); Mbeya City (n = 3); Mbarali District Council (n = 8); Kyela District Council (n = 6); Rungwe District Council (n = 7) and, Busekelo District Council (n = 4). The selected RCH clinics were estimated to provide services to approximately 1036 pregnant women.

Study population
All pregnant women aged 15-49 years who attended the selected RCH clinics within their first and second trimesters (less than 28 weeks of gestation) were invited to participate in the study. A total of 574 pregnant women were eligible, and 420 agreed to take part. Pregnant women who refused to consent and those who were unable to communicate due to illness or taking medication were excluded from the study. Participants in their second trimester, a period during which fetal neurodevelopment is impacted by adequate maternal thyroid function, were included. To eliminate the effects of gestational age on thyroid hormone, participants beyond eight weeks of gestation were excluded.

Sample size and sampling procedure
The prevalence of iodine deficiency among women of reproductive age reported in Tanzania was estimated at 40%. Based on this figure and the population of pregnant women in this region, a sample size of 574 was calculated using the Lwanga and Lemeshow formula with: margin error of 5%; confidence level of 95%; design effect of 1.5 and; an additional of 10% to account for non-response. Only 420 pregnant women agreed to participate and this sample size was considered satisfactory assuming intracluster correlation coefficient (ICC) of 0.10 and, a power of 80%.

The sampling procedure involved two steps: First, a list of 251 government, private and faith-based health facilities providing RCH services in Mbeya region was obtained and used in a random selection of the health facilities to be involved in the study from each district. Given the sampling frame of health facilities in Mbeya, probability proportional to size was performed to allocate the number of facilities per District for inclusion in the survey. Out of 251 health facilities that offer RCH services (eligibility criteria) in Mbeya, forty two facilities were randomly selected for the study. An additional two reserved clusters were included in the survey. Therefore, a total of 44 health facilities offering RCH services located in the Mbeya region were visited and surveyed.

The second step involved the selection of pregnant women for each selected health facility. An eligibility form was used to list all pregnant women attending RCH services in the selected health facility. The resulting list of pregnant mothers served as the sampling frame for the selection of participants who met the inclusion criteria. Systematic Random Sampling was then carried out by using the list of mothers to randomly select required pregnant women for each facility to participate in the survey based on probability and proportion to size sampling for the specific facility.

Data collection
Data were collected through interviews guided by a structured questionnaire and, laboratory analysis of urine samples. A standard structured questionnaire was constructed in English and translated into Kiswahili, a language that is spoken by almost 95% of Tanzanians (see Extended data). To ensure the quality of the translation, back-translation was performed by independent translators and reviewed by field staff in Mbeya. Pre-testing was done to evaluate the quality of the translations in terms of comprehensibility, readability, and relevance to assess face validity.

The interviews were administered by a trained Nurse Midwife in face-to-face interviews with participants, before the collection of urine samples. Initial interviews were administrated to determine various social demographic characteristics and dietary factors concerning iodine status, including participant’s age, marital status, education, household assets possessions, socioeconomic status, parity, stage of pregnancy, and dietary habits.

Urine sample collection and laboratory analysis
A trained Nurse Midwife collected urine samples from consented study participants. The urine samples were collected in a disposable plastic screw caped container of 100 ml. Before urine collection, the approximate volume of urine sample required was pre-marked by a trained Nurse Midwife on urine containers and instructed the participant on collecting her urine in the container. The collected urine sample was stored in the cool-box with a temperature of approximately 2-8°C for 2-4 hours. At the temporary laboratory, the sample was processed, transferred into two 2 ml vials, and then labeled by the trained laboratory technician. The sample into vials was kept stored at -20°C. All urine samples were shifted to TFNC.
laboratory (located in Dar es Salaam) for further analysis within one month. The urine samples were analyzed using the ammonium persulfate digestion method, as previously described by Sandell-Kolthoff reaction. TFNC laboratory is registered and successfully participated in the quality assurance program for Ensuring the Quality of Urinary Iodine Procedures (EQUIP) offered by the Centres for Disease Control and Prevention (CDC), Atlanta, Georgia, USA. The assay accuracy was assessed using reference quality-control urine specimens obtained from the CDC. The assay detection limit was <5.0 μg/L with the coefficient of variation <10%, when compared to the reference method.

Variables
Outcome/response variable

Median UCI as a response variable was split into three categories as per WHO recommended level of iodine micronutrient. The median urine iodine concentration (mUIC) indicated the level of iodine in urine (μg/L) (see Underlying data).

UIC 1 (Iodine <150 μg/L) = Insufficient iodine
UIC 2 (150< Iodine <249 μg/L) = Sufficient iodine
UIC 3 (Iodine >250 μg/L) = Above WHO recommended/excessive iodine intake

Independent variables/predictors

The study includes a set of independent variables to understand the extent and variations between the levels of iodine micronutrients among the participants. Socio-demographic variables assessed included age, residency (district), education level, occupation status, number of pregnancies, visits to the ANC and, upper mid-arm circumference (MUAC), which is the most accurate way to measure fat-free mass outside of a laboratory. Household wealth was also assessed. To do so, durable household assets that indicate wealth such as a radio, television, and telephone were recorded as (1) “available and in working condition” or (0) “not available and/or not in working condition.” Principal component analysis, PCA was then conducted to categorize households into five quartiles of wealth, with 1 being the lowest and 3 the highest. Diet, in specific consumption of certain foods, such as fish, dairy products and processed meat and, refined and baked foods was also assessed among the participants, using 24-hour recalls.

Data analysis

The data were analyzed using Stata v 15.1 (RRID: SCR_012763). Stata is proprietary software but an open-access alternative in which the sequence could have been generated is Microsoft Excel (RRID: SCR_016137). Descriptive statistics were used to summarize the data of study participants. Pearson’s chi-square test and p-values were used to test for the significance of each of the potential risk factors in bivariate analysis. Multinomial logistic regression models were used to adjust for confounders and predict the true association between the dependent and independent variables. All tests were two-tailed, and the significance level was set at p ≤ 0.05.

Ethical approval and informed consent

Ethical clearance was obtained from the National Institute for Medical Research (NIMR) with reference number NIMR/HQ/R.8a/Vol. IX/2589 and appropriate authorization was given from the Regional, Council and health facility level. All eligible subjects were given information about the survey and were asked to sign a written informed consent form before participation.

Results

Descriptive of the study participants

The socio-demographic profile of overall sample is shown in Table 1. In this study, 420 agreed to participate (response rate of 73%). More than half of the respondents belonged to age 15-24 years. The mean age of the pregnant women was 25.49 (± 6.37) years. The majority of the respondents (70%) had primary education, two third of the respondents has been pregnant more than once. The household socio-economic composition of the sample shows a better distribution of all categories of respondents with about one third belong to the poorest quintile. More than two third of the respondents were self-employee (84.5%) followed by not employed (11.9%), and formal employee (3.6%). Improved source of water was reported by 71% of the participants. The distribution of respondents according to dietary habit, more than half of the respondents were reported that they consumed fish (68%) and, more than 90% consumed dairy products.
Table 1. Frequency distribution of the study participant in Mbeya (n = 420).

| Variables                                      | Category            | n   | %    |
|------------------------------------------------|---------------------|-----|------|
| Age group                                      | 15-24               | 215 | 52.18|
|                                                | 25-34               | 147 | 35.68|
|                                                | 35-49               | 50  | 12.14|
| Education level                                | No formal education | 34  | 8.10 |
|                                                | Primary education   | 301 | 71.67|
|                                                | Secondary and above | 85  | 20.24|
| Marital status                                 | Married             | 238 | 56.67|
|                                                | Cohabit             | 133 | 31.67|
|                                                | Single              | 39  | 9.29 |
|                                                | Divorced            | 10  | 2.38 |
| Occupational status                            | Formal employment   | 15  | 3.57 |
|                                                | Self-employment     | 355 | 84.52|
|                                                | Not employed        | 50  | 11.90|
| Antenatal care center (ANC) visit              | 1 visit             | 163 | 38.81|
|                                                | 2-3 visits          | 226 | 53.81|
|                                                | More than 3 visits  | 31  | 7.38 |
| Residence                                      | Chunya District Council | 45  | 10.71|
|                                                | Mbeya District Council | 97  | 23.10|
|                                                | Mbarali District Council | 93  | 22.14|
|                                                | Kyela District Council | 50  | 11.90|
|                                                | Rungwe District Council | 68  | 16.19|
|                                                | Busokelo District Council | 33  | 7.86 |
|                                                | Mbeya City          | 34  | 8.10 |
| Number of pregnancies                          | Primigravida        | 104 | 24.76|
|                                                | Multigravida        | 316 | 75.24|
| Type of water source                           | Improved            | 302 | 71.90|
|                                                | Unimproved          | 118 | 28.10|
| Mid-upper arm circumference (MUAC) categorization | MUAC < 23 cm       | 16  | 3.81 |
|                                                | MUAC ≥ 23 cm-MUAC < 33 cm | 383 | 90.19|
|                                                | MUAC ≥ 33 cm        | 21  | 5.0  |
| Consumption of fish                            | No                  | 287 | 68.3 |
|                                                | Yes                 | 133 | 31.7 |
| Consumption of Dairy products                  | No                  | 381 | 90.7 |
|                                                | Yes                 | 39  | 9.8  |
| Consumption of Processed meat                  | No                  | 410 | 97.6 |
|                                                | Yes                 | 10  | 2.4  |
| Urinary Iodine Concentration (UIC) categorization | Insufficient (UIC 0–149 μg/l) | 72  | 17.14|
|                                                | Sufficient (UIC 150–249 μg/l) | 102 | 24.29|
|                                                | Above recommended (>250 μg/l) | 246 | 58.57|
| Variable               | Category                      | Insufficient (Urinary Iodine Concentration (UIC) 0–149 μg/l) | sufficient (UIC 150–249 μg/l) | Above recommended (>250 μg/l) | Chi-square | P-value |
|------------------------|-------------------------------|-------------------------------------------------------------|--------------------------------|--------------------------------|------------|---------|
|                        |                               | % | n   | %  | n   | % | n   | %  | n   |                 |            |         |
| Age group              | 15-24                         | 17.2 | 37  | 26.9 | 58  | 55.8 | 120 |                  | 4.0208     | 0.403    |
|                        | 25-34                         | 16.3 | 24  | 22.4 | 33  | 61.2 | 90  |                  |            |          |
|                        | 35-49                         | 14.0 | 7   | 16.0 | 8   | 70.0 | 35  |                  |            |          |
| Education level        | No formal education           | 26.4 | 9   | 17.6 | 6   | 55.8 | 19  |                  | 4.314      | 0.634    |
|                        | Primary education             | 15.6 | 47  | 24.9 | 75  | 59.4 | 179 |                  |            |          |
|                        | Secondary and above           | 18.8 | 16  | 24.7 | 21  | 56.5 | 48  |                  |            |          |
| Wealth Index           | 1 tercile                     | 20.7 | 29  | 26.4 | 37  | 52.8 | 74  |                  | 4.7325     | 0.316    |
|                        | 2 tercile                     | 15.7 | 22  | 20.0 | 28  | 64.2 | 90  |                  |            |          |
|                        | 3 tercile                     | 15.0 | 21  | 26.4 | 37  | 58.5 | 82  |                  |            |          |
| Marital status         | Married                       | 18.4 | 44  | 22.2 | 53  | 59.2 | 141 |                  | 2.71       | 0.838    |
|                        | Cohabit                       | 15.0 | 20  | 28.5 | 38  | 56.3 | 75  |                  |            |          |
|                        | Single                        | 17.9 | 7   | 23.0 | 9   | 58.9 | 23  |                  |            |          |
|                        | Divorced                      | 10.0 | 1   | 20.0 | 2   | 70.0 | 7   |                  |            |          |
| Occupational status    | Formal employment             | 20.0 | 3   | 33.3 | 5   | 46.6 | 7   |                  | 4.132      | 0.388    |
|                        | Self-employment               | 17.4 | 62  | 22.5 | 80  | 56.0 | 213 |                  |            |          |
|                        | Not employed                  | 14.0 | 7   | 34.0 | 17  | 52.0 | 26  |                  |            |          |
| Antenatal care center (ANC) visit | 1 visit                  | 17.1 | 28  | 23.9 | 39  | 58.9 | 96  |                  | 3.6999     | 0.498    |
|                        | 2-3 visits                    | 18.5 | 42  | 24.7 | 56  | 56.6 | 128 |                  |            |          |
|                        | More than 3 visits            | 6.4  | 2   | 22.5 | 7   | 70.9 | 22  |                  |            |          |
| Residence              | Chunya DC                     | 6.6  | 3   | 22.2 | 10  | 71.1 | 32  |                  | 31.987     | 0.001    |
|                        | Mbeya DC                      | 21.6 | 21  | 32.9 | 32  | 45.3 | 44  |                  |            |          |
|                        | Mbarali DC                    | 11.8 | 11  | 13.9 | 13  | 74.1 | 69  |                  |            |          |
|                        | Kyela DC                      | 12.0 | 6   | 20.0 | 10  | 68.0 | 34  |                  |            |          |
|                        | Rungwe DC                     | 27.9 | 19  | 25.0 | 19  | 47.0 | 32  |                  |            |          |
|                        | Busokelo DC                   | 24.2 | 8   | 27.2 | 9   | 48.4 | 16  |                  |            |          |
|                        | Mbeya city                    | 11.7 | 4   | 32.3 | 11  | 55.8 | 19  |                  |            |          |
Table 2. Continued

| Variable                      | Category          | Insufficient (Urinary Iodine Concentration (UIC) 0–149 μg/l) | sufficient (UIC 150–249 μg/l) | Above recommended (>250 μg/l) | Chi-square | P-value |
|-------------------------------|-------------------|-------------------------------------------------------------|--------------------------------|------------------------------|------------|---------|
|                               |                   | % n                                                         | % n                           | % N                          |            |         |
| Number of pregnancies         | Primiglavida      | 16.3 17                                                    | 22.1 23                        | 61.5 64                      | 0.527      | 0.768   |
|                               | Multiglavida      | 17.7 55                                                    | 25.0 79                        | 57.5 182                     |            |         |
| Type of water source          | Improved          | 18.5 56                                                    | 23.5 71                        | 57.9 175                     | 0.567      | 0.457   |
|                               | Unemployed        | 13.5 16                                                    | 26.2 31                        | 60.1 71                      |            |         |
| Mean- upper arm circumference (MUAC) categorization | MUAC < 23 cm | 12.5 2                                                      | 18.7 3                         | 68.7 11                      | 0.987      | 0.912   |
|                               | MUAC ≥ 23 cm-MUAC < 33 cm | 17.4 67                                               | 24.2 91                        | 58.2 223                     |            |         |
|                               | MUAC ≥ 33 cm      | 14.2 3                                                      | 28.5 6                         | 57.1 12                      |            |         |
| Consumption of fish           | No                | 13.7 38                                                    | 26.8 74                        | 59.4 164                     | 7.5619     | 0.023*  |
|                               | Yes               | 23.6 34                                                    | 19.4 28                        | 56.9 82                      |            |         |
| Consumption of Dairy products | No                | 17.1 60                                                    | 23.7 83                        | 59.0 206                     | 0.2912     | 0.865   |
|                               | Yes               | 16.9 12                                                    | 26.7 16                        | 56.3 40                      |            |         |
| Consumption of Processed meat | No                | 17.2 71                                                    | 23.8 98                        | 58.8 242                     | 2.0475     | 0.359   |
|                               | Yes               | 11.1 1                                                     | 44.4 4                         | 44.4 4                       |            |         |
| Consumption of refined and baked | No      | 18.9 14                                                    | 24.3 18                        | 56.7 42                      | 0.2158     | 0.898   |
|                               | Yes               | 16.7 58                                                    | 24.2 84                        | 58.9 204                     |            |         |

*Represents p value: p < 0.05.
Urinary iodine concentration (UIC)

The median UIC in the present study was 279.4 μg/L, and it ranged from 26.1-1915 μg/L. According to the UIC results, 17.14% of participants had an insufficient iodine intake, 24.29% had sufficient urine iodine concentration, and 58.57% had above the WHO recommended level of iodine in urine (Table 1).

Bivariate analysis

Table 2 presents a cross-tabulation of the median UIC status (mUIC) and socio-demographic, economic and dietary factors among pregnant women in Mbeya. Of 215 participants aged between 15-24 years, 17% had UIC (0–149 μg/l) that would be considered insufficient, and 55.8% had UIC (>250 μg/l) above the WHO recommended levels. The residence profile of the sample shows that, Chunya and Mbarali DCs have the highest percentage (above 70%) of the WHO recommended UIC among the pregnant women in Mbeya. On other hand, Rungwe DC had the highest percentage (27.9%) of participants with insufficient urine iodine concentrations. From the 133 participants who had fish in their diet, UIC was insufficient in 23%, sufficient in 19.4%, and 56.9% had above the WHO recommended level.

Multivariate analysis

The multivariate analysis are presented in Tables 3a and 3b. The chi-square model (63.51) was 0.0176, with p < 0.05.

| Independent                  | Category     | OR    | 95% confidence interval for OR | P-value |
|------------------------------|--------------|-------|--------------------------------|---------|
| Consumption of fish          | No           | 1     |                                |         |
|                              | Yes          | 2.60  | 1.31 – 5.15                    | 0.006*  |
| Consumption of Dairy products| No           | 1     |                                |         |
|                              | Yes          | 0.96  | 0.41 – 2.28                    | 0.940   |
| Consumption of Processed meat| No           | 1     |                                |         |
|                              | Yes          | 0.32  | 0.03 – 3.19                    | 0.334   |
| Consumption of refined and baked| No     | 1     |                                |         |
|                              | Yes          | 0.79  | 0.33 – 1.91                    | 0.609   |
| Residence                    | Mbeya district council (DC) | 1     |                                |         |
|                              | Chunya DC    | 0.38  | 0.08 – 1.65                    | 0.199   |
|                              | Mbarali DC   | 1.15  | 0.38 – 3.44                    | 0.793   |
|                              | Kyela DC     | 0.85  | 0.25 – 2.92                    | 0.809   |
|                              | Rungwe DC    | 2.43  | 0.95 – 6.19                    | 0.061   |
|                              | Busokelo DC  | 1.79  | 0.52 – 6.11                    | 0.351   |
|                              | Mbeya city   | 0.77  | 0.18 – 3.24                    | 0.732   |
| Age group                    | 15-24        | 1     |                                |         |
|                              | 25-34        | 1.11  | 0.50 – 2.44                    | 0.782   |
|                              | 35-49        | 1.45  | 0.42 – 4.98                    | 0.553   |
| Wealth Index                 | 1 quantile   | 1     |                                |         |
|                              | 2 quantile   | 1.62  | 0.62 – 4.26                    | 0.321   |
|                              | 3 quantile   | 1.28  | 0.42 – 3.90                    | 0.663   |
| Education level              | No formal education | 1     |                                |         |
|                              | Primary education | 0.29 | 0.08 – 0.99                    | 0.049*  |
|                              | Secondary and above |       |                                |         |
### Table 3a. Continued

| Variable | Category | OR  | Lower bound | Upper bound | P-value |
|----------|----------|-----|-------------|-------------|---------|
| Mean upper arm circumference (MUAC) categorization | MUAC < 23 cm | 1.27 | 0.18 | 8.90 | 0.807 |
| | MUAC ≥ 23 cm-MUAC < 33 cm | 1.17 | 0.10 | 13.31 | 0.896 |
| | MUAC ≥ 33 cm | 1.01 | 0.25 | 4.05 | 0.985 |
| Number of pregnancies | Primigravida | 0.83 | 0.34 | 2.01 | 0.683 |
| | Multigravida | 0.74 | 0.13 | 4.27 | 0.745 |

*Represents p value: p < 0.05.

### Table 3b. Multivariate analysis on factors associated with values above the WHO recommendation for mUIC among pregnant women in Mbeya (n = 420).

| Variable | Category | OR  | Lower bound | Upper bound | P-value |
|----------|----------|-----|-------------|-------------|---------|
| Consumption of fish | No | 1 | | | |
| | Yes | 1.24 | 0.71 | 2.15 | 0.438 |
| Consumption of Dairy products | No | 1 | | | |
| | Yes | 0.90 | 0.46 | 1.73 | 0.754 |
| Consumption of Processed meat | No | 1 | | | |
| | Yes | 0.50 | 0.11 | 2.31 | 0.379 |
| Consumption of refined and baked | No | 1 | | | |
| | Yes | 0.99 | 0.50 | 1.96 | 0.998 |
| Residence | Mbeya DC | 1 | | | |
| | Chunya DC | 2.05 | 0.84 | 4.96 | 0.110 |
| | Mbarali DC | 4.09 | 1.85 | 9.01 | 0.000* |
| | Kyela DC | 2.15 | 0.88 | 5.23 | 0.089 |
| | Rungwe DC | 1.49 | 0.67 | 3.29 | 0.321 |
| | Busokelo DC | 1.55 | 0.56 | 4.26 | 0.390 |
| | Mbeya city | 1.45 | 0.54 | 3.94 | 0.456 |
| Age group | 15-24 | 1 | | | |
| | 25-34 | 1.47 | 0.81 | 2.69 | 0.201 |
| | 35-49 | 2.51 | 0.99 | 6.33 | 0.050* |
| Wealth Index | 1 tercile | 1 | | | |
| | 2 tercile | 1.41 | 0.66 | 3.03 | 0.367 |
| | 3 tercile | 2.08 | 0.91 | 4.71 | 0.079 |
| Education level | No formal education | 1 | | | |
| | Primary education | 1.04 | 0.37 | 2.94 | 0.929 |
| | Secondary and above | 1.18 | 0.35 | 3.95 | 0.777 |
| MUAC categorization | MUAC < 23 cm | 1 | | | |
| | MUAC ≥ 23 cm-MUAC < 33 cm | 1.01 | 0.25 | 4.05 | 0.985 |
| | MUAC ≥ 33 cm | 0.74 | 0.13 | 4.27 | 0.745 |
| Number of pregnancies | Primigravida | 0.64 | 0.32 | 1.26 | 0.203 |

*Represents p value: p < 0.05.
Table 3a presents a multivariate analysis of the factors related to the group of women who are below the WHO recommendation for mUIC among pregnant women. After taking into account confounding factors, it was found that dietary and socio-demographic factors were significantly associated with the low WHO recommendation for mUIC among pregnant women. The analysis showed that pregnant women who consume fish were more likely to have a low WHO recommendation for mUIC, with an Adjusted OR of 2.60 (95% CI 1.31-5.15). In contrast, pregnant women who had at least primary education were less likely to have a low WHO recommendation for mUIC, with an Adjusted OR of 0.29 (95% CI 0.08-0.99). Table 3a presents a multivariate analysis of the factors related to the low WHO recommendation for mUIC among pregnant women. After taking into account confounding factors, it was found that dietary and socio-demographic factors were significantly associated with the low WHO recommendation for mUIC among pregnant women. The analysis showed that pregnant women who consume fish were more likely to have a low WHO recommendation for mUIC, with an Adjusted OR of 2.60 (95% CI 1.31-5.15). In contrast, pregnant women who had at least primary education were less likely to have a low WHO recommendation for mUIC, with an Adjusted OR of 0.29 (95% CI 0.08-0.99).

Table 3b presents a multivariate analysis of the factors related to the group of women who are above the WHO recommendation for mUIC among pregnant women. After taking into account confounding factors, it was found that only socio-demographic factors were significantly associated with the above WHO recommendation for mUIC among pregnant women. Thus, pregnant women resident in Mbarali DC, aged between 35-49 years and belonging to the highest socio-economic status [Adjusted OR = 4.09 (95% CI 1.85-9.01)], [Adjusted OR = 2.51 (95% CI 0.99-6.33)] and [Adjusted OR = 2.08 (95% CI 0.91-4.71)] respectively were at greatest risk of excess mUIC.

Discussion
This is the first population-based cross-sectional study to assess the magnitude of iodine status and the association with socio-demographic factors and diet in Tanzanian pregnant women. The findings of the study are important since iodine insufficiency is the most prevalent micronutrient insufficiency, affecting 28.9% of the world population, particularly affecting women living in developing countries. Iodine deficiency disorders in Tanzania are high with the most recent figures indicating that more than 40% of the population in the country lives in geographical regions prone to iodine insufficiency. However, this data is largely outdated, as more recent data as well as the most recent efforts to reduce iodine insufficiency have focused on primary school children in Tanzania, whilst the iodine micronutrient status among pregnant women has been limited in recent years. A reanalysis of the 2010 Tanzania demographic and health survey reported that 54% of pregnant women had subclinical iodine deficiency.

The present research looks for potential socio-demographic and dietary factors associated with levels of mUIC both below and above WHO recommendations. Our study found that residence in Mbarali district, age between 35-49 years, and belonging to high socio-economic status were associated with an increasing odds of pregnant women having excess mUIC levels. This could be explained by the fact that the Mbarali district is home to the Ruaha National Park, which attracts food products to its business district that are preserved by iodized salt. As previous documented the frequency and intake of food products preserved or snacks sprinkled with iodated salt were one of the four scenarios of excessive iodine intakes, the other three were: close to salt factories; losses less than expected because of not passing through all the steps in the salt marketing chain, and districts close to large salt processing factories adhering to USI. Thus, it is important to continue monitoring the distribution, packaging and handling iodated salt and, similarly to monitor thyroid function and its associated disorders in this population since excessive iodine is thought to matter most at the time of fetal development.

This study also looked for evidence of the factors likely to be influencing the prevalence of insufficient mUIC among pregnant women in Mbeya. We found that consumption of fish was associated with lower mUIC. The poor iodation technologies and supply of potassium iodate in many small and medium salt producers could be the reason behind insufficient iodine observed in this survey. Moreover, during pregnancy there are variations in the functionality of the thyroid. This can increase the risk of insufficient iodine intake for some mothers. As such, predicting UIc based on usage of iodized salt alone, may not be accurate. However, other studies have documented that freshwater fish may contain Iodine at levels that can improve daily Iodine intake.

In countries with successful USI programs, studies have reported an optimal median UIC in pregnant women in comparison to Tanzania. As such, USI remains the most cost-effective strategy for achieving reduced IDD. However, the full implementation of USI remains a challenge in many sub-Saharan African countries including Tanzania, largely due to the lack of adequate enforcement and, the inadequate monitoring of small-scale salt producers who often do not comply with USI legislation.
This analysis also indicated that pregnant women who had a primary school education were at lower risk of iodine insufficiency; however, further studies are needed to investigate this association. Similar evidence has been reported in previous studies among primary school children in Tanzania alerts policymakers to consider adjusting the amount of iodine added to salt along with the obligation of reducing discretionary foods and salt intake.

WHO recommended an increased iodine intake for pregnant women, although evidence is weak. Indeed, detrimental effects from more than adequate and excessive iodine intake have been reported in general populations. Shi et al. have reported on the associations between UIC and thyroid health among pregnant women and recommend a lower limit for maternal iodine intake during pregnancy than that currently advised by the WHO. This is also an area in need of further investigation. The question remains how much iodized salt pregnant women in Mbarali district should consume, and at what concentration. As our findings illustrate, it is extremely difficult for USI to avoid not only deficiency but also excess, especially in mixed urban and rural settings in areas with complex salt production by small and large producers.

The strength of this study is in the fact that its large population-based sample size managed to demonstrate important factors that could explain factors associated with both excessive and insufficient iodine among pregnant women. However, there were limitations as follows: first, the use of UIC to determine individual iodine status could be limited due to the potential for misclassification of participants because of day-to-day variations. Second, UIC reflects recent iodine intake or exposure rather than chronic individual iodine status. Third, the use of iodized salt was not assessed in this study. Finally, it would have been useful to have a non-pregnant control group to help ascertain whether lower mean UIC concentrations during pregnancy could be attributed to pregnancy itself or the diet.

Conclusion
This study demonstrated a significant association between geographical factors (residence in the Mbarali district) and median urine iodine concentration above WHO recommended. Further, this study found association between inadequate iodine in diet and insufficient median urine iodine concentration as indicated by the World Health Organization recommendation. Therefore, educational programs on iodine intake should be strengthened as attending at least primary education was found to be a protective factor for insufficient median urine iodine concentration. This study also recommends further longitudinal studies. Further, attending at least primary education was found to be a protective factor for insufficient median urine iodine concentration. Controlling risk factors through strengthening the USI program to include monitoring excessive iodine exposures will reduce the detrimental effects of iodine during pregnancy. This study also recommend for further longitudinal studies. It illustrates how difficult it is to adjust salt iodation levels so as to avoid both deficiency and excess and the importance of continued monitoring and adjustment of iodation levels at regional and even local levels as needed.

Data availability
Underlying data
Open Science Framework (OSF): Factors associated with inadequate urinary iodine concentration among pregnant women in Mbeya region Tanzania. DOI: https://osf.io/7ysb9/.

This project contains the following underlying data:

- MBMNS_MUIC10082021: This is the SPSS database file that contained all the laboratory assessment variables for the medium urine iodine concentrations.

This project also contains the following extended data:

- Questionnaire English version: This file contains all the questions used to interview pregnant women in Mbeya.
- Questionnaire Swahili version: This file is the Swahili version of Questionnaire.

Data are available under the terms of the Creative Commons Zero “No rights reserved” data waiver (CC0 1.0 Public domain dedication).
Author contributions
Conceptualization, TL, RM, AH. SEJ and GHL; project administration and resources, AS, RN, FK and GHL; formal analysis and writing—original draft, TL, RM, AH, SEI, HAP, AS, RN, FK, ET and GHL; reviewed and edited the manuscript. GB and, RB. All authors: Reviewed and agreed upon the final manuscript.

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We sincerely appreciate health workers assistance in the laboratory data collection and the participation of all pregnant women in this study.

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Current Peer Review Status: ✔️ ✔️

Version 5

Reviewer Report 28 August 2024

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Ted Greiner
Member, Executive Committee; Editor-in-Chief of Association journal World Nutrition (https://worldnutritionjournal.org/index.php/wn), World Public Health Nutrition Association (Ringgold ID: 26716), London, UK

I approve this 5th version.

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Public Health Nutrition

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.

Version 4

Reviewer Report 17 June 2024

https://doi.org/10.5256/f1000research.163953.r270358

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Ted Greiner
Member, Executive Committee; Editor-in-Chief of Association journal World Nutrition (https://worldnutritionjournal.org/index.php/wn), World Public Health Nutrition Association (Ringgold ID: 26716), London, UK
1. "Table 3a. Multivariate analysis on factors associated with the low WHO recommendation" Should end with "values below" or "women below" the WHO recommendation, since you are not commenting on the recommendation itself. The same is true for Table 3b.

Similarly, below the tables, "factors related to the low WHO" should be something like "factors related to the group of women who are below the WHO" and similar for the next paragraph regarding those above the recommendation. The paragraph about 3a is repeated a second time.

2. You write that ref. 19 found "54% of pregnant women with iodine deficiency" but the title of that article should be repeated (subclinical). If this is based on goiter rather than UIC, I suggest mentioning this because goiter in Tanzanian adults is likely related more to past than present IDD. Is it correct that this analysis was done in 2010? (It was published in 2017.) Rather than saying recent attention to pregnant women has been overlooked, I suggest saying it has been limited.

3. "distract" should presumably be district.

4. After saying "In countries with successful USI programs, studies have reported an optimal median UIC in pregnant women." I suggest giving ref. 37 (which is incomplete) if it says that. Then, in comparison, give the median from your study.

5. In the conclusions, the first mention of "This study also recommend for further longitudinal studies." should be deleted. Instead of "recommend for", I suggest "recommends".

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Public Health Nutrition

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 31 Jul 2024

Ray Masumo

We appreciate the time and effort that you and the reviewers dedicated to providing valuable feedback on our manuscript. Thank you very much. Here is a point-by-point response to the reviewers' comments and concerns.

**Results**

**Comment 1:** "Table 3a. Multivariate analysis on factors associated with the low WHO recommendation" Should end with "values below" or "women below" the WHO recommendation, since you are not commenting on the recommendation itself. The same is true for Table 3b.

Similarly, below the tables, "factors related to the low WHO" should be something like "factors related to the group of women who are below the WHO" and similar for the next paragraph regarding those above the recommendation. The paragraph about 3a is repeated a second time.

**Response:** We agree with this comment and have included your suggestion.

**Discussion:**
Comment 2: You write that ref. 19 found “54% of pregnant women with iodine deficiency” but the title of that article should be repeated (subclinical). If this is based on goiter rather than UIC, I suggest mentioning this because goiter in Tanzanian adults is likely related more to past than present IDD. Is it correct that this analysis was done in 2010? (It was published in 2017.) Rather than saying recent attention to pregnant women has been overlooked, I suggest saying it has been limited.

Response: We agree with this comment and have rewritten the discussion section to stipulate that 54% of pregnant women had subclinical iodine deficiency.

Comment 3: "distract" should presumably be district.

Response: Thank you so much for pointing this out and, we have corrected it.

Comment 4: After saying "In countries with successful USI programs, studies have reported an optimal median UIC in pregnant women." I suggest giving ref. 37 (which is incomplete) if it says that. Then, in comparison, give the median from your study.

Response: We agree with this comment and have rewritten the paragraph as suggested.

Conclusion:

Comment 5: In the conclusions, the first mention of "This study also recommend for further longitudinal studies." should be deleted. Instead of "recommend for", I suggest "recommends".

Response: Thank you for pointing this out. We agree with this comment and edited the sentence as suggested.

Competing Interests: The authors declare that there are no conflicts of interest.
1. I think it would be useful to give some of the early provincial school-based survey data from Tanzania showing that Mbeya had one of the highest prevalences of goiter, thus indicating the value of having chosen it for this study.

2. Is there no more modern reference than your #5? Its data are over 30 years old.

3. “Although USI is arguably the successful [health] intervention in global history”

4. “UNICEF documented that [in] many African countries ”

5. “whose diets contain sufficient [should presumably read “substantial”] amounts of iodine-depleting foods”

6. “more than 10% of Tanzania households [which] remain at risk”

7. “It is also necessary to set upper as well as lower limits for maternal iodine intake to ensure optimal health outcomes are achieved” - This does not seem to be a task related to the present paper. On the other hand, its findings could be useful in future decision making regarding whether levels of iodine added to fortified salt should be increased or decreased, especially if such decisions can be taken at regional or local salt facility levels.

8. “All pregnant women aged 15-49 years who attended [the selected RCH] clinics within their first and second trimesters ”

9. “420 agreed to take part, as per the calculated sample size” - The final clause in this statement is premature and in any case incorrect and needs to be reworded or deleted.

10. “medium urine iodine concentration” Presumably should be “median”?

11. “Median UCI as a response variable was split into three categories as per WHO recommended level of iodine micronutrient. A new variable called medium urine iodine concentration (UIC) was developed to indicate the level of iodine in urine (μg/L) (see Underlying data).21” - This is unclear and seems unnecessary. Surely each UIC was simply placed into one of the three existing WHO categories.

12. Is the wealth index in Table 1 really quintiles? If so, which one is completely absent? If it is terciles, which seems likely, remove it from the table, as 33% in each category is literally the definition of a tercile, not a finding.

13. In Table 2, the n's are missing from secondary education.

14. I don't see the point in Table 3. It cannot be interpreted on its own. It does not even mention fish. Seeing it does not add any information or clarity to what is presented in the text and it only includes a few values, which could be given in the text if important.

15. “This research looks for evidence of the factors influence excess of UIC above the WHO recommended level.” Suggestion: “evidence of the factors likely to be influencing the prevalence of excess UIC”
16. “Geographical factors i.e. residence in Mbarali district, and the aged between 35-49 years were play an important role in increasing the risk of pregnant women having excess UIC above the WHO recommended level: [Adjusted OR = 4.09 (95% CI 1.85-9.01)] and, [Adjusted OR = 2.51 (95% CI 0.99-6.33)] respectively.” - This is confusing. It is written as if it's evidence from the present study, but this was not included in the results section. Then it is referenced as if it is Assey's finding. The next sentence (which is the one that presumably should be cited for Assey) is also confusing. Why would being closed to earlier access to iodated salt be associated with increased risk of excess?

17. In this sentence: “The poor iodation technologies and supply of potassium iodate in many small and medium salt producers could be the reason behind consumption of freshwater fish and insufficient iodine observed in this survey” I suggest deleting “consumption of freshwater fish and“ since it is illogical.

18. “This analysis also indicated that pregnant women who had a primary school education were at lower risk of iodine insufficiency [Adjusted OR = 0.29 (95% CI 0.08-0.99)], “ was also not presented in the results section.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Yes

Are sufficient details of methods and analysis provided to allow replication by others?
Yes

If applicable, is the statistical analysis and its interpretation appropriate?
Yes

Are all the source data underlying the results available to ensure full reproducibility?
Yes

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: My areas of expertise are infant feeding and combatting micronutrient deficiencies (A, Fe, I) at public health levels. I am co-author on several publications related to IDD in Tanzania and worked on the issue some in the field there, for example a school goiter survey. I was involved with UIC measurement surveys, but am not myself expert on nor have I ever personally utilized laboratory methods in research.

I confirm that I have read this submission and believe that I have an appropriate level of
expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Author Response 22 Apr 2023

Ray Masumo

We appreciate the time and effort that you have dedicated to providing constructive feedback on our manuscript entitled ‘Factors associated with inadequate urinary iodine concentration among pregnant women in Mbeya region Tanzania’. Thank you very much.

Here is a point-by-point response to the reviewers’ comments and concerns.

**General comment:**

*Comment 1:* This is a useful, reasonably well-done study on an important issue. The OR data referred to in the discussion and any other OR data that was analyzed need to be presented in the Results section.

*Response:* Thank you very much for pointing this out and we have incorporated your suggestion throughout the manuscript.

**Specific comments:**

*Comment 1:* I think it would be useful to give some of the early provincial school-based survey data from Tanzania showing that Mbeya had one of the highest prevalences of goiter, thus indicating the value of having chosen it for this study.

*Response:* We agree with this comment and have added more information on the early provincial school-based survey data from Tanzania showing that Mbeya had one of the highest prevalence of goiter.

*Comment 2:* Is there no more modern reference than your #5? Its data are over 30 years old.

*Response:* Thanks for pointing this out. We have replaced reference #5 with the recent reference.

*Comment 3:* “Although USI is arguably the successful [health] intervention in global history”

*Response:* Thank you very much for pointing this out and we have incorporated your suggestion.

*Comment 4:* “UNICEF documented that [in] many African countries”

*Response:* We agree with this comment and incorporated the suggestion.

*Comment 5:* “whose diets contain sufficient [should presumably read “substantial”] amounts of iodine-depleting foods”
Response: We agree with this comment and replaced the word ‘sufficient’ as suggested.

Comment 6: “More than 10% of Tanzania households [which] remain at risk”

Response: Thank you very much for pointing this out and, we have incorporated your suggestion.

Comment 7: “It is also necessary to set upper as well as lower limits for maternal iodine intake to ensure optimal health outcomes are achieved” - This does not seem to be a task related to the present paper. On the other hand, its findings could be useful in future decision-making regarding whether levels of iodine added to fortified salt should be increased or decreased, especially if such decisions can be taken at regional or local salt facility levels.

Response: Thank you for pointing this out and we have rephrased the statement for clarity.

Comment 8: “All pregnant women aged 15-49 years who attended [the selected RCH] clinics within their first and second trimesters”

Response: We agree with this comment and have incorporated your suggestion.

Comment 9: “420 agreed to take part, as per the calculated sample size” - The final clause in this statement is premature and in any case incorrect and needs to be reworded or deleted.

Response: Thank you for this suggestion and we have incorporated your suggestion.

Comment 10: “medium urine iodine concentration” Presumably should be “median”?

Response: We agree with this comment and make the correction as suggested.

Comment 11: “Median UCI as a response variable was split into three categories as per WHO recommended level of iodine micronutrient. A new variable called medium urine iodine concentration (UIC) was developed to indicate the level of iodine in urine (μg/L) (see Underlying data).21” - This is unclear and seems unnecessary. Surely each UIC was simply placed into one of the three existing WHO categories.

Response: We highly appreciate the reviewers' insightful and helpful comments on our manuscript. We have rewritten the statement for clarity.

Comment 12: Is the wealth index in Table 1 really quintiles? If so, which one is completely absent? If it is terciles, which seems likely, remove it from the table, as 33% in each category is literally the definition of a tercile, not a finding.

Response: We agree with this comment and make the correction as suggested.

Comment 13: In Table 2, the n’s are missing from secondary education

Response: Thank you for pointing that out, and we added the missing n's and percentages
Comment 14: I don't see the point in Table 3. It cannot be interpreted on its own. It does not even mention fish. Seeing it does not add any information or clarity to what is presented in the text and it only includes a few values, which could be given in the text if important.

Response: We agree with this comment and re-write the description of Table 3.

Comment 15: “This research looks for evidence of the factors influence excess of UIC above the WHO recommended level.” Suggestion: “evidence of the factors likely to be influencing the prevalence of excess UIC”

Response: We agree with this comment and incorporated your suggestion.

Comment 16: “Geographical factors i.e. residence in Mbarali district, and the aged between 35-49 years were play an important role in increasing the risk of pregnant women having excess UIC above the WHO recommended level: [Adjusted OR = 4.09 (95% CI 1.85-9.01)] and, [Adjusted OR = 2.51 (95% CI 0.99-6.33)] respectively.” - This is confusing. It is written as if its evidence from the present study, but this was not included in the results section. Then it is referenced as if it is Assey’s finding. The next sentence (which is the one that presumably should be cited for Assey) is also confusing. Why would being closed to earlier access to iodated salt be associated with increased risk of excess?

Response: We agreed with the comment and we have re-write the paragraph for clarity.

Comment 17: In this sentence: “The poor iodation technologies and supply of potassium iodate in many small and medium salt producers could be the reason behind consumption of freshwater fish and insufficient iodine observed in this survey” I suggest deleting “consumption of freshwater fish and” since it is illogical.

Response: We agree with this comment and incorporate the suggestion.

Comment 18: “This analysis also indicated that pregnant women who had a primary school education were at lower risk of iodine insufficiency [Adjusted OR = 0.29 (95% CI 0.08-0.99)],” was also not presented in the results section.

Response: Thank you for pointing that out, and we have re-write the paragraph for clarity.

Competing Interests: We declare no competing interest.
Urine samples
  ○ please indicate time of the day the samples were collected. Was it morning urine or random (i.e. collected at any time of the day)?

Variables
  ○ 'Median UCI' - misspelt

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.
Department of Human Nutrition and Consumer Sciences, Sokoine University of Agriculture, Morogoro, Tanzania

Abstract:
1. Use of the word 'insufficient' should be consistent throughout the article.
2. Conclusion does not state explicitly the factors associated with insufficient/sufficient UIC.

Introduction:
1. Provide explanation as to why highland regions have highest prevalence of IDD considering that Tanzania has been implementing salt iodisation programmes for many years?

Method:
1. Change 'Ante-natal Care Clinics' to 'Reproductive and Health Clinics' and use it consistently throughout the document.
2. Explain adequately how sampling procedure was carried out.
3. Was the questionnaire pre-tested before translation?
4. "interviews were done by health professional" - which cadre?
5. Provide more information about the conditions for storage of the urinary samples in the field, transportation and storage at the laboratory before analysis and for how long were the samples stored before analysis. What distance from the field to the laboratory? This is important because iodine in urine is known to undergo changes after some time.
6. Was there any effort to ensure that women at various stages of pregnancy were well represented in the sample? It will also be useful to know of the sample size recruited, what was the stage of pregnancy for each participant? This information is missing.
7. Why Mbeya region? Provide justification.

Results:
1. Area of residence seemed to have an influence on iodine status of pregnant women, it was expected to see a good description of the study areas in this manuscript. The information is missing. Could the authors strive to provide this information?
2. It will also be useful to know the stage of pregnancy (1st, 2nd, 3rd, trimester) of participants and if there were any association/interaction between area of residence, other factors and UIC.
3. Presentation of Tables should be improved; instead of brackets, authors could include columns for easy of reading.
4. What was the consumption of iodised salt? This could be one of the contributing factors to high levels of UIC observed in some areas of the study. But also consumption of foods especially vegetables of the brassica group that are known to have compounds that interact with iodine in the gut.
5. Clarification about consumption of processed meat.

6. Clearly stipulate factors that are associated with UIC in this section. Factors are not very clear.

Discussion:
1. How were the identified factors influenced iodine status? These have not been adequately articulated in this manuscript.

2. Was the use of iodised salt investigated in the present study? What is the level of consumption among pregnant women? What is the availability and accessibility to iodised salt in the study areas?

3. Authors indicated some strengths of the study; large sample size; but also identified limitations? One of the limitations was that they did not investigate use of iodised salt in the study area. This is a serious omission considering that iodised salt contributes to iodine intake and therefore UIC at least for a large part of the population. Additionally, there was no control group, which again raises concern over the design of this study.

4. Conclusion: It is a repeat of statement of results and not conclusion. Authors should look at the objectives of the study and provide a concrete conclusion as to whether the objectives were attained and what are the implications to individual women and society in general.

Is the work clearly and accurately presented and does it cite the current literature?
Partly

Is the study design appropriate and is the work technically sound?
Partly

Are sufficient details of methods and analysis provided to allow replication by others?
Partly

If applicable, is the statistical analysis and its interpretation appropriate?
Partly

Are all the source data underlying the results available to ensure full reproducibility?
Partly

Are the conclusions drawn adequately supported by the results?
Partly

Competing Interests: No competing interests were disclosed.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.
Author Response 05 Aug 2022

Ray Masumo

We appreciate the time and effort that you and the reviewer have dedicated to providing valuable feedback on our manuscript. Thank you very much.

Here is a point-by-point response to the reviewer’s comments and concerns.

Abstract

Comment 1: The use of the word ‘insufficient’ should be consistent throughout the article.
Response: The word ‘insufficient’ instead of ‘deficiency’ will be used throughout the manuscript.

Comment 2: Conclusion does not state explicitly the factors associated with insufficient/sufficient UIC
Response: The conclusion will carefully be rephrased and show factors associated with insufficient/sufficient UIC.

Introduction:

Comment 1: Provide an explanation as to why highland regions have highest prevalence of IDD considering that Tanzania has been implementing salt iodisation programs for many years?
Response: The explanation has been provided on page 11, discussion section, paragraph 4 ‘However, the full implementation of USI remains a challenge in many sub-Saharan African countries including Tanzania, largely due to the lack of adequate enforcement and, the inadequate monitoring of small-scale salt producers who often do not comply with USI legislation’.

Method:

Comment 1: Change ‘Ante-natal Care Clinics’ to ‘Reproductive and Health Clinics’ and use it consistently throughout the document.
Response: The word ‘Ante-natal Care Clinics’ will replace ‘Reproductive and Health Clinics’ throughout the document.

Comment 2: Explain adequately how sampling procedure was carried out.
Response: We agree, and the sampling procedures will be explained in more detail.

Comment 3: Was the questionnaire pre-tested before translation?
Response: Thank you very much for pointing this out. The questionnaire was pre-tested after translation.

Comment 4: Interviews were done by health professional” - which cadre?
Response: Interviews were done by trained Nurse Midwives (we will specify the cadre of health professionals).

Comment 5: Provide more information about the conditions for storage of the urinary samples in the field, transportation, and storage at the laboratory before analysis and for how long were the samples stored before analysis. What distance from the field to the laboratory? This is
important because iodine in urine is known to undergo changes after some time.

Response: We agree - more information on the conditions of the urinary samples stored in the field, transportation, and storage at the laboratory before analysis will be added.

Comment 6: Was their any effort to ensure that women at various stages of pregnancy were well represented in the sample? It will also be useful to know of the sample size recruited, what was the stage of pregnancy for each participant? This information is missing.

Response: Thank you very much for pointing this out. The inclusion and exclusion criteria of this study were mentioned on page 4, paragraph 2 ‘Participants in their second trimester, a period during which fetal neurodevelopment is impacted by adequate maternal thyroid function, were included. To eliminate the effects of gestational age on thyroid hormone, participants beyond eight weeks of gestation were excluded.

Comment 7: Why Mbeya region? Provide justification.

Response: This study is the part of IMAN project piloted in Mbeya and supported by the UNICEF-Tanzania and the Ministry of Health - Tanzania aims to demonstrate how the country can sustainably scale up delivery of a comprehensive package of interventions to improve maternal nutrition (Interventions, Platforms, and Enabling Environment/System strengthening).

Results:

Comment 1: Area of residence seemed to have an influence on iodine status of pregnant women, it was expected to see a good description of the study areas in this manuscript. The information is missing. Could the authors strive to provide this information?

Response: We agree and more information on the area of residence will be added.

Comment 2: It will also be useful to know the stage of pregnancy (1st, 2nd, 3rd, trimester) of participants and if there were any association/interaction between area of residence, other factors and UIC.

Response: The study participants were only pregnant women in the second trimester and the reason behind this was to avoid the effects of gestational age on thyroid hormone.

Comment 3: Presentation of Tables should be improved; instead of brackets, authors could include columns for easy of reading.

Response: We agree with this comment and will remove the bracket.

Comment 4: What was the consumption of iodised salt? This could be one of the contributing factors to high levels of UIC observed in some areas of the study. But also consumption of foods especially vegetables of the brassica group that are known to have compounds that interact with iodine in the gut.

Response: Consumption of iodized salt and vegetables of the Brassica group will be the limitation of the study.

Comment 5: Clarification about consumption of processed meat.

Response: Here we referred to meats that have been preserved by smoking, salting, curing, or addition of chemical preservatives.
Comment 6: Clearly stipulate factors that are associated with UIC in this section. Factors are not very clear.
Response: We agree with this comment and will rephrase the paragraphs to stipulate clearly the factors associated with UIC.

Discussion:
Comment 1: How were the identified factors influenced iodine status? These have not been adequately articulated in this manuscript.
Response: We agree with this comment and will rephrase the discussion section to articulate clearly on factors that influence iodine status.

Comment 2: Was the use of iodised salt investigated in the present study? What is the level of consumption among pregnant women? What is the availability and accessibility to iodised salt in the study areas?
Response: We have noted these observations and, they will be part of the study's limitations.

Comment 3: Authors indicated some strengths of the study; large sample size; but also identified limitations? One of the limitations was that they did not investigate use of iodised salt in the study area. This is a serious omission considering that iodised salt contributes to iodine intake and therefore UIC at least for a large part of the population. Additionally, there was no control group, which again raises concern over the design of this study.
Response: Thank you so much for pointing this out. We will add more information that clarifies the limitation of our study design.

Comment 4: Conclusion: It is a repeat of statement of results and not a conclusion. Authors should look at the objectives of the study and provide a concrete conclusion as to whether the objectives were attained and what are the implications to individual women and society in general.
Response: We agree, and we will carefully rewrite the conclusion section based on the study objectives.

Competing Interests: No competing interest
the manuscript.

Comment 2: Conclusion does not state explicitly the factors associated with insufficient/sufficient UIC
Response: Thank you for pointing this out. We agree with this comment and have rewritten the conclusion as suggested.

Introduction:
Comment 1: Provide explanation as to why highland regions have highest prevalence of IDD considering that Tanzania has been implementing salt iodisation programmes for many years?
Response: Agree. We have revised the introduction section to clearly emphasize this point.

Method:
Comment 1: Change 'Ante-natal Care Clinics' to 'Reproductive and Health Clinics' and use it consistently throughout the document.
Response: We agree with this comment and have incorporated your suggestion throughout the manuscript.

Comment 2: Explain adequately how sampling procedure was carried out.
Response: We agree, and have rewritten the sampling procedures.

Comment 3: Was the questionnaire pre-tested before translation?
Response: Thank you very much for pointing this out. The questionnaire was pre-tested after translation.

Comment 4: Interviews were done by health professional" - which cadre?
Response: Interviews were done by a trained Nurse Midwife. We have incorporated this suggestion throughout the manuscript.

Comment 5: Provide more information about the conditions for storage of the urinary samples in the field, transportation and storage at the laboratory before analysis and for how long were the samples stored before analysis. What distance from the field to the laboratory? This is important because iodine in urine is known to undergo changes after some time.
Response: We agree with this comment and have added more information on the conditions of the urinary samples stored in the field, transportation, and storage at the laboratory before analysis.

Comment 6: Was their any effort to ensure that women at various stages of pregnancy were well represented in the sample? It will also be useful to know of the sample size recruited, what was the stage of pregnancy for each participant? This information is missing.
Response: Thank you very much for pointing this out. The inclusion criteria of this study clearly indicated that ‘To eliminate the effects of gestational age on thyroid hormone, participants beyond eight weeks of gestation were excluded.

Comment 7: Why Mbeya region? Provide justification.
Response: Thank you for pointing this out and we have added the following statement in the manuscript for clarity. This study is part of the project on improving maternal and
adolescent nutrition in Mbeya supported by UNICEF Tanzania and the Ministry of Health-Tanzania.

**Results:**

**Comment 1:** Area of residence seemed to have an influence on iodine status of pregnant women, it was expected to see a good description of the study areas in this manuscript. The information is missing. Could the authors strive to provide this information?

**Response:** Thank you for pointing this out and we have added a sub-section of the study site in the methods section.

**Comment 2:** It will also be useful to know the stage of pregnancy (1st, 2nd, 3rd, trimester) of participants and if there were any association/interaction between area of residence, other factors and UIC.

**Response:** You have raised an important point here. However, we believe that excluding participants of beyond eight weeks of gestation was more appropriate to avoid the effects of gestational age on thyroid hormone.

**Comment 3:** Presentation of Tables should be improved; instead of brackets, authors could include columns for easy of reading.

**Response:** We agree with this comment and have incorporated your suggestion.

**Comment 4:** What was the consumption of iodised salt? This could be one of the contributing factors to high levels of UIC observed in some areas of the study. But also consumption of foods especially vegetables of the brassica group that are known to have compounds that interact with iodine in the gut.

**Response:** Thank you for this suggestion. It would have been interesting to explore this aspect. However, in the case of our present study, the assessment of iodised salt and vegetables of the brassica group was out of scope and has been included in the limitation of the study.

**Comment 5:** Clarification about consumption of processed meat.

**Response:** Agree. Here we referred to processed meat as that which has been preserved by smoking, salting, curing, or addition of chemical preservatives.

**Comment 6:** Clearly stipulate factors that are associated with UIC in this section. Factors are not very clear.

**Response:** We agree with this comment and have rewritten the result section to stipulate the factors associated with UIC.

**Discussion:**

**Comment 1:** How were the identified factors influenced iodine status? These have not been adequately articulated in this manuscript.

**Response:** We agree with this comment and have rewritten the discussion section to stipulate the identified factors that influence iodine status.

**Comment 2:** Was the use of iodised salt investigated in the present study? What is the level of consumption among pregnant women? What is the availability and accessibility to iodised salt in
the study areas?

Response: You have raised an important point here. However, the use of iodised salt (availability and accessibility) was not investigated in this study, and we have included it as part of the study's limitations.

Comment 3: Authors indicated some strengths of the study; large sample size; but also identified limitations? One of the limitations was that they did not investigate use of iodised salt in the study area. This is a serious omission considering that iodised salt contributes to iodine intake and therefore UIC at least for a large part of the population. Additionally, there was no control group, which again raises concern over the design of this study.

Response: Thank you so much for pointing this out and, we highly appreciate the reviewers’ insightful and helpful comments on our manuscript. It would have been interesting to explore and we have included it in the study's limitations. We will add more information that clarifies the limitation of our study design.

Comment 4: Conclusion: It is a repeat of the statement of results and not conclusion. Authors should look at the objectives of the study and provide a concrete conclusion as to whether the objectives were attained and what are the implications to individual women and society in general.

Response: Thank you for pointing this out. We agree with this comment and have rewritten the conclusion as suggested.

Competing Interests: None