RESEARCH ARTICLE

Factors associated with inadequate urinary iodine concentration among pregnant women in Mbeya region Tanzania. [version 1; peer review: 1 approved with reservations]

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Abstract

Background: Deficient and excess iodine intake during pregnancy can lead to serious health problems. In Tanzania, information available on iodine status during pregnancy is minimal. The aim of this study was to assess the iodine status and its association with sociodemographic factors in pregnant women in the Mbeya region, Tanzania. **Method:** A cross sectional survey involving 420 pregnant women (n=420) aged between 15-49 years registered in antenatal care clinics was conducted. Data were collected via interviews and laboratory analysis of urinary iodine concentration (UIC). **Results:** Median UIC was 279.4µg/L (+/-26.1) to 1915µg/L. Insufficient iodine intake (UIC below 150µ

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g/L) was observed in 17.14% of participants, sufficient intake in 24.29% and 58.57% had intakes above the recommended level (>250µ g/L). Rungwe district council (DC) had the highest proportion of patients (27.9%) with low iodine levels, while Chunya and Mbarali DCs had the greatest proportion of those with UIC's, over the WHO recommended level. Fish consumption and education status were associated with increased risk of insufficient iodine while individuals in Mbalali DC aged between 35-49 years were associated with increased risk of UIC above recommended level. **Conclusion:** Both deficient and excess iodine intake remains a public health problem, especially in pregnant women in Tanzania. Therefore, educational programs on iodine intake are needed to ensure this population has an appropriate iodine intake to prevent any health risks to the mother and the unborn child.

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

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Any reports and responses or comments on the article can be found at the end of the article.

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Introduction

Iodine deficiency is a significant global public health concern.[1] This element is found in hormones produced by the thyroid gland namely, triiodothyronine (T3) and thyroxine (T4),[1,2] and must be consumed in the diet as it cannot be made naturally in the body.[1] A diet low in iodine results in deficiencies 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 functional and developmental abnormalities.[3]

In terms of daily intake of iodine, the World Health Organization (WHO) recommends 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 are recommended 250 µg[4] daily. By ensuring that individuals have an adequate intake of iodine in their diets, IDDs can be prevented.[5] Although cretinism is the most severe form of iodine deficiency, minor iodine deficiency can also result in reduced intellectual ability, limited work capacity due to mental and neurological impairment.[4] In 1994, from the 1572 million people globally who suffered from iodine deficiency (28.9% of global population), 11.2 million were affected by overt cretinism, and 43 million people had at least some degree of intellectual impairment.[5]

In Tanzania, the most recent figures indicate that more than 40% of the population live in geographical regions prone to iodine deficiency.[6] The prevalence of IDD is greatest in the highland regions such as Iringa, Arusha, Mbeya, Rukwa and Ruvuma.[7] 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.[7] As recommended by WHO, Iodine Global Network (IGN) and United Nations Children's Fund (UNICEF), median Urinary Iodine Concentration (UIC) is considered the most practical biochemical marker for the assessment and monitoring of iodine nutrition in the population.[8] According to the National IDD survey conducted in 2004, about 25% of primary school children in Tanzania had UIC below 100 µg/L.[6]

Universal salt iodization (USI), whereby all the salt used for human consumption is iodized, is the most used intervention to increase iodine intake.[9] This intervention is widespread, as 68% of households have access to iodized salt.[10] USI is an effective way of delivering iodine to individuals and in term, improving cognition in populations exposed to iodine deficiency.[10,11] 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 is estimated at USD 1000. There are also large gains in per Disability-Adjusted Life Years (DALYs), at USD 34-36.[12] 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.[13]

In 1995, Tanzania legislation on USI was enacted.[14] 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.[15]

Nutritional deficiencies are prevalent among pregnant women in Tanzania, particularly, in areas of low socioeconomic status. However, there is a dearth of information regarding the burden of, and factors associated with iodine deficiency in this population. 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.[16,17] There are also concerns relating to excessive iodine consumption 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.[18,19] 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. It is also necessary to set upper as well as lower limits for maternal iodine intake to ensure optimal health outcomes are achieved.[19] 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. to assess the likelihood of IDD or otherwise, differing across socioeconomic groups and locations in Tanzania.

Methods

Study design

This was a cross-sectional survey involving pregnant women aged 15-49 years registered in antenatal care clinics (ANC). Study participants were recruited in all seven district councils (DC) of the Mbeya region (Chunya district, Ileje district,

Mbarali district, Mbeya urban district, Mbozi district, Momba district and the Rungwe district), from September until October 2020. The Mbeya region has 17 hospitals, 23 health centres, and 278 dispensaries, where 251 health facilities provide reproductive and child health services. The study was conducted at 42 Reproductive and Child Health (RCH) clinics in the seven districts of the Mbeya region. The selected RCH clinics provide services to approximately 1036 pregnant women.

Study population and sample size

Pregnant women aged 15-49 years that were within their first and second trimesters (less than 28 weeks of gestation), who attended ANC in the Mbeya region were recruited into the study. Overall, 574 participants were invited to participate, from which 420 (n = 420) agreed to take part. 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. Additionally, individuals who did not give consent, or were not able to communicate due to illness, and those taking medication were excluded. The sample size for the whole survey was pre-calculated based on the Lwanga and Lemeshow formula.[20]

Sample size and sampling procedure

In the Mbeya region, 251 governmental and faith-based health facilities that provided RCH services were included in a list, which was used to randomly select health facilities per district. In the survey, 42 facilities were randomly selected to take part, with two additional sites later invited, giving a total of 44 facilities in the final survey. Probability proportional to size was performed, due to the sampling frame of public health facilities in Mbeya, to allocate the number of facilities per district in the survey. Next, pregnant women from each selected health facility were invited to take part in the research. All pregnant women attending the ANC were asked to complete an eligibility form. Those that were eligible to take part were included in a Systematic Random Sampling procedure. This was done by obtaining an accurate and complete list of the pregnant women who had attended ANC in each health facility, and randomly selecting the required number of women per 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).[21] 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 health professional trained 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

Most of iodine consumed in the diet (90%) is lost through urine. As such UI is used as an indicator of iodine intake, expressed either as (μg/L), in terms of its relationship to creatinine excretion (μg iodine/g creatinine), or as 24-hour excretion (μg/day), termed urinary iodine excretion (UIE). It is impractical to collect 24-hour samples in field studies, therefore UI acts as a practical alternative to assess UI (expressed as the median, in μg/L) in a representative sample of the target group. After interviews were completed, a trained member of nursing staff took spot urine samples from consented participants. Urine samples were collected in a disposable plastic screw caped 100ml urine container. The urine samples were transported to a temporary laboratory for processing and shipment to central Tanzania Food and Nutrition Centre (TFNC) laboratory for analysis. At the temporary laboratory, the urine samples were transferred into screw-capped plastic vials and frozen at −20°C until shipped to TFNC laboratory for analysis. The urine samples were analyzed using the ammonium persulfate digestion method, as previously described by Sandell-Kolthoff reaction.[22] TFNC laboratory is registered and successfully participated in the quality assurance program for Ensuring the Quality of Urinary Iodine Procedures (EQUIP)[23] 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.[23]

Variables

Outcome/response variable

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 (MUIC) was developed to indicate the level of iodine in urine (μg/L) (see underlying data).[21]

MUIC 1 (Iodine <150μg/L) = Insufficient/deficiency iodine

MUIC 2 (150< Iodine <249 μg/L) = Sufficient/adequacy iodine

MUIC 3 (Iodine >250 μg/L) = 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, processed meat and, refined and baked foods were 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 a 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 cofounders and predict the true association between the dependent and independent variables. All tests were two-tailed, and the significance level was set at $p \leq 0.05$.

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

In this study, 420 agreed to participate (response rate of 73 %), with the mean age of 25.49 (± 6.37) years. In terms of demographics, 70% of participants had primary education, 75% has been pregnant more than once, 68% reported that they consumed fish and, more than 90% consumed dairy products. Improved source of water was reported by 71% of the participants (Table 1).

Urinary iodine concentration (UIC)

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

Bivariate analysis

Of 215 participants aged between 15-24 years, 17% had UIC (0–149 μg/l) that would be considered inadequate, and 55.8% had UIC (>250 μg/l) above the recommended levels. Table 2 presents a cross-tabulation of the prevalence of median UIC, MUIC and various independent factors. Chunya and Mbarali DCs have the highest percentage (above 70%) of the WHO recommended UIC among the participants in the sample. Rungwe DC had the highest percentage (27.9%) of participants with inadequate urine iodine concentrations. From the 133 participants who had fish in their diet, UIC was inadequate in 23%, adequate in 19.4%, and 56.9% had above the recommended level.

Multivariate analysis

The fitted models and the estimated effects from the multivariate analysis are presented in Table 3. The chi-square model (63.51) was 0.0176, with $p < 0.05$.

Table 1. Frequency distribution of the study participant in Mbeya (n = 420).

Variables	Category	% (n)
Age group	15-24	52.18 (215)
	25-34	35.68 (147)
	35-49	12.14 (50)
Education level	No formal education	8.10 (34)
	Primary education	71.67 (301)
	Secondary and above	20.24 (85)
Wealth Index	1quantile	33.3 (140)
	2quantile	33.3 (140)
	3quantile	33.3 (140)
Marital status	Married	56.67 (238)
	Cohabit	31.67 (133)
	Single	9.29 (39)
	Divorced	2.38 (10)
Occupational status	Formal employment	3.57 (15)
	Self-employment	84.52 (355)
	Not employed	11.90 (50)
Antenatal care center (ANC) visit	1 visit	38.81 (163)
	2-3 visits	53.81 (226)
	More than 3 visits	7.38 (31)
Residence	Chunya District Council	10.71 (45)
	Mbeya District Council	23.10 (97)
	Mbarali District Council	22.14 (93)
	Kyela District Council	11.90 (50)
	Rungwe District Council	16.19 (68)
	Busokelo District Council	7.86 (33)
	Mbeya City	8.10 (34)
Number of pregnancies	Primiglavida	24.76 (104)
	Multiglavida	75.24 (316)
Type of water source	Improved	71.90 (302)
	Unimproved	28.10 (118)
Mid-upper arm circumference (MUAC) categorization	MUAC < 23cm	3.81 (16)
	MUAC ≥ 23cm-MUAC < 33cm	90.19 (383)
	MUAC ≥ 33cm	5.0 (21)
Consumption of fish	No	68.3 (287)
	Yes	31.7 (133)
Consumption of Dairy products	No	90.7 (381)
	Yes	9.8 (39)
Consumption of Processed meat	No	97.6 (410)
	Yes	2.4 (10)
Urinary Iodine Concentration (UIC) categorization	Insufficient (UIC 0–149 μg/l)	17.14 (72)
	Sufficient (UIC 150–249 μg/l)	24.29 (102)
	Above recommended (>250μg/l)	58.57 (246)

Table 2. Predictors of urine iodine concentration level (MUIC) among pregnant women in Mbeya (n = 420).

		Insufficient (Urinary Iodine Concentration (UIC) 0–149 μg/l)	sufficient (UIC 150–249 μg/l)	Above recommended (>250μg/l)	Chi-square (X^2)	P value
Variable	**Category**	**% (n)**	**% (n)**	**% (n)**		
Age group	15-24	17.21(37)	26.98 (58)	55.81(120)	4.0208	0.403
	25-34	16.33 (24)	22.45(33)	61.22(90)		
	35-49	14.00(7)	16.00 (8)	70.00 (35)		
Education level	No formal education	26.47 (9)	17.65 (6)	55.88 (19)	4.314	0.634
	Primary education	15.61 (47)	24.92 (75)	59.47 (179)		
	Secondary and above	16	21	48		
Wealth Index	1quantile	20.71 (29)	26.43 (37)	52.86 (74)	4.7325	0.316
	2quantile	15.71 (22)	20.00 (28)	64.29 (90)		
	3quantile	15.00 (21)	26.43 (37)	58.57 (82)		
Marital status	Married	18.49 (44)	22.27 (53)	59.24 (141)	2.71	0.838
	Cohabit	15.04 (20)	28.57 (38)	56.39(75)		
	Single	17.95 (7)	23.08 (9)	58.97 (23)		
	Divorced	10.0 (1)	20.0 (2)	70.0 (7)		
Occupational status	Formal employment	20.0(3)	33.33(5)	46.67 (7)	4.132	0.388
	Self-employment	17.46 (62)	22.54 (80)	60.0(213)		
	Not employed	14.0 (7)	34.0 (17)	52.0 (26)		
Antenatal care center (ANC) visit	1 visit	17.18(28)	23.93 (39)	58.90 (96)	3.3699	0.498
	2-3 visits	18.58 (42)	24.78 (56)	56.64 (128)		
	More than 3 visits	6.45 (2)	22.58 (7)	70.97 (22)		
Residence	Chunya DC	6.67 (3)	22.22(10)	71.11 (32)	31.987	0.001
	Mbeya DC	21.62 (21)	32.99 (32)	45.36 (44)		
	Mbarali DC	11.83 (11)	13.98 (13)	74.19(69)		
	Kyela DC	12.0(6)	20.0 (10)	68.0 (34)		
	Rungwe DC	27.94 (19)	25.0 (19)	47.06 (32)		
	Busokelo DC	24.24 (8)	27.27 (9)	48.48 (16)		
	Mbeya city	11.76 (4)	32.35 (11)	55.8 (19)		

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Table 2. *Continued*

		Insufficient (Urinary Iodine Concentration (UIC) 0–149 μg/l)	sufficient (UIC 150–249 μg/l)	Above recommended (>250μg/l)	Chi-square (X^2)	P value
Variable	**Category**	**% (n)**	**% (n)**	**% (n)**		
Number of pregnancies	Primiglavida	16.35 (17)	22.12(23)	61.54 (64)	0.527	0.768
	Multiglavida	17.71 (55)	25.0 (79)	57.59 (182)		
Type of water source	Improved	18.54 (56)	23.51 (71)	57.95 (175)	0.567	0.457
	Unemployed	13.56 (16)	26.27 (31)	60.17 (71)		
Mean- upper arm circumference (MUAC) categorization	MUAC < 23cm	12.50 (2)	18.75 (3)	68.75(11)	0,987	0.912
	MUAC ≥ 23cm-MUAC < 33cm	17.49(67)	24.28 (91)	58.22 (223)		
	MUAC ≥ 33cm	14,29(3)	28.57 (6)	57.14 (12)		
Consumption of fish	No	13.77 (38)	26.81 (74)	59.42 (164)	7.5619	0.023*
	Yes	23.61(34)	19.44 (28)	56.94 (82)		
Consumption of Dairy products	No	17.19(60)	23.78 (83)	59.03 (206)	0.2912	0.865
	Yes	16.90(12)	26.76 (16)	56.34 (40)		
Consumption of Processed meat	No	17.27 (71)	23.84 (98)	58.88 (242)	2.0475	0.359
	Yes	11.11 (1)	44.44 (4)	44.44(4)		
Consumption of refined and baked	No	18.92(14)	24.32 (18)	56.76 (42)	0.2158	0.898
	Yes	16.76(58)	24.28(84)	58.96 (204)		

Table 3. Multinomial logistic regression models for iodine intake among pregnant women in Mbeya (n = 420).

Model fitting information						
Model	**-2logLikelihood**		**Chi-Square**			**P-value**
Intercept Only	391.00997					
Final	359.25317		63.51			0.0176
Parameters estimates						
Dependent	**Independent**			**95% confidence interval for Exp(B)**		
	Variable	**Category**	**Exp (B)**	**Lower bound**	**Upper bound**	**P- value**
Insufficient	Consumption of fish	No				
		Yes	2.60	1.31	5.15	0.006*
	Consumption of Dairy products	No				
		Yes	0.96	0.41	2.28	0.940
	Consumption of Processed meat	No				
		Yes	0.32	0.03	3.19	0.334
	Consumption of refined and baked	No				
		Yes	0.79	0.33	1.91	0.609
	Residence	Mbeya district council (DC)	1	1	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				
		25-34	1.11	0.50	2.44	0.782
		35-49	1.45	0.42	4.98	0.553
	Wealth Index	1quantile				
		2quantile	1.62	0.62	4.26	0.321
		3quantile	1.28	0.42	3.90	0.663
	Education level	No formal education				
		Primary education	0.29	0.08	0.99	0.049*
		Secondary and above				
	Mean upper arm circumference (MUAC) categorization	MUAC < 23cm				
		MUAC ≥ 23cm-MUAC < 33cm	1.27	0.18	8.90	0.807
		MUAC ≥ 33cm	1.17	0.10	13.31	0.896
	Number of pregnancies	Primiglavida				
		Multiglavida	0.83	0.34	2.01	0.683

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Table 3. *Continued*

Parameters estimates						
Dependent	**Independent**			**95% confidence interval for Exp(B)**		
	Variable	**Category**	**Exp (B)**	**Lower bound**	**Upper bound**	**P- value**
Above recommended	Consumption of fish	No				
		Yes	1.24	0.71	2.15	0.438
	Consumption of Dairy products	No				
		Yes	0.90	0.46	1.73	0.754
	Consumption of Processed meat	No				
		Yes	0.50	0.11	2.31	0.379
	Consumption of refined and baked	No				
		Yes	0.99	0.50	1.96	0.998
	Residence	Mbeya DC				
		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				
		25-34	1.47	0.81	2.69	0.201
		35-49	2.51	0.99	6.33	0.050*
	Wealth Index	1quantile				
		2quantile	1.41	0.66	3.03	0.367
		3quantile	2.08	0.91	4.71	0.079
	Education level	No formal education				
		Primary education	1.04	0.37	2.94	0.929
		Secondary and above	1.18	0.35	3.95	0.777
	MUAC categorization	MUAC < 23cm				
		MUAC ≥ 23cm-MUAC < 33cm	1.01	0.25	4.05	0.985
		MUAC ≥ 33cm	0.74	0.13	4.27	0.745
	Number of pregnancies	Primiglavida				
		Multiglavida	0.64	0.32	1.26	0.203

The reference category contains: sufficient/adequate/sufficient iodine concentration.* Represents p value: *p<0.05.

The predicted probability of having inadequate urine iodine level was 2.60 (95% CI 1.31-5.15), in participants who consumed freshwater fish. Additionally, inadequate iodine level was 0.29 (95 % CI 0.08-0.99) in participants who had a primary school education. The probability of having increased iodine levels amongst participants living in Mbarali DC was 4.09 (95% CI 1.85- 9.01), whilst for individuals aged 35-49 years, the probability was 2.51 (95% CI 0.99-6.33). The likelihood of having an inadequate iodine level based on DC, resulted in a significant likelihood of having above recommended iodine level for individuals in Mbarali DC [4.09 (95% CI 1.85-9.01)], whilst those living in Rungwe DC had a significant (borderline) likelihood of having inadequate iodine levels [2.43 (95% CI 0.95-6.19)].

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 deficiency is the most prevalent micronutrient deficiency, affecting 28.9% of the world population,[24] particularly affecting women living in developing countries.[25] Iodine deficiency in Tanzania is also high with the most recent figures indicating that more than 40% of the population in the country lives in geographical regions prone to iodine deficiency.[6] However, this data is largely outdated, as more recent data as well as the most recent efforts to reduce iodine deficiency have focused on primary school children in Tanzania.[6] Whilst the iodine micronutrient status among pregnant women has been overlooked in recent years.

In this study, pregnant women living in the Mbarali district were more likely to be above the recommended level of UIC [4.09 (95% CI 1.85-9.01)], particularly among individuals aged between 35-49 years [2.51 (95% CI 0.99-6.33)]. Thus, it is important to monitor thyroid function and its associated disorders in this population. Contrary to these results, in 2010, a reanalysis of the Tanzania demographic and health survey reported 54% of pregnant women with iodine deficiency.[16] The discrepancy could be attributed to differences in study methodologies as well as the 10-year lapse between the studies, since significant USI interventions were applied in this period.

In this study a strong association between consumption of freshwater fish and UIC of <150µg/l [odd ratio = 2.60 (95% CI 1.31-5.15)], indicated that pregnant women who consumed fish were at higher risk of iodine deficiency. This finding could be explained by the notion that iodine levels in freshwater fish depend on the locality and the regularity of consumption of fish.[26,27] Moreover, during pregnancy there are variations in the functionality of the thyroid. This can increase the risk of inadequate iodine intake for some mothers. As such, predicting UIC based on usage of iodized salt alone, may not be accurate.[28–30] Other studies have documented that freshwater fish may contain Iodine in levels that can improve daily Iodine intake.[26]

In countries with successful USI programs, studies have reported an optimal median UIC in pregnant women. As such, USI remains the most cost-effective strategy for achieving reduced IDD.[31,32] However, the full implementation of USI remains a challenge in many sub–Saharan African countries including Tanzania,[33] 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.[6]

This analysis also indicated that pregnant women who had a primary school education were at higher risk of iodine deficiency [odd ratio= 0.29 (95% CI 0.08-0.99)], However, further studies are needed to investigate this association. Excessive iodine intake in pregnant women is also an important area of current research.[34,35] The WHO recommended an increased iodine intake for pregnant women, although evidence is weak.[36] However, detrimental effects from more than adequate and excessive iodine intake have been reported in general populations.[37–39] 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.[40] This is also an area in need of further investigation. The question remains if pregnant women in Mbarali district should continue using iodinated salt, and if so at what concentration.

The strength of this study is in its large population-based sample size. The study limitations are 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. Additionally, 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 UI concentrations during pregnancy could be attributed to pregnancy itself or the diet.

Conclusion

The aim of this study was to explore iodine levels in pregnant women living in the Mbeya region of Tanzania. Findings indicate that 17.14% of participants had an insufficient iodine intake whilst, 24.29% had sufficient/adequate urine iodine concentration, and 58.57% had above the recommended levels of iodine. There were differences found between district

councils, with the Rungwe DC having the highest percentage (27.9%) of participants with inadequate urine iodine concentrations. Protective factors for IDD included consumption of freshwater fish and having a primary education, whilst factors increasing the risk of excessive iodine intake included being older in age (35-49 years). Due to these findings, this study recommends strategic efforts to ensure that the current USI program addresses the problem of iodine deficiency in pregnant women, and monitor excessive iodine exposure that might have detrimental effects during pregnancy.

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/.[21]

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.

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, SEJ, HAP, AS, RN, FK, ET and GHL; reviewed and edited the manuscript. GB and, RB. All authors: Reviewed and agreed upon the final manuscript.

Acknowledgments

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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?

Joyce Kinabo
Department of Human Nutrition and Consumer Sciences, Sokoine University of Agriculture, Morogoro, Tanzania

Abstract:

1. Use of the word 'insufficient' should be consistent through out 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 through out 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 know to undergo changes after some time.

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.

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

Author Response 23 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 reviewers' comments and concerns.

Abstract
Comment 1: *Use of the word 'insufficient' should be consistent throughout the article.*
Response: We agree with this comment and have incorporated your suggestion throughout 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