International Journal of Biomedical Research
ISSN: 0976-9633 (Online); 2455-0566 (Print)
Journal DOI: https://doi.org/10.7439/ijbr
CODEN: IJBRFA

Original Research Article

Assessment of knowledge, attitude and practice of iodized salt utilization and associated factors at household level in Bure town administration, North West, Ethiopia

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Abstract

Background: Iodine is one of the trace elements which are needed for thyroid hormone production and synthesis. Inadequate iodine in the body leads to deficiency of these hormones, which affect human vital organs basically muscle, heart, liver, kidney, and the developing brain.
Objective: To assess knowledge, attitude and practice of iodized salt utilization and associated factors at household level.
Methods: Community based cross-sectional study was conducted from January to June, 2019 in Bure Town administration. A total of 597 households was selected using systematic sampling technique. Data was entered into Epi info version 3.5.1 and exported to SPSS version 23 for cleaning and analysis.
Result: Residence of the respondents, marital status and Occupational status of the respondents were showed a significant effect for poor knowledge and Age of the respondents, Residence of the respondents were showed a significant effect for Negative attitude and educational status of the respondents, Residence of the respondents and Occupational status of the respondents were showed a significant effect for poor practice.
Conclusion: Knowledge, attitude and practice on utilization of iodized salt at household level were poor in Bure Town Administration. Occupational status, marital status, and residency of participants were associated factor with knowledge and Age and residency of participants were associated factor with Attitude on iodized salt utilization at the household level and occupational status, educational status, and residency of participants were associated factor with practice about iodized salt utilization at the household level.
Keywords: Iodine Salts, Knowledge, Attitudes, Practice.

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***Article History:**
Received: 25/02/2022
Revised: 29/03/2022
Accepted: 29/03/2022
DOI: https://doi.org/10.7439/ijbr.v13i3.5740

QR Code

How to cite: Manaye Y, Manaye E, Menberu T, Getnet T and Mohammed A. Assessment of knowledge, attitude and practice of iodized salt utilization and associated factors at household level in Bure town administration, North West, Ethiopia. *International Journal of Biomedical Research* 2022; 13(3): e5740. DOI: 10.7439/ijbr.v132i3.5740 Available from: https://ssjournals.com/index.php/ijbr/article/view/5740

1. Introduction

Iodine is one of the trace elements in human body, used for the production and synthesis of thyroid hormone, which play a determining role in the process of the early growth and development of most organs and which is gained from consumed diet, while the human body does not make iodine. Iodine is found in different foods and is found naturally in soil and seawater. [1]

Iodine can be gained through utilization of foods that naturally contain it such as fish, seafood, kelp, some drinking water, cow's milk and vegetables grown in sufficiently Iodine containing soil) or upon it iodine is added (commonly stated as table salt).[2]

Globally, 38% of the world's population lives with insufficient iodine intake. In Africa more than 150,000 million people are affected and with its 1.1million deficient people bear the most burden of the region. Even though iodine content of iodized salt is sufficient, there is an iodine loss of approximately 20% between production site and household use and another 20% loss during improper cooking before consumption [9,10].

Regional coverage of iodized salt varies from 90% in Asia and the Pacific region to 40–60% in Sub-Saharan Africa. The level of utilization also varies from 10 to 90% in different countries. For instance, the utilization of iodized salt is less than 10% in Sudan, Mauritania, Guinea-Bissau, and Gambia, whereas Burundi, Kenya, Nigeria, Tunisia, Uganda, and Zimbabwe have achieved the USI target [11].

In Ethiopia, around 28 million people suffer from goiter, and more than35 million people are at risk of iodine deficiency, and one out of every 1000 is a cretin, and about 50,000 perinatal deaths are occurring annually due to low iodine intake. About 34.5%to 37% of the childbearing women in the country have goiter. In Ethiopia, utilization of adequately iodized salt use showed a marked increase from 15% in 2011 to 89% in 2016.[12-14]. Inconsistencies of the practice are detected among dwellings and economic status. As an illustration, iodized salt utilization is the highest in Tigray (55.2%) and Somali (49.4%) and the lowest in Gambelia (9.5%), SNNPR (13.7%), and Amhara regions (15%)[15].

The consequence of low intake of iodine in the diet includes mental retardation, goiter, growth retardation, reproductive failure, and increased childhood mortality. Iodine deficiency disorders are the major public health problems in developing countries[14,16].

In view of the low prevalence of use of iodized salt, the Ethiopian government formulated a national nutrition program. The program includes USI as one strategic objective which aimed to increasing the proportion of households using iodized salt[17].

2. Materials and Methods

2.1 Study designs

Cross sectional community-based study was employed to assess KAP on iodized salt utilization and associated factors at household level in Bure town.

2.2 Study area and period

The study was conducted in Burie Town administration from January to June 2019. Bure is Located in the West Gojjam Zone of the Amhara Region, It is about 152 Km away from Bahir Dar City, the capital of the Amhara National Regional State and 410 Km far from Addis Ababa-the capital city of Ethiopia in the North-Western direction.

2.3 Populations

2.3.1 Source population

All households living in Bure town administration was the source population of this study.

2.3.2 Study population

All households in randomly the selected kebeles of Bure town administration were the study population.

2.4 Inclusive criteria

All households having at least one resident in the age of 18 years and above who involve in the preparation of food for household consumption and who had lived at least 6 months in Bure town administration was included.

2.5 Exclusive criteria

Households with participants who have hearing difficulty for interview were excluded.

2.6 Sample size determination and sampling technique

The sample size for this study was determined the following assumptions:

Proportion of knowledge (p1) (28.7 %), proportion of attitude (p2) (62.6%) and proportion of practice (p3) (83.3%) taken from previous study towards households iodized salt utilization [22,31,36]. Confidence level = 95%, Margin of error (D) =5%, Non-response rate =10%

$n = \frac{Z^2 p(1-p)}{(d)^2}$ Where'' n'' is overall sample size

So, the sample size calculated was 362.Finally, by adding non response rate of 10% and design effect of 1.5, the final sample size will be 597.

2.7 Dependent variable

KAP of iodized salt utilization.

2.8 Independent variables

Socio-demographic characteristics (Age, sex, educational status, residence, religion, marital status, occupational status, family size),

Dietary factors (knowing source of iodine nutrient, availability of iodized salt) and Sources where information regarding iodized salt heard (Health workers, Friends/neighbors, Mass media, printed materials, Merchants and schools).

2.9 Data collection procedures

The data was collected using structured questionnaire by a face-to-face interviewing technique. The questionnaire was prepared in English language then translated to Amharic language and then translated back to English to check the validity. The questionnaire consists of questions about knowledge, attitude and practice on iodized salt utilization.

2.10 Data processing and analysis

Data was coded and entered in to Epi-data version 3.5.1 and was exported to SPSS version 21.0 for cleaning analysis. Descriptive statistics like frequency, proportion, and cross tabulation was computed. Binary logistic regression analysis was used to assess the association between the dependent variable with each independent variable.

Finally, variables, which show association in bivariate logistic regression at P-value of less than 0.2 was entered in to multivariable logistic regression model and declared statistically significant at P-Value < 0.05.

2.11 Ethical considerations

This document submitted to Bahir Dar University postgraduate research review board for ethical approval. Following the approval, Official letter of co-operation was written to concerned bodies and informed verbal consent was received from the respondents, after the necessary explanation about the purpose and absence of risks by being participants in the study.

3. Results

3.1 Socio demographic characteristics

A total of 597food caterers were interviewed, which was 100% response rate. Majority of the respondents were in the age group of ≥45 years; while majority (531, [88.9%]) of the respondents were female and Christian (509, [85.3%]). From study participants, about 255 (42.7%) were single and regarding to educational status of respondent's majority (169, [28.3%]) had read and write.

3.2 Knowledge, of iodized salt utilization

Almost all respondents 590(98.8%) they had heard of iodized salt. More than half (64.3%) of the respondents were know the benefit of iodized salt.

The majority of food caterers (306, [51.3%]) know about importance of using iodized salt that is preventing IDD such as goiter, abortion, cretinism& dwarfism). In addition, 456(76.4%) of the caterers doesn't know iodine evaporate when iodized salt stored in open container **(Figure 1)**.

Figure 1: Magnitude of Knowledge, of Iodized Salt at Household Level in Bure Town Administration

3.3 Attitude, of Iodized Salt Utilization

Among total respondents 379(63.5%) they had preferred packed salt and more than half of respondents 329(55.1) the said that Reasons for salt preference related with Health benefit.

Majority of respondents 503(84.5%) they disagree all types of salt have iodine. But 326(54.6%) of respondents agree with it is possible to develop health problems related to iodine deficiency through a chronic lack of iodine in your body **(Figure 2)**.

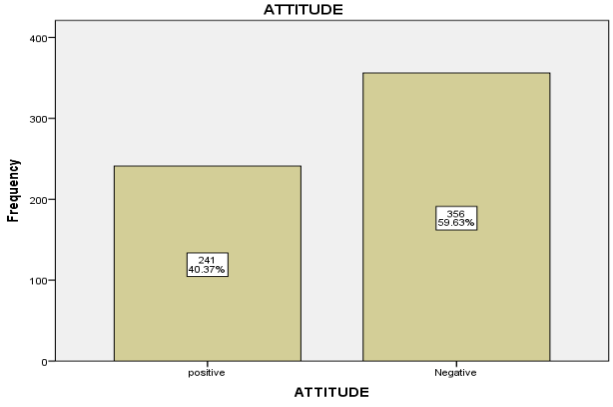

Figure 2: Magnitude of Attitude, of Iodized Salt at Household Level in Bure Town Administration

3.4 Practice of Iodized Salt utilization

Among total respondents almost all 595(96%) they used salt to cook meal eaten. And 365(61.1%) of respondents they used Iodize salt.

More than half of respondents 327(54.8%) they were asked the seller to check the salt weather it is iodized or not. Majority of respondents 442(74%) get iodized salt by purchasing in small shop, 406(68%) of respondents stored iodized Salt in dry place. While 306(51.3%) of respondents they never observe expiry date of iodized salt **(Figure 3)**.

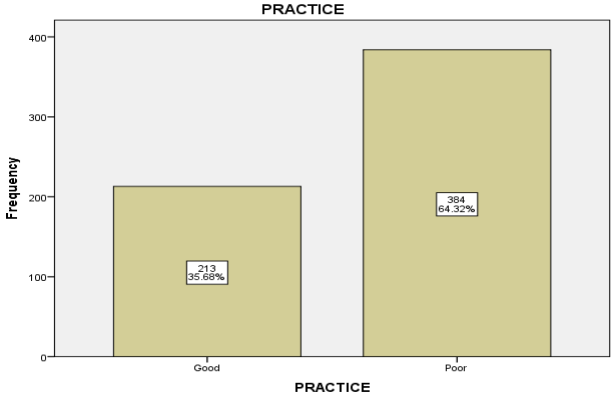

Figure 3: Magnitude of practice, of Iodized Salt at Household Level in Bure Town Administration

3.5 Factors Associated with Knowledge, Attitude and Practice of Iodized Salt Utilization at Household Level

3.5.1 Factors Associated with Knowledge of Iodized Salt Utilization

In the bivariable (crude) logistic-regression analysis, Religion, Marital status, Residence of the respondent and Occupational status of the respondent were showed significant effect at P-value of less or equal to 0.2.

The variables with p-value 0.2 or less in the bivariable result were entered in to multivariable logistic-regression analysis.

Residence of the respondents showed a significant effect. participants those who had lived in rural area were 7.7 times more likely to have Poor knowledge of iodine salt utilization compared to those who had lived in urban area with [p ≤ 0.001, AOR = 7.7, 95% CI: 4.4-13.1].

Participants who are Single had 7 times more likely to have poor knowledge of iodine salt utilization compared to those who are widowed with [p =<0.001, AOR = 7.0, 95% CI: 2.8 – 17.0]. Participants who are married had 21% less likely to have poor knowledge of iodine salt utilization compared to those who are widowed with [p =<0.001, AOR = 0.79, 95% CI: 0.27 – 2.2].

Participants those who had merchant and farmer more likely to have poor knowledge of iodine salt utilization compared to those who had Job seeker with [p ≤ 0.001, AOR = 14, 95% CI: 6.5-33.3], [p ≤ 0.001, AOR = 7.0, 95% CI: 2.5-19](**Table 1**).

Table 1: Bivariate and multivariable logistic regression output showing that factors associated with knowledge of iodized salt utilization at house hold level, in Bure Town Administration, 2022

Variable	Category	Knowledge of Iodine salt utilization		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Good	Poor				
Residence	Urban	92	295	1		1	
	Rural	140	70	6.4(4.4-9.2)	<0.001	7.7(4.4-13.0)	<0.001
Marital status	single	105	150	1.07(0.64-1.7)		7.0(2.8-17.7)	<0.001
	Divorced	73	146	1.5(0.89-2.5)		4.9(2.3-10.1)	
	Married	20	24	0.9(0.4-1.9)		0.79(0.27-2.2)	
	Widowed	34	45	1	0.19	1	
Religion	Orthodox	213	296	0.27(0.07-0.97)			
	Muslim	16	54	0.67(0.17-2.6)			
	Protestant	3	15	1	0.002	1	
Occupational status	House wife	54	99	1.6(0.9-2.7)		2.2(0.9-5.3)	
	Farmer	6	55	8.0(3.1-20.5)		7.0(2.5-19.0)	
	Merchant	13	107	7.2(3.5-14.6)		14(6.5-33.3)	
	Employed	91	23	0.22(0.12-0.41)	< 0.001	0.51(0.21-1.2)	< 0.001
	House servant	26	33	1.1(0.57-2.14)		1.2(0.56-2.7)	
	Job seeker	42	48	1		1	

3.5.2 Factors Associated with Attitude of Iodized Salt Utilization

Participants those who were age group between 18-24 years 60% less likely to have poor Attitude about iodine salt utilization compared to those who were ≥ 45 years with [p ≤ 0.001, AOR = 0.40, 95% CI: 0.24-0.7].and participants those who were age group between 25-34 years 78% less likely to have poor Attitude about iodine salt utilization compared to those who were ≥ 45 years with [p = 0.012, AOR = 0.22, 95% CI: 0.13-0.36]. and participants those who were age group between 35-34 years 81% less likely to have poor Attitude about iodine salt utilization compared to those who were ≥ 45 years with [p = 0.06, AOR = 0.19, 95% CI: 0.11-0.34].

Other significant variable in multivariable, Residence of the respondents showed a significant effect. Participants those who had lived in urban area were 71% less likely to have poor Attitude about iodine salt utilization compared to those who had lived in rural area with [p ≤ 0.001, AOR = 0.29, 95% CI: 0.2-0.44]. **(Table 2).**

Table 2 Bivariate and multivariable logistic regression output showing that factors associated with Attitude of iodized salt utilization at house hold level, in Bure Town Administration, 2022

Variable	Category	Attitude about Iodine salt utilization		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Positive	Negative				
Age	18-24 yrs	56	39	0.41(0.25-0.7)	<0.001	0.4(0.24-0.7)	
	25-34 yrs	99	71	0.17(0.10-0.3)		0.22(0.13-0.4)	
	35-44 yrs	48	85	0.16(0.096-0.3)		0.19(0.1-0.34)	<0.001
	≥ 45 yrs	38	161	1		1	
Religion	Orthodox	185	324	6.1(1.9-18.8)		1	
	Muslim	42	28	2.3(0.7-7.8)			
	Protestant	14	4	1	<0.001	1	
Residence	Urban	41	169	0.22(0.15-0.33)	<0.001	0.29(0.2-0.44)	<0.001
	Rural	200	187	1		1	
Family size	≤ 5	166	219	0.72(0.51-1.02)	0.06	1	
	>5	75	137	1		1	

3.5.2 Factors Associated with Practice of Iodized Salt Utilization

In the bivariable (crude) logistic-regression analysis, Education status, Residence of the respondent, Occupation of the respondent and Family size of the respondent were showed significant effect at P-value of less or equal to 0.2.

The variables with p-value 0.2 or less in the bivariable result were entered in to multivariable logistic-regression analysis.

Participants those who had unable read and write had 3 times more likely to have poor practice about iodine salt utilization compared to those who had Collage and above with [p ≤ 0.007, AOR = 3.2, 95% CI: 1.3-7.3].and participants those who had Read and write only had 2.7 times more likely to have poor practice about iodine salt utilization compared to those who had Collage and above with [p ≤ 0.003, AOR = 2.7, 95% CI: 1.4-5.5]. and participants those who had Primary level had 1.9 times more likely to have poor practice about iodine salt utilization compared to those who had Collage and above with [p ≤ 0.07, AOR = 1.9, 95% CI: 0.9-3.8]. and participants those who had Secondary level had 1.4 times more likely to have poor practice about iodine salt utilization compared to those who had Collage and above with [p ≤ 0.32, AOR = 1.4, 95% CI: 0.7-3.11].

Other significant variable in multivariable, Residence of the respondents showed a significant effect. participants those who had lived in rural area were 3 times more likely to have poor practice about iodine salt utilization compared to those who had lived in rural area with [p ≤ 0.001, AOR = 3.0, 95% CI: 1.8-4.8].

Occupational status of the respondents showed a significant effect in logistic-regression analysis. Participants those who had farmer were 8 times more likely to have poor practice of iodine salt utilization compared to those who had Job seeker with [p ≤ 0.001, AOR = 8.0, 95% CI: 2.4-30.0].and participants those who had house servant were 57% less likely to have poor practice of iodine salt utilization compared to those who had Job seeker with [p ≤ 0.04, AOR = 0.43, 95% CI: 0.19-0.96]. **(Table 3).**

Table 3: Bivariate and multivariable logistic regression output showing that factors associated with Practice of iodized salt utilization at house hold level, in Bure Town Administration, 2022

variable	Category	Practice about Iodine salt utilization		COR (95% CI)	P-value	AOR (95% CI)	P-value
		Good	Poor				
Education	Unable read and write	21	93	7.4(3.6-15.1)	<0.001	3.2(1.3-7.3)	<0.001
	Read and write	51	118	3.8(2.0-7.2)	<0.001	2.7(1.4-5.5)	
	Primary (Grad 1-8)	58	87	2.5(1.3-4.7)	<0.001	1.9(0.9-3.8)	
	Secondary (Grad 9-12)	46	64	2.3(1.2-4.4)	<0.001	1.4(0.7-3.11)	
	Collage and above	37	22	1		1	
Residence of the respondents	Urban	115	95	1		1	
	Rural	98	289	3.5(2.5-5.0)	<0.001	3.0(1.8-4.8)	<0.001
Occupation	House wife	83	70	0.3(0.17-0.54)	<0.001	0.6(0.32-1.2)	
	Farmer	3	58	7.0(2.0-24.5)	<0.001	8.0(2.4-30.0)	
	Merchant	24	96	1.4(0.76-2.7)	<0.001	2.0(0.9-4.1)	
	Employed	44	70	0.57(0.31-1.05)	0.012	1.7(0.8-3.9)	
	House servant	35	24	0.25(0.12-0.5)	0.5	0.43(0.19-0.96)	<0.001
	Job seeker	24	66				
Family size	≤ 5	121	264	1.6(1.2-2.3)	0.004		
	>5	92	120	1		1	

4. Discussions

It is apparent that the use of iodized salt by individuals and households is the major approach in the control of IDDs globally. Thus, strengthening salt iodization programs and improving monitoring is a crucial step to eradicate the problem [39].

The purpose of this study was to determine the knowledge, Attitude and practice of Iodine salt utilization and its associated factor at household level in Bura town administration.

This study found that from the total respondents 365(61.1) % of the respondents had poor knowledge of iodized salt utilization. The finding was lower than study done in Mecha, Gonder town and Laelay Maychew district which were 72.3%, 74.8% and 64.2%, respectively [22,29,30]. And also, this finding lower than study done abroad the country which were 72.9% and 74% in Iraq and Tehran respectively [39,40]. The variation might be due to the nature of study settings in that household from slum areas and poor communities were included in that study. This means, slum areas are characterized by poor infrastructure and inadequate communication channels compared to the current study, the setting of our study, where the respondents had opportunities to increase their knowledge through promotions of iodized salt on the media. In fact, promotions on the media increase public awareness.

Our finding was lower than 90.4% reported in Ghana[41]. This might be due to the accessibility of different media nearby for the target group in the study area. Even if there was minimal increment in knowledge on the iodized salt use over the years, it was low, suggesting that awareness creation and educational activities on the use of iodized salt were not yet enough mainly in the rural communities.

In the current study, Residence of the respondents showed a significant effect. Participants those who had lived in rural area were 7 times more likely to have poor knowledge of iodine salt utilization compared to those who had lived in urban area.

This finding was similar with the study done Mecha and Sudan that explains participants who live in the rural area was more likely to have poor knowledge on the use of iodized salt utilization[22,42]. The reason behind this might be that participants who live in the rural area were difficult to get easily accessible to health education and awareness creation which is now in different type of social media about Iodine salt utilization. But there is no study to oppose the current finding regarding to residence of the respondents.

Other significant variable was marital status, being married. Participants who are married had 21 % less likely to have poor knowledge of iodine salt utilization compared to those who are widowed. Although no other studies have been found that had reported the association of Married with poor knowledge of iodine salt utilization during literature review, Logical it is proven that respondents who are married had more opportunity to share idea/information about iodine salt utilization with their partner.

Another study done in Deber tabour town the opposite of the current one in this study showed that the, marital status was strongly associated with knowledge. Those widowed were 96% less likely to have poor knowledge as compared to married ones[32]. This may be due to accessibility of information; on the other hand, workload at home for married ones that could hinder them from information.

Occupational status of the respondents showed a significant effect. Participants those who had employed were 49 % less likely to have poor knowledge of iodine salt utilization compared to those who had Job seeker. Study that has done in south Ethiopia and Mecha district also supported the current study [21,22]. This may be due to employed participants had better exposure to knowledge and more concerned about their health. But no other studies have been found that opposed the current finding.

This study found that from the total respondents 356(59.6%) % of the respondents had Negative Attitude about iodized salt utilization. It had also showed almost similar result with the study done in southern Ethiopia which was 57.4%[21].

Our finding was slightly higher than study done in Dabat and Sudan elaborate that 37.4% and 51% of households had Negative attitude about iodized salt utilization [28,31]. The difference might be due to market availability, accessibility and level of awareness in each study area and country.

Participants those who were age group between 18-24 years 60% less likely to have poor Attitude about iodine salt utilization compared to those who were ≥ 45 years.

This study in line with another study done in Mecha district that explain if the age increase from time-to-time respondents had positive attitude about iodine salt utilization[22].

But another study done Debre tabor town and south Ethiopia showed that the opposite of the current finding that is being young age and were more likely with positive Attitude toward Iodine salt utilization[21,32].

Residence of the respondents showed a significant effect. participants those who had lived in urban area were 71% less likely to have poor Attitude about iodine salt utilization compared to those who had lived in rural area this study supported by study done in south Ethiopia, and Mecha district Participants from urban households are more likely to have positive attitude toward Iodine salt utilization. This may be related to information exposure differences between the 2 communities in that urban households have better access to educational media. And broadcasting of specific information targeting the particular population group and geographical areas through mass media.

This study found that from the total respondents 384(64.3%) of the respondents had poor Practice about iodized salt utilization. The finding was higher than study done in Gidam, Oromia region and Addis Ababa city which were 49.4% and 23.7%[18,43] respectively . This might be due to respondents that participate in the current study it may have good accessibility of different media nearby for the target group in the study area.

Our finding was lower than 74% reported in Mecha district [22].and another study reported was the opposite of the current finding .that was good practice were 98.9% reported in Tripura, India[19]. The discrepancy might be due to in geographical location, educational status of the respondents, accessibility of awareness creation and health promotion it may be high in that study.

In the current study educational status of the respondents showed a significant effect. participants those who had unable read and write had 3 times more likely to have poor practice about iodine salt utilization compared to those who had Collage.

The finding was similar with the study done North Shewa, south Ethiopia and Gidam district it explains that Participants who did not attended formal educations were

more likely to do poor practice on the use of iodized salt than those who attend formal education. This finding was also similar with the study done in Sudan and Iraqi which identified education as a predictor variable to practice about iodized salt [40,42].

This might be due to the fact that higher levels of education provided better nutritional awareness about the benefits of iodine, increased awareness on the health benefits of iodine in diets, and raised the use of iodized salt. In addition, women who had the highest educational status had good employment opportunities which might be indicative of better socio-economic status.

The other reason for this might be the educated head of households might have learnt and read about the importance of iodized salt. Individuals who become more educated they have experience to practice the utilization of iodine salt[18,44,45]. But no other studies have been opposing the current finding during literature review.

Residence of the respondents showed a significant effect. Participants those who had lived in rural area were 3 times more likely to have poor practice about iodine salt utilization compared to those who had lived in urban area. This supported with another study done in North shoa zone and Mecha district [37,45].

This could be related to better awareness due to access to media among urban residents which might enhance their level of understanding regarding the importance of iodized salt and information access. In addition, urban respondents have access to iodized salt everywhere and every time.

Occupational status of the respondents showed a significant effect. Participants those who had house servant were 57% less likely to have poor practice about iodine salt utilization compared to those who had Job seeker. The finding was in line with the study done in another area it explain Participants who were house servant and house wife less likely to have poor practice about iodine salt utilization merchants[37]. This is because participants who were house servant were had many exposure/experiences for cooking so this exposure was comfortable to have good practice iodine salt utilization. But there is no found another study to oppose the current finding.

In this study, expose salt to sunlight, packaging, purchasing from open markets, place of storage and duration of storage has not shown significant effect for KAP of iodine salt utilization but in other study that variable has significant effect for iodine salt utilization[18,37,45].

The reason behind it may be the study period is so longer than in the current study and the sample size also large to compare than the current study.

5. Conclusions and Recommendation

Based on the finding of this study, can conclude that the knowledge, attitude and practice on utilization of iodized salt at household level were poor in Bure Town Administration.

Occupational status, marital status, and residency of participants were identified as predictors associated with knowledge on iodized salt utilization at the household level.

Age of respondents and residency of participants were identified as predictors associated with Attitude on iodized salt utilization at the household level.

Occupational status, educational status, and residency of participants were identified as predictors associated with practice about iodized salt utilization at the household level.

Government should take measure on companies which produced and distributed inadequately iodized salt to the community.

Declarations

Ethical approval and consent to participate: Procedures followed the ethical standards of the Ethical Review Board of Bahir dar University. Following the approval, an Official letter of co-operation was written to concerned body. From those participants who are agreed to be included in the study written informed consent was taken from each study participant during data collection.

Consent to Publish: Not applicable

Availability of data and material: The data supporting this finding can be available at any time with a request.

Competing interests: The authors declare that they have no competing interests.

unding: This is from a developing country; our salary couldn't cover the fee for publication. This paper is original and has a great impact on designing prevention strategies for policymakers and it will be used as the baseline data for future researchers. Therefore, we request your journal to publish this paper-free.

Author's contribution: YM conceived the idea of the study, prepared the study proposal, collected data in the field performed the data analysis, and drafted the manuscript. EM assisted with the preparation of the proposal and the interpretation of data, participated in data analysis, and critically reviewed the manuscript. TM, TG&AM participated in the critical comments of the proposal and manuscript preparation. All authors read and approved the final manuscript

Acknowledgments

We would like to express our heartfelt gratitude to Bahir Dar University president for giving us this chance to do this research. Our appreciation also goes to Buria district manager for their generous provision of information.

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