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Original Research Article

Regional Differences of Drinking Water Iodine and Its Association with Thyroid Disorder and Serum Iodine

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Abstract

The study aims to evaluate relationship between drinking water iodine and serum iodine with thyroid disorders in patients with symptomatic thyroid disease in Erbil province, Iraq. Outpatients attending Rizgariy and Hawler teaching hospital, Erbil province, were participated in this cross sectional study and samples of drinking water were collected randomly from different geographical region of Erbil province**.** Biochemical analyses included; serum thyroid hormones, serum iodine and drinking water iodine. Level of water and serum iodine were deficient 24.1± 6.8 µg/l (SD)µg/l and 24.4 ± 21.4 (SD) µg/l respectively. Highest level of the water iodine was in south west of Erbil city and the lowest one was in the east districts. Water iodine showed significant negative correlation with thyroid stimulating hormone (TSH) in patients with abnormal thyroid function and significant increase risk of hypothyroidism in regions with low water iodine. 20% of patient had hypothyroidism. Serum iodine didn't correlated with water iodine while there was significant negative correlation of it with TSH hormone. Deficiency of drinking water iodine reflects effect of environmental factors on water quality. It is a potential risk factor for developing thyroid disorder especially hypothyroidism in reproductive age of housewives. Continued monitoring treatment and iodized salt programs could prevent hypo and hyperthyroidism.

Key Words: Water and serum iodine, Thyroid disorder, Erbil /Kurdistan / Iraq

الخلاصة

تهدف الدراسة الى استبيان العلاقة بين محتوى اليود في ماء الشرب ومصل الدم وامراض الغدة الدرقية فى محافظة اربيل / العراق. كانت الدراسة وصفية و شملت على عينات الدم من المرضى الذين يعانون من اعراض مرض الغدة الدرقية والتي تم الحصول عليها من مستشفى رزكاري والجمهوري في محافظة اربيل، وعينات من ماء الشرب جمعت بشكل عشوائي من البيوت لتغطية مناطق مختلفة للمرضى في محافظة اربيل لغرض تحليل مستوى اليود في الدم وماء الشرب ومستوى هورمونات الغدة الدرقية . اظهرت نتائج الدراسة نقص فى محتوى اليود في الدم وماء الشرب ، وكانت 21.4 ± 24.4 µg/l و 6.8 ±24.1 µg/l على التوالي ،وتبين بان اعلى مستوى لليود في ماء الشرب كان في منطقة جنوب شرقي مدينة اربيل ، واقل مستوى كان في مناطق الغربية خارج المدينة . واظهرت التحاليل بان ٢٠% من المرضى لهم خمول فى نشاط الغدة الدرقية . بينت نتائج التحليل الإحصائي على وجود علاقة معنوية عكسية ما بين هورمون محفز الدرقية (TSH) ومستوى اليود في ماء الشرب والدم. ودلت النتائج ايضا بان العوامل البيئية تؤثر على نوعية مياه الشرب وبالتالي على محتوى اليود الذي له علاقة وثيقة مع امراض الغدة الدرقية ومعالجتها وانعكاسها على محتوى اليود في الدم. وتؤكد النتائج ايضا على اهمية متابعة برنامج علاج نقص اليود بدقة و بشكل مستمر .

Introduction

Iodine is an essential micronutrient; 150 microgram is required daily for normal growth, metabolism, and regulation of thyroid hormones in human and animals [1]. It is an essential part of two important thyroid hormones; thyroxin or tetra-idothyronin (T4) and tridothyronine (T3). Thyroid stimulating hormone (TSH) is a hormone initiating the entire metabolic pathways to produce T4 and T3.The active iodide transport from blood circulation into

thyroid by TSH in spite of much higher iodide concentration in the gland [2].

The iodine content of food depends on the iodine content of the soils in which it is grown. The requirement of iodine is met from food and water, when the soil content of iodine is adequate, [3]. Erosion of soils causes loss of iodine from soils, groundwater and foods grown locally in these areas which do not provide adequate amount of iodine when consumed [4].

Significant close relationship exist among environment (for example drinking water quality), and human health and thyroid diseases [5]. Thyroid disease is closely associated with absorption of food iodine, and it is an important direct index of human's natural iodine intake. Food iodine is closely related to iodine concentration of water, soil and salt. It is also an indirect index of environmental pollution [6].

Deficiency of iodine has several important health consequences that are together called Iodine Deficiency Disorders (IDD) like goiter, hypothyroidism, cretinism and socioeconomic retardation (Sharbari Basu et al, 2007) and these effects are preventable by correction of the iodine deficiency [4].

Goiter is known to be prevalent in Kurdistan region / Iraq [7]. Erbil province / Iraq considered among the endemic area for goiter and related to iodine deficiency, which resulted in mountainous area from leaching of iodine from soils by heavy rains [8]. Recent studies showed that Iraq is a country with sever IDD. Difficulty of the study and progress due to lack in the required data, and it is still a major public health problem in Duhok./ Iraq [4].

Erbil province is currently served by two types of water resources for drinking; ground water and surface water from great Zab River and Rawanduz River. Three water treatment plants (WTP) have been constructed with intake of raw water from Efraz river (Efraz; 1, 2, 3) [9]. Erbil city imports an average of 85% of its water from the Efraz river and there are several forces negatively impact the quality of water. [5]

This study was conducted as a result of lack of studies to assess the level of drinking water iodine in Erbil province in order to investigate its relation to thyroid disorders and serum iodine in patients with symptomatic hypothyroism disease and to identify effects of managements in Erbil/ Iraqi Kurdistan region.

Material and Methods:

Sample collection:

A- Erbil city geographically is divided to six area considering source of drinking water (center, north, east, south, south west, and west) , and four major districts (North, East, South, and West) to determine drinking water iodine concentration. A total of 50 of drinking water samples from 10 area (covered the dwelling areas of the outpatient hospital samples) were collected randomly from houses, and stored at -20 C^0 for analysis through one week.

B- Fifty five (55) convenient outpatient samples with > 4 positive signs of hypothyroidism diseases; (weight gain, loss of appetite, tiredness, hoarseness of voice, bradycardia, rough skin, menorrhagia) diagnosed by physician, attending Rizgary teaching hospital from 1st July to 30th August of 2010 (one day / week) were participated in this cross sectional study after taking their consent and formal consent from the hospital.

Study instrument: Structured interview questionnaire was used to obtain socio-demographic variables (age, sex, occupation, and residence) and background information about iodized salt use, and diet history.

Biochemical analysis:

a- Determination serum levels of thyroid hormones for outpatients, using Mini Vedas ELFA (Enzyme Linked Fluorescent Assay) and immune-radiometric assay.

b- Determination of total iodine in serum samples and in drinking water by Kinetic-catalytic method of (Takashi et al, 2004) [10].

Statistical analysis

The data have been analyzed by the use of statistical package of social science (SPSS) version 18.and included descriptive statistic, inferential Statistics, independent T-test and ANOVA test for comparing means. Linearly regression for measuring risk of iodine deficiency on thyroid hormones levels**.** P value < 0.05 considered statistically significant

Results and Discussion

Drinking water iodine concentration and regional differences

Table 1 represents iodine levels of drinking water in major geographical region of Erbil province. The minimum mean value was 16.7± 3.4 µg/l in the east districts of Erbil province to a maximum 31.6±5.9 µg/l in the south west of the Erbil city. The mean iodine level in the water samples was low 24.1± 6.8 µg/l, and was in the range (1-50 µg/l), which is considered a potential risk factor for developing goiter [3]. [11] Reported that water iodine is important for iodine intake in many countries and its concentration ranged between (< 1.0 and 139 µg/l).

There was high significant difference between the regions in iodine content of drinking water. South west of Erbil city, and south districts of the Erbil province had higher levels of iodine than other regions, while the lower mean levels were in the east of the city and east districts than other region of the Erbil province. This result may due to regional differences in quality of water which depends on water source from which is drown (geological formation and climate), treatment of water, and pollution of water . It is in line with [12] who stated that chemical differences in the environment (soil, food staff, and drinking water) affect iodine bioavailability and [4] who stated that iodine content of food differs with geographic location.

Table 1: Iodine content of drinking water samples in Erbil provinc

Study area	No.	Mean± SD	Mean ±SE	F- value	P-value
Erbil city					
Center	6	30.2±3.8	30.2 ±1.6	3.75	**≤ 0.01****
North	7	25.5± 5.7	25.5±2.2		
East	4	17.0± 8.9	17.0±4.4		
South	3	20.0± 4.1	20.0±2.4		
South West	3	**31.6±5.9**	31.6±3.4		
West	4	21.2± 3	21.2±1.5		
Districts of Erbil province					
North	11	23.6± 6.9	23.6±2.1		
Districts of East	4	**16.7± 3.4**	16.7±1.7		
South Districts	4	29.9± 3.5	29.9±1.8		
Districts of West Erbil proviience	4	23.2± 4.3	23.2±2.1		
Total	50	**24.1± 6.8**	24.1±1.0		

No. = Number or Frequency of sample, Sig = Significant, ** = High significant value for P value

One way ANOVA (post hoc) multiple comparison test (Table 2) showed that drinking water in the center and south west of the city differ significantly with regions that had lower levels of drinking water iodine, and were; east, south, west, of the city . This due to water source of drinking water in the south west, center of the city, which is mostly Efras river while is ground water in the east, south and west of the Erbil city. This difference may due to pollution, as indicated by their water quality indices measured by [5], and included higher nitrate content, higher

turbidity, and higher alkalinity than (WHO) guide line and 1raqi standard range and attributed pollution to long distance winding through unprotected watershed containing towns and farms. Further study [13] regarded high values of water nitrite as a warning sewage contamination and the effect of urban water discharge that containing high amount of nitrate. [6] Concluded that iodine content of water indirectly reflects environmental pollution especially of the water of ditches and river.

Table 2: multiple comparison tests of the studied areas in Erbil province

Studied area comparisons		**Mean Difference ± SE**	
East (E) with other city regions (R)		**E-R ± SE**	**Sig.**
East	Center of the city	-13.17±3.6 **	0.00
	North	-8.5±3.5 *	0.02
	South	-3.01±4.26	0.48
	South west	-14.6±4.26**	0.00
	West	-4.15± 3.9	0.30
South West (S) with other regions(R)		S-R ± SE	Sig
South West	Center of Erbil province	1.40± 3.94	0.72
	North of the city	6.08± 3.84	0.12
	East	14.56± 4.26 **	0.00
	South	11.56± 4.55 *	0.02
	West	10.4* ± 4.26*	0.02
Comparisons among districts		Mean Difference ±SE	
East Districts (E) with other Districts (D)		E-D± SD	Sig
East Districts	North District	-6.9± 3.25*	0.039
	South	-13.2± 3.9**	0.002
	West	-6.5± 3.9	0.108
South Districts (S) with other Districts (D)		S-D± SD	Sig
South Districts	North Districts	6.23± 3.3	0.063
	East Districts	13.18±3.9*	0.002
	West Districts	6.7±3.9	0.097

* = Significant value for P value

Among the districts; south had the highest level of iodine and differ significantly from mountainous area in the east districts and hill area of west districts of Erbil province while north district showed no significant difference with both south and east districts of Erbil province, figurer 1. These differences may due to iodine content of environment and soil which indirectly reflected on chemical properties of water and cause alkaline pH, high conductivity and high calcium and sulphate ions. This view the results of other studies; [14] and [15] who concluded that endemic iodine deficiency diseases occur among the population of the northern Iraq and affected by various environmental factors including pH, dissolved salts especially elements calcium and sulfur species, which determine the bioavailability of iodine for the biological processes. Also consistent with [16] who concluded that highest concentrations of iodine were in pH > 7.5 of water and positively correlated with conductivity of ground water.

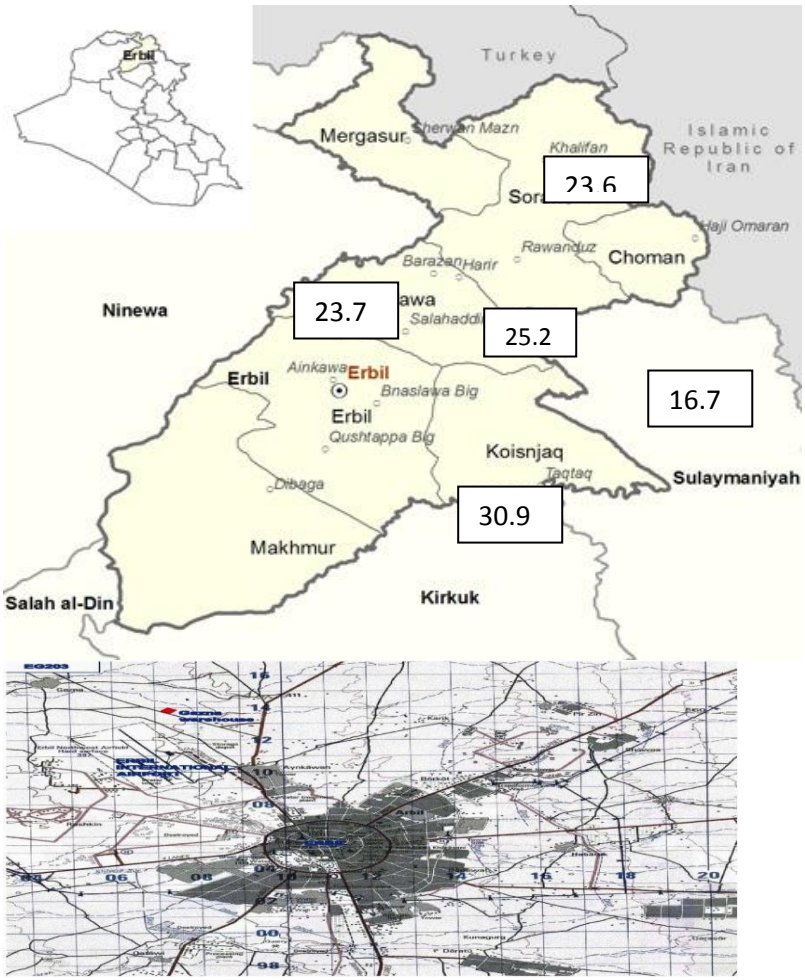

Figure 1: Maps of Erbil province and mean levels of iodine in drinking water (µg/l) in the center and districts

Association of thyroid hormones with drinking water iodine:

Table 3 shows mean levels of thyroid hormones in studied population. They were categorized into two groups; normal thyroid function status and abnormal status according to reference range of thyroid hormones T_4 (60-120 nmol/l), T_3 (0.95- 2.5 nmol/l), and TSH (0.3-5 µIU/l). Approximate to half 44.4% of studied population had abnormal thyroid function test and 45.8% out of it had high levels of TSH hormone (> 5 µIU/ml) which correspond to 20% of all samples. There was significant difference in the mean levels of T_3 and TSH between patient with normal and abnormal thyroid function tests.

Table 3 also shows mean levels of drinking water iodine of regions where patients dwelling and its significant negative correlation with TSH. Linear regression analysis after adjusting for gender and ages showed significant risk of low water iodine in regions where patients had high levels of TSH. These results may due to lack of substrate for thyroid hormones synthesis and indicates that iodine deficiency may be a major cause of hypothyroidism. It is in agreement with [1] who observed significant high value of TSH in hypothyroidism patients and concluded that iodine deficiency could be associated with an increase of hypothyroidism. Also [17] concluded that iodine deficiency disorders is the cause of hypothyroidism and [7] reported that incidence of goiter in Erbil Gov. would be between 20-30% with clinical evidence of few of hypothyroidism.

Table 3: Thyroid hormones and drinking water iodine levels in normal and abnormal categories

Thyroid hormones status	Thyroid hormones levels			Mean± SD	t-value	Sig.	Relation of water iodine with hormones	
Normal	No.	Minimum	Maximum					
T_4 nmol./l	30	71.77	110.6	89.7± 10.1			N.S.	
T_3 nmol/l	30	1.00	2.37	1.7 ± 0.3	-2.1	< 0.05		
TSH µIU/ml	30	.61	3.09	1.5± 0.66	-2.6	< 0.05		
Abnormal	No.	Minimum	Maximum	Mean± SD			R value	Sig.
T4 nmol/l	25	11.02	266.0	88.5±51.9				
T3 nmol/l	25	.30	5.86	2.3± 1.24				
TSH µIU/l	25	.04	80.00	12.97± 21.7			-0.42	< 0.05
Iodine content of water (µg/l)	No.	Water iodine levels					Risk of water deficiency in abnormal category with high levels of TSH	
							OR	95% CI
Normal	30	17.2	34.9	26.3± 5.6	1.23	N.S.		Lower Upper
Abnormal	25	8.7	34.9	24.3± 6.6			-1.4*	-0.05 -2.7

R= Pearson's correlation OR = Odds ratio or risk of iodine decrease among abnormal category

Socio-demographic characteristic of studied population

Table 4A shows, age groups, ranged between (13 - 67) years, with mean (37.4± 15.5) years. Most of patients with normal thyroid function were in age group (41-50) years; while abnormal thyroid function patients' age was (39.0±17.6) years and most were in age group (21-30) years. Majority of patients were; house wives and married (Table 4A & B). These views the same result of further researchers that abnormal thyroid function was highest in third decade of life (21-30) years and decrease by ages especially among women in reproductive age which occupied 80% of studied abnormal sample and were four times more than males. This may due to the effects of sex hormones levels, and pregnancy as found by [8] among age (34.5) years and [19] who concluded that prevalence of thyroid disease in Erbil city was at age groups of (20-39) years, and [18] who found hyperthyroidism 4 times more common among females than in males in Erbil city from period (1998 - 2010). Significant correlation between thyroid hormones (T_4 and TSH) with ages among patients with abnormal thyroid function conforms that TSH decrease with ages as concluded by [17] in area with mild and moderate iodine deficiency.

Table 4 A: Socio-demographic characteristic and their relations with thyroid hormones

Age Group	**Normal Group**		**Relations with hormones**	**Abnormal Group**					**Relations with hormones**	
				(TSH µIU/l)					**Age with TSH**	
	No.	**%**	N.S.	< 0.3	0.3-5	> 5	**Total**	**%**	R value	Sig
≤ 20	5	16.7		0	2	2	4	16.7	**-.43**	**≤ 0.05**
21-30	7	23.3		0	3	5	**8**	**32**	**Age with T4**	
31-40	7	23.3		0	0		2	8.3	**0.4**	**≤ 0.05**
41-50	**8**	**26.7**		3	0	0	3	12.5		
51-60	3	10.0		2	1	2	5	20.8		
≥ 61				2	0	1	3	12.5		
Total	30	100		7	6	11	25	100		

Gender	**Normal**			**Abnormal**			**Total**		
	No.	**%**		**No.**	**%**		**No.**	**%**	
Male	8	26.7		5	20		13	23.6	
Female	22	**73.3**		20	**80.0**		42	76.4	

Marital status	**Normal**			**Abnormal**				
	No.	**%**		**No**	**%**		No.	%	
Married	23	**76.7**		19	**76.0**		42	76.4	
Not Married	7	23.3		6	24.0		13	23.6	

Type of salts	**No.**	**%**	**Relations of salts with water iodine**			**No.**	**%**	**Relations with water iodine**
Iodized salt	**17**	**56.7**	**Chi Square**			**15**	**60.0**	**N.S.**
Not iodized	10	33.3	**39.5**	**≤ 0.05**		10	40	
Mixed	3	10	**With TSH**			0	0	
			Eta test	**Value**				
Total	30	100	**0.54**	**Strong**		25	100	

Eta test for relation between nominal and interval, N.S. = No Significant

(Table 4A) using iodized salt by most than half of patients may be attributed to regular monitoring and assessment of the level of iodine in the salt utilized by household across Iraq by governorate. It is consistence with Multiple Indicators Cluster Survey (MICS) conducted every five year by ministry of planning and Health and UNICEF who found 37.5% of Kurdistan region utilize adequate iodized salt and reached to 76.7% in Duhok Governorate [20]. Significant negative association between types of salts intake and iodine content of water from their dwelling region and strong relation between iodized salt and TSH hormone of normal patients confirm lack of hypothyroidism among these patients and may be resulted from correction effect of water iodine deficiency by long duration use of iodized salt in addition to the effects of; concentration of iodine in the salt, type of foods ingested and genetic susceptibility. This is online with [21 and 22] and [1] who supported the use of iodized salt as a corrective strategy in area with IDD, and with [18] who found lowest cases in (2008-2009) years of thyroid diseases in iodine deficiency area and attributed it to iodizing table salts program which play an important role in prevention of goiter and eventually hyperthyroidism. Beside adaption effect of the normal thyroid gland in less sever iodine deficiency to keep thyroid hormone

production within the normal range as stated with [23].

According to residence status Table 4B; most of patients were from the center and north of the Erbil city , there was no significant difference between two categories in residence in spite of presence of patients from areas with lowest water iodine content (south of the city and east districts) in abnormal category. This result may due to the hospital position in the center where hormones analyzed and Ifraz river pollution in the center and north of the city with compounds that decrease bioavailability of iodine such as nitrate as concluded by [24] that high nitrate level was associated with inhibition of iodine intake by thyroid gland and thyroid hypertrophy. Also view the same result of [8] who found two third of thyroid patients from inside of the Erbil city and attributed it the position of the hospital in the center of the city and [4] who found mild iodine deficiency in primary school children, 71.1% of them were from urban area.

Table 4 B : Socio-demographic characteristic of studied population

Occupation Status	**Normal**		**Abnormal**		
	No.	**%**	**No**	**%**	**Total**
Government	8	26.7	4	16.0	12
House wife	**16**	**53.3**	**15**	**60.0**	**31**
Student	1	3.3	3	12.0	4
Self employed	4	13.3	2	8.0	6
Retired	1	3.3	1	4.0	2
Total	30	100	25	100	55
Residence	**No.**	**%**	**No.**	**%**	**Total**
Center of the city	**10**	**33.3**	**6**	**24.0**	**16**
North of the city	**5**	**16.6**	**5**	**20.0**	10
East of the city	3	10.0	2	8.0	5
South of the city	3	10.0	**6**	**24.0**	9
South West of the city	2	6.7	1	4.0	3
North Districts	3	10.0	1	4.0	4
East Districts	2	6.7	**4**	**16.0**	6
South Districts	2	6.7	----	-------	2
Total	30	100	25		55

Serum Iodine levels: Table 5 shows deficiency of serum iodine and was lower than normal range (45-100 µg/l) measured by [25]. The highest level was in married house wife women at fourth decade of life in rural area, and they used iodized salts. There was relation between serum iodine and ages, also significant correlation of it with TSH hormone. There was low relation of serum iodine with residence and type of salts used. These results confirm prevalence of thyroid disorder in reproductive ages as consequence of water iodine deficiency, especially in rural area that were far from management centers (city) as stated by [8], and had low awareness to complexity of disease. This view has been supported with [26] who stated that, education should be one of the main pathways of communicating information to alleviate IDD.

Table 5: Serum iodine levels & its relation to thyroid hormones and socio-demographic characteristic

Serum iodine (µg/l)	Thyroid function status	Mean ± SD of serum I_2	Differences	Relations serum I_2 with TSH
Mean average		24.4±21.4		R Value Sig.
Cases	Normal Abnormal	17.1± 5.2 28.5± 17.9	N.s.	-0.65 < 0.05*
Age group (years)	≤ 20 21-30 31-40 ≥41	12.0±5.23 24.7±15.01 41.1±36.48 14.1± 4.3	N.s.	Serum I_2 with age Eta test value 0.55 Strong
Gender	Male Female	17.4± 4.4 28.4± 26.5	N.s.	N.s.
Marital status	Married Not married	29.3±23.4 11.1±4.0	N.s.	N.s.
Occupation	Employed House wife	19.9± 11.4 29.6±30.4	N.s.	N.s.
Residence	Urban Rural	18.0± 10.5 41.3 ±36. 3	N.s.	Serum I_2 with residence Eta test Value 0.40 Low
Type of salts	Iodized Not iodized Mixed salts	31.4±26.9 16.4±7.7 15.0± 2.2	N.s.	Serum I_2 with Type of salt Eta test Value 0.42 Low

N.S. = No significant

Negative correlation of serum iodine with TSH hormone in spite of no relation with water iodine of their dwelling region indicates that serum iodine increase in hyperthyroidism and decreases in hypothyroidism. This result parallel with [1] that found negative significant correlation of serum and urinary iodine with TSH hormone and concluded its use as indicator for thyroid dysfunction. The result also reveals effects of other factors; genetic, malnutrition, iodized salt, goitrogens, treatments (hormone replacement therapy, medication), and prolonged adaption of normal thyroid gland to mild and moderate iodine deficiency especially in elderly people. This conclusion supported with further researchers [1, 14, 22] who attributed no correlation between drinking water iodine and urinary iodine in goiters patients to other factors and causes.

33.3% of abnormal thyroid function patients were hyperthyroidism patients who did thyroidectomy. This result confirms no relation of water iodine with serum iodine and reveals effects of treatment, and intake of iodized salts and foods. It is consistence with [18] who stated that development of various forms of hyperthyroidism depends to a great extent on the iodine intake of the population and attributed most cases of hyperthyroidism to a program of iodinization of table salt sponsored by UNICEF, also [21] who suggested that an increase in the prevalence of iodine-induced hyperthyroidism is temporary and that within a few years of population exposure to iodized salt, the prevalence of hyperthyroidism reverts to baseline levels or even lower. Further study [23] and [27] concluded that hyperthyroidism may ensue if iodine deficiency is not extremely severe.

Advantage of the study: It is new trial for measuring level of iodine in drinking water in Erbil province, and identifying its association with serum iodine. Limitation of the study: The study was a cross sectional study and sample size of the water and sample of patients participated in this study were small.

Conclusion

Deficiency of iodine content of drinking water especially in mountainous area of east districts of Erbil province reflects environmental differences in water ; alkalinity, conductivity properties and pollution . Potentially affect serum iodine bioavailability and may cause thyroid disorder among reproductive ages of housewives. Continued monitoring treatment and iodized salt programs (duration of uses and iodine salt concentration) can provide high-quality outcomes, and prevent potential adverse effects such as hypothyroidism and hyperthyroidism.

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