Journal of Medical Research and Health Sciences
Received 12 Aug 2021 | Revised 30 Aug 2021 | Accepted 25 Sep 2021 | Published Online 16 Oct 2021

DOI: https://doi.org/10.52845/JMRHS/2021-4-10-4
JMRHS 2 (10), 1500–1510 (2021)

ISSN (O) 2589-9031 | (P) 2589-9023

RESEARCH ARTICLE

OPEN ACCESS JOURNAL

Evaluation of Twenty Chemical Elements in Thyroid with Hashimoto's thyroiditis using X-Ray Fluorescent and Neutron Activation Analysis

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Abstract

Background: Hashimoto's thyroiditis (HT) is an internationally important health problem.

Objectives: Role of chemical elements (ChE) in etiology and pathogenesis of HT is unclear. The aim of this exploratory study was to assess whether there were significant changes in thyroid tissue levels of twenty ChE (Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn) are present in the HT transformed thyroid.

Methods

Twenty ChE of thyroid tissue were determined in 8 patients with HT. The control group included thyroid tissue samples from 105 healthy individuals. Measurements were conducted using combination of non-destructive methods such as energy dispersive X-ray fluorescent analysis and instrumental neutron activation analysis.

Results

Conclusions

Reduced mean values of Ca and I content almost in two times, while elevated level of Ag, Cu, Hg, and Na in 21, 1.2, 30, and 1.5 times, respectively, were found in thyroid with HT in comparison with normal level.

There are considerable changes in some ChE contents in tissue of thyroid with HT. Thus, it is reasonable to assume that the levels of these ChE in affected thyroid tissue can be used as HT markers. However, this topic needs additional studies.

Keywords: Hashimoto's thyroiditis, Intact thyroid, Chemical elements, Energy dispersive X-ray fluorescent analysis, Neutron activation analysis.

1 | INTRODUCTION

Hashimoto's thyroiditis (HT), also called chronic lymphocytic or autoimmune thyroiditis, is part of the spectrum of chronic autoimmune thyroid diseases (1). Hashimoto's disease is associated with thyroid autoantibodies production like the most common, thyroid peroxidase and thyroglobulin antibodies, and with lymphocytic inltration (1). Although the HT was described over 100 years ago the exact mechanism of progressive thyroid tissue destruction as a result of HT is still not sufficiently elucidated. Clinical differentiation between HT, Riedel's struma and other thyroid benign and malignant nodules is often difficult (2, 3). We hypothesized that imbalance of chemical elements (ChE) contents in thyroid tissue may play a significant role in etiology and pathogenesis of HT. Furthermore, specific levels of ChE contents in autoimmune transformed thyroid tissue may be used as HT biomarkers.

For over the 20th century, there was the governing opinion that all thyroid nodules (TN), including HT, are the straightforward sequel of iodine (I) deficiency. Though, it was found that TN is a frequent disease even in those countries and regions where the inhabitants are never exposed to I shortage (4). Moreover, it was shown that iodine excess has severe effects on human health and is associated with the development of thyroidal disfunctions and autoimmunity, nodular and diffuse goiter, benign and malignant tumors of gland (5–8). It was also demonstrated that besides the iodine deficiency and excess many other dietary, environmental, and occupational factors are associated with the TN incidence (9–11). Among them, a disruption of evolutionary stable input of many chemical elements (ChE) in the human body after the industrial revolution plays a significant role in the etiology of thyroidal disorders (12).

In addition to I, many other ChE is involved in essential physiological functions (13). Crucial or toxic (phologistic, goitrogenic, mutagenic, carcinogenic) properties of ChE depend on tissue-specific need or tolerance, respectively (13). Deficiency, overload, or an imbalance of the ChE may result in cellular dysfunction, degeneration, death, benign or malignant transformation (13–15).

In our earlier studies, the complex of in vivo and in vitro nuclear analytical and related methods was developed and used for the investigation of iodine and other ChE contents in the normal and pathological thyroid (16–22). Iodine level in the normal thyroid was scrutinized in relation to age, gender, and some non-thyroidal diseases (23, 24). Hereafter, variations of ChE content with age in the thyroid of males and females were studied, and age- and gender-dependence of some ChE was perceived (25–41). In addition, a significant difference between some ChE contents in normal and cancerous thyroid was demonstrated (42–47).

So far, the etiology and pathogenesis of HT has to be considered as multifactorial. The present study was performed to clarify the role of some ChE in the HT etiology. Having this in mind, our aim was to assess the silver (Ag), bromine (Br), calcium (Ca), chlorine (Cl), cobalt (Co), chromium (Cr), coper (Cu), iron (Fe), mercury (Hg), I, potassium (K), magnesium (Mg), manganese (Mn), sodium (Na), rubidium (Rb), ammonium (Sb), scandium (Sc), selenium (Se), strontium (Sr), and zinc (Zn) contents in HT affected thyroid tissue using energy dispersive X-ray fluorescent analysis (EDXRF) combined with non-destructive instrumental neutron activation analysis with high resolution spectrometry of sort-lived radionuclides (INAA-SLR) and long-lived radionuclides (INAA-LLR). A further aim was to compare the levels of these twenty ChE in the HT transformed thyroid with those in normal (intact) thyroid (NT).

2 | MATERIAL AND METHODS

All patients with HT (n=8, 7 females and 1 male, mean age MSD was 4010 years, range 34-55) were hospitalized in the Head and Neck Department of the

Supplementary information The online version of this article (https://doi.org/10.52845/JMRHS/2021-4-10-4) contains supplementary material, which is available to authorized users.

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MRRC. Thick-needle puncture biopsy of suspicious lesion of the gland was performed for every persons, to allow morphological examination of affected thyroid tissue and to determine their TE contents. For all patients the diagnosis has been confirmed by clinical and morphological results obtained during studies of biopsy and resected materials. Histological conclusion for all thyroidal lesions was the HT.

Normal thyroid samples were removed at necropsy from 105 deceased (mean age 4421 years, range 2-87), who had died suddenly. The majority of deaths were due to trauma. Histological examination was used in the NT group to match the age criteria, as well as to confirm the absence of micro-nodules and underlying cancer.

All studies were approved by the Ethical Committees of the Medical Radiological Research Centre (MRRC), Obninsk. All the procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments, or with comparable ethical standards.

All thyroid samples were divided into two parts using a titanium scalpel (48). One was used for morphological study while the other was for TE evaluation. All samples for TE analysis were weighed, freeze-dried and homogenized (49).

The content of Br, Cu, Fe, Rb, Sr, and Zn were determined by EDXRF. Details of the relevant facility for this method, source with ^{109}Cd radionuclide, methods of analysis and the results of quality control were presented in our earlier publications concerning the EDXRF of ChE contents in human thyroid and prostate tissue (25, 26, 50).

The content of Br, Ca, Cl, I, K, Mg, Mn, and Na were determined by INAA-SLR using a horizontal channel equipped with the pneumatic rabbit system of the WWR-c research nuclear reactor (Branch of Karpov Institute, Obninsk). Details of used neutron flux, nuclear reactions, radionuclides, gamma-energies, spectrometric unit, sample preparation and measurement were presented in our earlier publications concerning the INAA-SLR of ChE contents in human thyroid, scalp hair, and prostate (27, 28, 51–53)

In a few days after non-destructive INAA-SLR all thyroid samples were repacked and used for INAA-LLR. A vertical channel of the WWR-c research nuclear reactor (Branch of Karpov Institute, Obninsk).was applied to determine the content of Ag, Co, Cr, Fe, Hg, Rb, Sb, Sc, Se, and Zn by INAA-LLR. Details of used neutron flux, nuclear reactions, radionuclides, gamma-energies, spectrometric unit, sample preparation and measurement were presented in our earlier publications concerning the INAA-LLR of ChE contents in human thyroid, scalp hair, and prostate (29, 30, 51, 54)

To determine contents of the ChE by comparison with a known standard, biological synthetic standards (BSS) prepared from phenol-formaldehyde resins were used (55).In addition to BSS, aliquots of commercial, chemically pure compounds were also used as standards. For each method ten certified reference material IAEA H-4 (animal muscle) and IAEA HH-1 (human hair) sub-samples were treated and analyzed in the same conditions that thyroid samples to estimate the precision and accuracy of results.

A dedicated computer program for INAA mode optimization was used (56). All thyroid samples were prepared in duplicate, and mean values of ChE contents were used. Mean values of ChE contents were used in final calculation for the Br, Fe, Rb, and Zn mass fractions measured by two methods. Using Microsoft Office Excel, a summary of the statistics, including, arithmetic mean, standard deviation, standard error of mean, minimum and maximum values, median, percentiles with 0.025 and 0.975 levels was calculated for ChE contents. The difference in the results between two groups (NT and HT) was evaluated by the parametric Student's t-test and non-parametric Wilcoxon-Mann-Whitney U-test.

3 | RESULTS

resents certain statistical parameters of theAg, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn mass fraction in normal thyroid and thyroid with Hashimoto's thyroiditis.

Comparison of values obtained for Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc,

Se, Sr, and Zn contents in the NT and HT group of samples with median of means reported by other researches (57–81) depicts in Table 2. A number of values for ChE mass fractions in literature were not expressed on a dry mass basis. However, we calculated these values using published data for water (75%) (82) and ash (4.16% on dry mass basis) (83) contents in thyroid of adults.

The ratios of means and the distinction between mean values of Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn mass fractions in the NT and HT group of samples are presented in Table 3.

4 | DISCUSSION

Previously found good agreement of the Br, Ca, Cl, I, K, Mg, Mn, and Na contents analyzed by INAA-SLR with the certified data of CRM IAEA H-4 (18, 25–30, 50–54) indicates an acceptable accuracy of the results obtained in the study of ChE of the thyroid samples presented in Tables 1-3.

The mean values and all selected statistical parameters were calculated for all twenty ChE (Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn) mass fractions in NT and HT groups of tissue samples (Table 1).

In a general sense values obtained for Br, Ca, Cl, Cr, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, and Zn contents in the normal human thyroid (Table 2) agree well with median of mean values reported by other researches (57–75).

Table 1. Some statistical parameters of Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn mass fraction (mg/kg, dry mass basis) in normal thyroid and thyroid with Hashimoto's thy-roiditis

Tissue	Element	Mean	SD	SEM	Min	Max	Median	P 0.025	P 0.975
Normal	Ag	0.0151	0.0140	0.0016	0.0012	0.0800	0.0121	0.0017	0.0454
n=105	Br	14.9	11.0	1.2	1.90	54.1	11.6	2.56	49.3
	Ca	1711	1022	109	414	6230	1458	460	3805
	Cl	3400	1452	174	1030	6000	3470	1244	5869
	Co	0.0399	0.0271	0.0030	0.0046	0.140	0.0327	0.0134	0.124
	Cr	0.539	0.272	0.032	0.130	1.30	0.477	0.158	1.08
	Cu	4.23	1.52	0.18	0.500	7.50	4.15	1.57	7.27
	Fe	223	93	10	51.0	512	221	74.2	433
	Hg	0.0421	0.0358	0.0041	0.0065	0.180	0.0304	0.0091	0.150
	I	1841	1027	107	114	5061	1695	230	4232
	K	6071	2773	306	1740	14300	5477	2541	13285
	Mg	285	139	17	66.0	930	271	81.6	541
	Mn	1.35	0.54	0.07	0.510	4.18	1.32	0.537	2.23
	Na	6702	1764	178	3050	13453	6690	3855	10709
	Rb	8.16	4.55	0.49	1.66	29.4	7.37	3.08	19.3
	Sb	0.111	0.072	0.008	0.0047	0.308	0.103	0.0117	0.280
	Sc	0.0046	0.0038	0.0008	0.0002	0.0143	0.0042	0.00035	0.0131
	Se	2.32	1.29	0.14	0.439	5.80	2.01	0.775	5.65
	Sr	4.55	3.22	0.37	0.100	13.7	3.70	0.483	12.3
	Zn	105.1	40.1	4.3	7.10	221	104.9	39.2	186
Hashimoto's	Ag	0.319	0.116	0.067	0.187	0.408	0.361	0.196	0.406
thyroiditis	Br	81.3	38.1	22.0	55.0	125	64.0	55.5	122
n=8	Ca	971	197	114	775	1169	968	785	1159
	Cl	8068	2571	1818	6250	9886	8068	6341	9795
	Co	0.0499	0.0172	0.0099	0.0321	0.0664	0.0512	0.0331	0.0656
	Cr	0.404	0.546	0.315	0.0750	1.03	0.103	0.0764	0.987
	Cu	5.05	0.21	0.15	4.90	5.20	5.05	4.91	5.19
	Fe	165	129	46	94.0	478	112	95.4	423
	Hg	1.27	0.39	0.23	0.894	1.68	1.23	0.911	1.66
	I	951	630	223	83.0	1787	1136	120	1759
	K	11785	9731	5618	5690	23007	6657	5738	22190
	Mg	530	276	159	326	844	419	331	823
	Mn	2.60	2.33	1.35	0.930	5.26	1.60	0.964	5.08
	Na	10211	1432	827	9286	11861	9486	9296	11742
	Rb	11.4	5.2	1.9	3.80	19.3	11.8	4.36	19.0
	Sb	0.0946	0.0493	0.0280	0.0377	0.126	0.1200	0.0418	0.126
	Sc	0.0214	0.0294	0.0170	0.00020	0.0550	0.0091	0.00065	0.0527
	Se	1.63	0.47	0.27	1.15	2.09	1.64	1.18	2.06
	Sr	3.70	2.73	1.0	0.740	6.66	4.81	0.749	6.61
	Zn	97.6	28.0	9.9	50.0	140	97.3	55.1	138

M – arithmetic mean, SD – standard deviation, SEM – standard error of mean, Min – minimum value, Max – maximum value, P 0.025 – percentile with 0.025 level, P 0.975 – percentile with 0.975 level.

Table 2 . Median, minimum and maximum value of means of twenty chemical element contents in normal thyroid and thyroid with Hashimoto's thyroiditis according to data from the literature in comparison with our results (mg/kg, dry mass basis)

Tissue	Published data [Reference]			This work
Element	Median of means (n)*	Minimum of means M or M±SD, (n)**	Maximum of means M or M±SD, (n)**	Males and females M±SD
Normal thyroid				
Ag	0.21 (12)	0.000784 (16) [57]	1.20±1.24 (105) [58]	0.0151±0.0140
Br	18.1 (11)	5.12 (44) [57]	284±44 (14) [59]	14.9±10.9
Ca	1600 (17)	840±240 (10) [60]	3800±320 (29) [60]	1692±1022
Cl	6800 (5)	804±80 (4) [61]	8000 (-) [62]	3400±1452
Co	0.306 (25)	0.016 (66) [63]	70.4±40.8 (14) [59]	0.0399±0.0271
Cr	0.69 (17)	0.088 (83) [64]	24.8±2.4 (4) [61]	0.539±0.272
Cu	5.94 (61)	0.16 (83) [64]	220±22 (10) [61]	4.23±1.52
Fe	252 (21)	56 (120) [65]	3360 (25) [66]	223±93
Hg	0.08 (13)	0.0008±0.0002 (10) [60]	396±40 (4) [61]	0.0421±0.0358
I	1888 (95)	159±8 (23) [67]	5772±2708 (50) [68]	1841±1027
K	4400 (16)	46.4±4.8 (4) [61]	6090 (17) [69]	6071±2773
Mg	390 (16)	3.5 (-) [70]	1520 (20) [71]	285±139
Mn	1.62 (40)	0.076 (83) [64]	69.2±7.2 (4) [61]	1.35±0.58
Na	8000 (9)	438 (-) [72]	10000±5000 (11) [73]	6702±1764
Rb	7.8 (9)	=0.85 (29) [60]	294±191 (14) [59]	8.20±4.54
Sb	0.15 (10)	0.040±0.003 (-) [72]	= 12.4(-) [74]	0.111±0.072
Sc	0.009 (4)	0.0018±0.0003 (17) [75]	0.014±0.005 (10) [60]	0.0046±0.0038
Se	2.32 (21)	0.436 (40) [63]	756±680 (14) [59]	2.32±1.29
Sr	0.61 (9)	0.055 (83) [64]	46.8±4.8 (4) [61]	4.55±3.22
Zn	110 (56)	2.1 (-) [70]	820±204 (14) [59]	105±40
Hashimoto's thyroiditis				
Ag	0.110 (1)	0.11±0.05 (19) [76]	0.11±0.05 (19) [76]	0.319±0.116
Br	-	-	-	81.3±38.1
Ca	-	-	-	971±197
Cl	-	-	-	8068±2571
Co	-	-	-	0.0499±0.0172
Cr	-	-	-	0.404±0.546
Cu	2.06 (3)	1.66 (31) [77]	4.8±2.8 (14) [76]	5.05±0.21
Fe	-	-	-	165±129
Hg	-	-	-	1.27±0.39
I	470(5)	140 (2) [78]	800 (10) [79]	951±630
K	-	-	-	11785±9731
Mg	-	-	-	530±276
Mn	0.80 (2)	0.768 (31) [80]	0.836±0.500 (51) [77]	2.60±2.33
Na	-	-	-	10211±1432
Rb	-	-	-	11.4±5.2
Sb	-	-	-	0.0946±0.0493
Sc	-	-	-	0.0214±0.0294
Se	1.03 (4)	0.408±0.209 (51) [77]	3.88±1.76 (7) [81]	1.63±0.47
Sr	-	-	-	3.70±2.73
Zn	54.9 (4)	22.4 (31) [77]	86.4±38.8 (14) [76]	97.6±28.0

M –arithmetic mean, SD – standard deviation, (n)* – number of all references, (n)** – number of samples.

The obtained means for Ag and Co were almost one order of magnitude lower whereas mean for Sr was 7.46 times higher than median of previously reported means for NT, but, nevertheless, inside the range of means (Table 2). Data cited in Table 2 for NT also includes samples obtained from patients who died from different non-endocrine diseases. In our previous study it was shown that some non-endocrine diseases can effect on ChE contents in thyroid (24). Moreover, in many studies the "normal" thyroid means a visually non-affected tissue adjacent to benign or malignant thyroidal nodules. However, there are no data on a comparison between the ChE contents in such kind of samples and those in thyroid of healthy persons, which permits to confirm their identity.

The data on ChE levels in thyroid with HT are very limited (Table 2). Results for Se obtained in the present study agree well with published data, while our value for Ag, Cu, I, Mn, and Zn are some higher than the upper limit of means from literature. Information on Br, Ca, Cl, Co, Cr, Fe, Hg, K, Mg, Na, Rb, Sb, and Sc contents in thyroid with HT was not found.

Table 3. Differences between mean values (M±SEM) of Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn mass fraction (mg/kg, dry mass basis) in normal thyroid and thyroid with Hashimoto's thyroiditis

Element	Thyroid tissue				Ratio
	Normal thyroid n=105	Hashimoto's thyroiditis n=8	Student's t-test $p\leq$	U-test p	Hashimoto's thyroiditis to normal thyroid
Ag	0.0151±0.0016	0.319±0.067	**0.046**	**=0.05**	21.1
Br	14.9±1.2	81.3±22.0	0.093	>0.05	5.46
Ca	1711±109	971±114	**0.0020**	**=0.01**	0.57
Cl	3400±174	8068±1818	0.234	>0.05	2.37
Co	0.0399±0.0030	0.0499±0.0099	0.420	>0.05	1.25
Cr	0.539±0.032	0.404±0.315	0.712	>0.05	0.75
Cu	4.23±0.18	5.05±0.15	**0.014**	**=0.01**	1.19
Fe	223±10	165±46	0.249	>0.05	0.74
Hg	0.0421±0.0041	1.27±0.23	**0.033**	**=0.01**	30.2
I	1841±107	951±223	**0.0045**	**=0.01**	0.52
K	6071±306	11785±5618	0.416	>0.05	1.94
Mg	285±17	530±159	0.264	>0.05	1.86
Mn	1.35±0.07	2.60±1.35	0.453	>0.05	1.93
Na	6702±178	10211±827	**0.046**	**=0.01**	1.52
Rb	8.16±0.49	11.4±1.9	0.128	>0.05	1.40
Sb	0.111±0.008	0.0946±0.0280	0.635	>0.05	0.85
Sc	0.0046±0.0008	0.0214±0.0170	0.425	>0.05	4.65
Se	2.32±0.14	1.63±0.27	0.103	>0.05	0.70
Sr	4.55±0.37	3.70±1.0	0.464	>0.05	0.81
Zn	105.1±4.3	97.6±9.9	0.501	>0.05	0.93

M – arithmetic mean, SEM – standard error of mean, Statistically significant values are in **bold**

The range of means of Ag, Br, Ca, Cl, Co, Cr, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn level reported in the literature for NT tissue vary widely (Table 2). This can be explained by a dependence of ChE content on many factors, including "normality" of thyroid samples (see above), the region of the thyroid, from which the sample was taken, age, gender, ethnicity, mass of the gland, and its functional activity. Not all these factors were strictly controlled in cited studies. However, in our opinion, the main reason for the inter-observer discrepancy can be attributed to the accuracy of the analytical techniques, sample preparation methods, and the inability to take standardized samples from affected tissues. It was insufficient quality control of results in these studies. In many scientific reports, tissue samples were ashed or dried at high temperature for many hours. In other cases, thyroid samples were treated with solvents (distilled water, ethanol, formalin etc). There is evidence that during ashing, drying and digestion at high temperature some quantities of certain ChE are lost as a result of this treatment. That concerns not only such volatile halogen as Br, but also other ChE investigated in the study (84, 85).

From Table 3, it is observed that in HT samples the mass fraction of Ca and I are approximately two times lower, while Ag, Cu, Hg, and Na contents are 21, 1.2, 30, and 1.5 times, respectively, higher than in NT. Thus, if we accept the ChE contents in the NT group as a norm, we have to conclude that under HT transformation the Ag, Ca, Cu, Hg, I, and Na levels in thyroid tissue notably changed.

Characteristically, elevated or reduced levels of ChE observed in affected tissues are discussed in terms of their potential role in the initiation and promotion of TN. In other words, using the low or high levels of the ChE in TN researchers try to determine the role of the deficiency or excess of each ChE in the TN etiology. In our opinion, abnormal levels of many ChE in TN, including HT, could be and cause, and

also effect of thyroid tissue transformation. From the results of such kind studies, it is not always possible to decide whether the measured decrease or increase in ChE level in pathologically altered tissue is the reason for alterations or vice versa. Nevertheless the differences between ChE levels in normal and affected thyroid tissue could be used as HT markers.

This study has some limitations. Firstly, analytical techniques used in this study measure merely twenty ChE (Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn) mass fractions. Future studies should be aimed toward using other analytical methods such as inductively coupled plasma atomic emission spectrometry (ICP-AES) and inductively coupled plasma mass spectrometry (ICP-MS), which will elongate the list of ChE investigated in NT and HT. Secondly, the sample size of HT group was relatively small and prevented investigations of ChE contents in HT group using differentials like gender, thyroid functional activity, stage of disease, dietary habits of healthy persons and patients with HT. Lastly, the generalization of our outcomes may be bounded to the Russian population. Despite these limitations, this study provides evidence on specific tissue Ag, Ca, Cu, Hg, I, and Na level alteration and shows the necessity to continue ChE research of HT.

5 | CONCLUSION

In this work, ChE measurements were carried out in the tissue samples of normal thyroid and HT using three non-destructive instrumental analytical methods: EDXRF, INAA-SLR, and INAA-LLR. It was shown that the combination of these methods is an adequate analytical tool for the non-destructive determination of Ag, Br, Ca, Cl, Co, Cr, Cu, Fe, Hg, I, K, Mg, Mn, Na, Rb, Sb, Sc, Se, Sr, and Zn content in the tissue samples of human thyroid, including needle-biopsy samples. It was observed that in thyroid with HT content of Ag, Cu, Hg, and Na significantly increased whereas the levels of Ca and I decreased in a comparison with the normal thyroid tissues. In our opinion, the increase in levels of Ag, Cu, Hg, and Na, as well as the decrease in levels of Ca and I in HT transformed thyroid tissue might demonstrate an involvement of these ChE in etiology and pathogenesis of HT. It was supposed that the changes in levels Ag, Ca, Cu, Hg, I, and Na in thyroid tissue can be used as HT markers.

Declaration of Conflicting Interests

The author has not declared any conflict of interests.

6 | FUNDING

The author received no financial support for this study and for publication of this article.

ACKNOWLEDGEMENTS

The author is extremely grateful to Profs. Vtyurin BM and Medvedev VS, Medical Radiological Research Center, Obninsk, as well as to Dr. Choporov Yu, former Head of the Forensic Medicine Department of City Hospital, Obninsk, for supplying thyroid samples.

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How to cite this article: Zaichick V. **Evaluation of Twenty Chemical Elements in Thyroid with Hashimoto's thyroiditis using X-Ray Fluorescent and Neutron Activation Analysis**. Journal of Medical Research and Health Sciences. 2021;1500–1510. https://doi.org/10.52845/JMRHS/2021-4-10-4