Vietnam Journal of Community Medicine, Vol. 66, English version No. 2, 31-35

ASSOCIATION BETWEEN LEAD CONCENTRATIONS IN BLOOD, THYROID TISSUE, AND THYROID CANCER

Lam Nguyen Nha Truc[1], Nguyen Van Chuyen[2*],
Nguyen Thi Thu Trang[2], Le Tuan Anh[2], Hoang Thi Truong[2], Vu Minh Tuan[2],
Doan Bao Ha[2], Nguyen Thi Thao[6], Ta Quang Thanh[3], Tran Quang Phuc[4], Nguyen Van Ba[5]

[1]Cho Ray Hospital - 201B Nguyen Chi Thanh, Dist 5, Ho Chi Minh City, Vietnam
[2]Vietnam Military Medical University - 160 Phung Hung, Ha Dong Ward, Hanoi City, Vietnam
[3]Bac Thang Long hospital - Group 1, Cao Lo Street, Dong Anh Dist, Hanoi City, Vietnam
[4]National Institue of Malariology Parastology and Entomology - 34 Trung Van, Nam Tu Liem Dist, Hanoi City, Vietnam
[5]Military hospital 175 - 786 Nguyen Kiem, Hanh Thong Ward, Ho Chi Minh City, Vietnam
[6]Ha Dong General Hospital - 2 Be Van Dan Street, Ha Dong Ward, Hanoi City, Vietnam

Received: 11/08/2025
Revised: 15/09/2025; Accepted: 20/12/2025

ABSTRACT

Background: Current research on lead (Pb) in relation to the thyroid and particularly thyroid cancer remains limited.

Objective: To compare Pb concentrations in blood and thyroid tissue samples between the patient and control groups; evaluate the association between Pb concentrations and thyroid cancer.

Methods: A cross-sectional descriptive study was conducted on 282 patients with benign and malignant thyroid tumors at stages 1, 2, and 4. Lead concentrations in blood and thyroid tissue were measured, and their correlation with thyroid cancer was analyzed.

Results: The blood Pb concentration in the patient group was 1.27 ± 2.33 µg/L, while in the control group, it was 0.65 ± 2.35 µg/L. The Pb concentration in thyroid tissue for the benign and malignant groups was 15.26 ± 72.87 µg/kg and 36.88 ± 74.32 µg/kg, respectively. Logistic regression analysis showed that blood Pb levels in the malignant thyroid tumor group were higher than in the benign group (OR = 1.270; 95% CI: 1.011–1.594; p = 0.040). High Pb concentrations in thyroid tissue were associated with thyroid cancer (OR = 1.006; 95% CI: 1.000–1.011; p = 0.043).

Conclusion: High Pb concentrations in thyroid tissue and blood samples are associated with thyroid cancer.

Keywords: Blood lead concentration, thyroid tissue lead concentration, thyroid cancer.

1. INTRODUCTION

Thyroid cancer is a common malignancy worldwide and in Vietnam. According to GLOBOCAN 2008, thyroid cancer ranks 9th among cancers in women with over 160.000 new cases annually, 20th among cancers in men with nearly 50.000 new cases annually, and 17th overall for both genders [1]. Exposure to heavy metals negatively impacts health, causing disorders in liver and kidney function, cardiovascular diseases, neurological decline, and cancers, particularly thyroid cancer [2]. The International Agency for Research on Cancer (IARC) has classified lead (Pb) as a potential carcinogen. A study in China demonstrated an association between urinary Pb and thyroid cancer [3]. Thus, Pb is a significant concern and may be a cause of thyroid cancer.

Numerous studies have explored the relationship between factors such as genetics, radiation exposure, estrogen hormones, dietary habits, and thyroid cancer [4]. However, these findings remain inconclusive. Research on the association between Pb in blood and thyroid tissue and thyroid cancer in Vietnam is limited. Therefore, the objectives of this study are to compare Pb concentrations in blood and thyroid tissue samples between patients with malignant and benign thyroid

*Corresponding author
Email: lamtruc0101@yahoo.com **Phone**: (+84) 908241565 **DOI:** 10.52163/yhc.v66i8.3233

tumors and to evaluate the association between Pb concentrations in blood and thyroid tissue with thyroid cancer.

2. SUBJECTS AND METHODS

2.1. Study Subjects

- Study Subjects: Thyroid tissue samples from 282 patients with TIRADS (Thyroid Imaging, Reporting and Data System) 4 and 5 thyroid tumors who underwent partial or total thyroidectomy at Cho Ray Hospital from October 1, 2024, to April 30, 2025, were included. At the time of diagnosis, patients had not received specific treatment.

- Exclusion Criteria: Incomplete medical records, secondary tumors, history of chronic diseases, pregnant or breastfeeding women, concurrent thyroid diseases such as acute thyroiditis, active Basedow's disease, hyperthyroidism or hypothyroidism, or refusal to participate in the study. The patient group (217 cases) consisted of patients with postoperative histopathological results indicating carcinoma, while the control group (65 cases) consisted of patients with benign thyroid tumors.

Patients underwent clinical and paraclinical examinations to screen for thyroid tumors (thyroid ultrasound, TIRADS 4 and 5 classification according to ACR TI-RADS, and fine-needle aspiration (FNA) classified according to Bethesda) [5]. Subsequently, patients underwent thyroidectomy with immediate biopsy to classify tumors as benign or malignant and stage malignant tumors (according to the TNM - AJCC/UICC classification system) [6]. Blood and thyroid tissue samples were preserved, mineralized, and analyzed for Pb concentration at the Department of Military Hygiene, Vietnam Military Medical University. Data were analyzed using SPSS 20 software.

2.2. Chemicals and Testing

Chemicals: Standard Pb solution 1 mg/mL (Merck); sulfuric acid (H_2SO_4 98%, Merck); nitric acid (HNO_3 65%, Merck); hydrogen peroxide (H_2O_2, Merck); perchloric acid ($HClO_4$ 70%, Merck). All chemicals were prepared as solutions for use within the day.

Testing: Pb concentrations were measured using an AAS ZA-3000 machine (Model AZ3000, Hitachi Ltd., Tokyo, Japan) at a wavelength of 283.3 nm.

The standard concentrations for lead (Pb) were 0, 50, 100, 200, and 300 ppb. A correlation coefficient of 99.99% indicated a highly linear relationship across the studied concentration range.

To check the accuracy of the method, the percentage recoveries were analyzed and quantified. The recovery coefficients for in samples of thyroid tissue and blood after adding the spiked sample were calculated, ranging from 94.05% to 95.06% for Pb. The values of these recovery coefficients indicated that the method was highly accurate and could be used for the analysis of heavy metals.

2.3. Sample Collection and Mineralization

Sample Collection: During surgery, 0.5 g of normal thyroid tissue surrounding the thyroid nodule was collected, wrapped in sterile gauze, and placed in a 50 mL Falcon tube containing physiological saline. To analyze heavy metals in blood and thyroid tissue samples, specimens were collected as follows: 2 mL of venous blood was drawn into tubes containing heparin as an anticoagulant. After collection, samples were stored at temperatures between 0 and 4 °C in sample storage boxes, then immediately transported to the laboratory and stored at –20 °C until analysis. Blood Pb concentrations were compared with the reference values from ISTISAN 10/22.

Microwave sample preparation: Approximately 0.5 g of thyroid tissue or 2 mL of blood was transferred into a microwave vessel and mineralized using a mixture of nitric acid (65%), sulfuric acid (98%), and perchloric acid (70%) at a 10:1:1 ratio in the Multiwave PRO microwave reaction system (Anton Paar GmbH, Graz, Austria). First, samples were placed into Teflon digestion tubes, then the digestion mixture (HNO_3, H_2SO_4, $HClO_4$, H_2O_2) was added. After gentle shaking for 20 minutes to initiate the digestion reaction, the tubes were placed in the Multiwave PRO system to complete sample digestion (USEPA, 1996). The temperature program was set as follows: heating to 170 °C for 5 minutes and holding for 10 minutes; then increasing to 200 °C and holding for 15 minutes, followed by cooling to room temperature. After digestion, the sample solution was expected to be clear and transparent. The digested samples were then diluted with 1% HNO_3 to a final volume of 5 mL prior to analysis.

2.4. Statistical Analysis

A cross-sectional descriptive study with a control group was conducted. Kolmogorov-Smirnov, Chi-square, and Mann-Whitney U tests were performed with a significance level of $p = 0.05$ using SPSS (IBM SPSS Statistics 20). Continuous variables were described as means ± standard deviation (SD). The correlation between Pb concentrations in thyroid tissue was evaluated using Spearman's correlation analysis. A p-value < 0.05 was considered statistically significant.

2.5. Ethics statement

This study was approved by the Ethics Committee under Decision No. 1178/QĐ-VSR of the National Institute of Malariology, Parasitology and Entomology on December 8, 2023, and by the Ethics Committee for Biomedical Research under approval No. 1912/GCN-HĐĐĐ dated December 3, 2024, of Cho Ray Hospital.

3. RESULTS

3. 1. Characteristics of Study Subjects

A total of 282 patients were included, with males accounting for 20.9% (n=59) and females 79.1% (n=223). Of these, 65 cases had benign thyroid tumors, and 217 had thyroid cancer. In the thyroid cancer group, males accounted for 20.7% (n=45) and females 79.3% (n=172), with a statistically significant difference between genders (p = 0.000).

Table 1. Average Age by Gender and Group

	Average Age	p
Male	43.89 ± 13.88	0.004
Female	49.31 ± 12.56	
Benign Group	51.73 ± 14.55	0.012
Cancer Group	47.11 ± 12.35	
Male with Cancer	41.89 ± 13.13	0.001
Female with Cancer	48.48 ± 11.8	

The average age of males was 43.89 ± 13.88 years, and for females, it was 49.31 ± 12.56 years (age range: 18–80 years). The control group had an average age of 51.73 ± 14.55 years, while the cancer group had an average age of 47.11 ± 12.35 years. The average age of males with thyroid cancer was 41.89 ± 13.13 years, and for females, it was 48.48 ± 11.8 year

3. 2. Histopathological Results and Thyroid Cancer Staging

Table 2. Histopathological Results and Thyroid Cancer Staging

Thyroid Cancer Group (n=217)		Number (n)	Percentage (%)
Cancer Type	Papillary	213	98.15
	Follicular	2	0.93
	Medullary	1	0.46
	Undifferentiated	1	0.46
T	T1	89	41.01
	T2	5	2.3
	T3	116	53.45
	T4	7	3.24
N	N0	183	84.33
	N1	34	15.67
M	M0	217	100
	M1	0	0
Stage	Stage 1	170	78.34
	Stage 2	46	21.2
	Stage 4	1	0.46

Papillary thyroid cancer accounted for the majority at 98.15% (n=213), followed by follicular thyroid cancer at 0.93% (n=2), and medullary and undifferentiated thyroid cancer each at 0.46% (n=1). According to TNM classification, T3 was the most common tumor invasion level at 53.45% (n=116), followed by T1 at 41.01% (n=89), T4 at 3.24% (n=7), and T2 at 2.3% (n=5). Regarding lymph node metastasis, N0 was predominant at 84.33%, and N1 accounted for 15.67% (n=34). All patients had no distant metastasis (M0). By TNM staging, Stage 1 accounted for 78.34%, Stage 2 for 21.2%, and Stage 4 for 0.46%, with no Stage 3 cases.

Table 3. Correlation Between Age, Gender, and Pb Concentrations in Tissue and Blood

	Year old	Gender
Blood Pb		
- Correlation coefficient	0.107	-0.04
- p	0.117	0.562
Pb model		
- Correlation coefficient	-0.036	-0.101
- p	0.598	0.136

Tested using Spearman's correlation

The correlation between age, gender, and blood Pb levels was very weak (correlation coefficients of 0.107 and -0.04, respectively) and not statistically significant (p = 0.117 and 0.562, respectively). Similarly, the correlation between age, gender, and tissue Pb levels was very weak (correlation coefficients of -0.036 and -0.101, respectively) and not statistically significant (p = 0.598 and 0.136, respectively).

3. 3. Association Between Pb and Thyroid Cancer

Table 4. Comparison of Pb Concentrations in Blood and Thyroid Tissue Between Cancer and Control Groups

Blood Pb (µg/l)		Tissue Pb (µg/kg)	
Min-Max	Mean ± SD	Min-Max	Mean ± SD
Cancer group (n=217)			
0 - 26.86	1.27 ± 2.33	0 - 364.53	36.88 ± 74.32
Control group (n=65)			
0 - 2.69	0.65 ± 2.35	0 - 101.62	15.26 ± 72.87
Reference interval ISTISAN 10/22			
	12.8 – 79.5		NA

NA: not available

The mean blood Pb concentration in the thyroid cancer group was 1.27 µg/L (n=217), while in the control group, it was 0.65 µg/L (n=65). No cases in either group exceeded the permissible blood Pb levels. Additionally, the mean Pb concentration in thyroid tissue was significantly higher in the cancer group (36.88 µg/kg) compared to the control group (15.26 µg/kg).

Table 5. Logistic Regression Analysis of the Association Between Pb and Thyroid Cancer

Study group (n = 282)		
OR (95%CI):		p value
Control group (n=65)	Thyroid Cancer group (n=217)	
Blood Pb (µg/L)		
1	1.270 (1.011 – 1.594)	0.040
Tissue Pb (µg/kg weight)		
1	1.006 (1.000 – 1.011)	0.043

Logistic regression analysis showed that blood Pb levels in the malignant thyroid tumor group were higher than in the benign group (OR = 1.270; 95% CI: 1.011–1.594; p = 0.040). High Pb concentrations in thyroid tissue were associated with thyroid cancer (OR = 1.006; 95% CI: 1.000–1.011; p = 0.043)

Table 6. Comparison of Pb Concentrations in Blood and Thyroid Tissue Across Thyroid Cancer Stages

		Blood Pb (µg/l)	Tissue Pb (µg/kg)
Mean ± SD	Stage 1 (n=170)	1.13 ± 4.43	41.03 ± 86.92
	Stage 2, 4 (n=47)	1.79 ± 1.77	21.88 ± 60.49
p value		0.915	0.113

The comparison of Pb concentrations in blood and thyroid tissue across thyroid cancer stages is shown in Table 6. Blood Pb levels in Stage 1 patients were significantly lower than in Stages 2 and 4 (1.13 µg/L vs. 1.79 µg/L). However, tissue Pb levels in Stages 2 and 4 were lower than in Stage 1.

4. DISCUSSION

4.1. Characteristics of Study Subjects

In this study, the female-to-male ratio was 3.94, and in the thyroid cancer group, it was 3.82. These results indicate that females are significantly more likely to develop thyroid cancer than males. Our findings align with those of Athanasios Bikas, who reported a female-to-male thyroid cancer ratio of up to 3.69 in the Hispanic community [7].

The average age of the study population was 43.89 ± 13.88 years, indicating that most thyroid cancer patients were middle-aged. The results showed that males tended to develop thyroid cancer at a significantly younger age than females (41.89 ± 13.13 years vs. 48.48 ± 11.8 years).

4.2. Histopathological Results and Thyroid Cancer Staging

Most patients were diagnosed at an early stage, with Stage 1 accounting for 78.34%, and Stages 2 and 4 comprising 21.2%. The majority of thyroid cancer cases were papillary (98.15%), a slow-progressing subtype with a good prognosis. Other subtypes accounted for a very small proportion. These findings are consistent with numerous domestic and international studies, which report that papillary thyroid cancer accounts for over 70% of cases [8]. Our study found no dependence of blood or tissue Pb concentrations on age or gender.

4.3. Association Between Pb and Thyroid Cancer

Blood Pb concentrations in the cancer and control groups were 1.27 µg/L and 0.65 µg/L, respectively. Both groups had blood Pb levels well below the permissible threshold, with no cases exceeding the limit. Tissue Pb concentrations in the cancer and control groups were 36.88 µg/kg and 15.26 µg/kg, respectively. Limited studies in Vietnam have examined Pb concentrations in blood and thyroid tissue in thyroid cancer patients, making direct comparisons challenging. We compared our results with international studies.

Logistic regression analysis demonstrated that increased blood and tissue Pb concentrations were associated with a higher risk of thyroid cancer, with statistically significant differences. Our findings align with those of Maryam Rezaei, who reported that Pb increases the risk of thyroid cancer. Similarly, a study in Argentina demonstrated that long-term Pb exposure significantly impairs thyroid function and is associated with thyroid cancer [9].

However, the biological mechanism linking Pb exposure to thyroid cancer remains unclear. Further research is needed to investigate the potential toxicological mechanisms of Pb on the thyroid.

Comparison of Pb Concentrations Across Thyroid Cancer Stages

We compared Pb concentrations in blood and thyroid tissue across thyroid cancer stages. The results showed no statistically significant differences in Pb concentrations between stages, suggesting that Pb in blood or tissue is not a factor in exacerbating thyroid cancer severity. Our findings are consistent with those of Hye-Kyung Chung, who reported no significant differences in blood or tissue Pb concentrations between Stage 1 and Stages 3–4 thyroid cancer patients (p = 0.419 and 0.334, respectively) [10].

This study has several strengths. First, it compared Pb concentrations in blood and thyroid tissue samples from 217 patients with malignant thyroid tumors and 65 patients with benign tumors. This cross-sectional descriptive study with a control group was approved by the Ethics Committee of Cho Ray Hospital. Second, logistic regression analysis was used to evaluate the association between Pb concentrations in blood and tissue samples and thyroid cancer, demonstrating that increased Pb concentrations are associated with a higher risk of thyroid cancer.

5. CONCLUSION

The incidence of thyroid cancer is significantly higher in females than in males. Papillary thyroid cancer accounts for the majority of malignant thyroid tumor cases. Most thyroid cancer patients were diagnosed at an early stage. Pb concentrations in blood and thyroid tissue were significantly higher in patients with malignant thyroid tumors compared to those with benign tumors. Our study demonstrated that increased Pb concentrations in blood and thyroid tissue are associated with a higher risk of thyroid cancer.

REFERENCES

[1] GLOBOCAN (2008). Estimates of worldwide burden of cancer in 2008:. International journal of cancer.

[2] Kim NH, Hyun YY, Lee KB (2015) Environmental heavy metal exposure and chronic kidney disease in the general population. J Korean Med Sci 30:272–277.

[3] Chi Zhang1 • Hua-Bing Wu1 • Meng-Xia Cheng. Association of exposure to multiple metals with papillary thyroid cancer risk in China. Environmental Science and Pollution Research (2019) 26:20560–20572

[4] Liu Yihao, Su Lei, Xiao Haipeng (2017). Review of factors related to the thyroid cancer epidemic. International journal of endocrinology, 2017(1): 5308635.

[5] Tessler Franklin N, Middleton William D, Grant Edward G, et al. (2017). ACR thyroid imaging, reporting and data system (TI-RADS): white paper of the ACR TI-RADS committee. Journal of the American college of radiology, 14(5): 587-595.

[6] Schneider David F, Chen Herbert (2013). New developments in the diagnosis and treatment of thyroid cancer. CA: a cancer journal for clinicians, 63(6): 373-394.

[7] Bikas Athanasios, Burman Kenneth D (2019), Epidemiology of thyroid cancer, in The Thyroid and Its Diseases: A Comprehensive Guide for the CliniancSpringer, 541-547.

[8] Li Hui, Li Xiang, Liu Jie, et al. (2017). Correlation between serum lead and thyroid diseases: papillary thyroid carcinoma, nodular goiter, and thyroid adenoma. International journal of environmental health research, 27(5): 409-419.

[9] López CM, Piñeiro AE, Núñez N, Avagnina AM, Villaamil EC, Roses OE (2000) Thyroid hormone changes in males exposed to lead in the Buenos Aires area (Argentina). Pharmacol Res 42:599–602

[10] Chung Hye-Kyung, Nam Ji Sun, Ahn Chul Woo, et al. (2016). Some elements in thyroid tissue are associated with more advanced stage of thyroid cancer in Korean women. Biological trace element research, 171(1): 54-62.