ORIGINAL RESEARCH ARTICLE

Comparison of Thyroid Function in Lead Poisoned Patients and Healthy Individuals in North India

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ABSTRACT

Background: Lead remains a pervasive environmental toxicant in India, with emerging evidence linking it to endocrine disruption. Its potential effect on thyroid function remains unclear, with inconsistent findings across studies. This study aimed to evaluate the association between blood lead concentration (BLC) and thyroid hormone levels in a North Indian population.

Methods: This retrospective study included 237 patients from Punjab who underwent simultaneous testing for BLC and thyroid hormones between January 2022 and December 2023. Patients were grouped by BLC (<10, 10–25, >25 µg/dL), and those with known thyroid disease or on thyroid-altering medications were excluded. BLC and thyroid hormones (fT3, fT4, TSH) were measured using validated instruments (LeadCare II, Roche Elecsys).

Results: Group 3 (BLC >25 µg/dL) had significantly higher fT4 levels (19.26 ± 4.95 pmol/L) and lower TSH levels (2.19 ± 1.77 µIU/L) compared to Group 1 (fT4: 16.26 ± 6.65 pmol/L; TSH: 3.60 ± 4.59 µIU/L; p <0.05). No statistically significant differences were observed in fT3 values between the groups (p = 0.513). Regression analysis showed a positive association between BLC and fT4 and a negative association with TSH. These findings suggest a trend toward subclinical hyperthyroid features in individuals with elevated lead levels.

Conclusion: Elevated BLC is associated with altered thyroid function, notably increased fT4 and decreased TSH concentrations, even in the absence of overt thyroid disease. These results support lead's role as a potential endocrine disruptor, with possible involvement of oxidative stress and neuroendocrine pathways.

Keywords: Lead poisoning, thyroid hormones, fT4, TSH, environmental exposure, endocrine disruption, North India

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INTRODUCTION

Lead is one of the most used toxic heavy metals in our environment. Its abundant distribution, easy availability, and important physio-chemical properties made it a great choice for different industries.[1] Despite increased awareness and efforts to limit its use globally, it is present in sectors like paints, batteries, glass, cosmetics, and fuel additives.[2] This continuous use and its non-biodegradable nature are causing an increase in lead accumulation in the environment and posing public health hazards.[1]

Lead entry into the bloodstream occurs through the dermal, digestive or respiratory route. Continuous exposure to its sources can cause lead poisoning. The World Health Organization advises that individuals with a blood lead concentration of 5 µg/dL or higher should have their sources of lead exposure identified, and measures should be implemented to decrease and eliminate this exposure.[3] Moreover, Centers for Disease Control and Prevention (CDC) has revised their guidelines and lowered the maximum acceptable blood lead level in children to 3.5 µg/dL, beyond which proper investigation and treatment of patients is now recommended.[4] However, there are research reports available that show that detrimental effects of lead can be seen at lower blood levels and hence no safe threshold can be established.[5]

Most of the lead enters the body either in mineral or organic form which accumulates in the red blood cells and eventually settles in the bones. This accumulated lead can affect various organ systems including haematological, cardiovascular, immunological, nervous, hepatobiliary, endocrinological and gastrointestinal.[2] Adverse effects of lead include anaemia, neuropathy, nephropathy, nervous encephalopathy etc. The extent and severity of the toxic effects depend on the duration and dosage of the exposure. Some studies have also associated lead exposure with carcinogenesis.[6,7]

The thyroid gland, the largest endocrine organ, regulates iodine homeostasis and primarily secretes thyroid hormones. It produces 90% thyroxine (T4), an inactive form, and 10% triiodothyronine (T3), the active hormone.[8] Thyroid hormones play a crucial role in maintaining homeostasis and exhibit various effects. They influence nearly all cells in the body through gene transcription. Both excessive and insufficient hormone production can have significant consequences.[9] Disorders related to abnormal thyroid hormone levels are prevalent, with hyperthyroidism affecting about 1-2% and hypothyroidism around 7-10% of adults worldwide.[10] As the prevalence of thyroid disorders is on an increasing trend, it is important to determine various factors influencing it. Different environmental, physiological and genetic factors associated with thyroid disorders have been identified already.[2] Numerous studies have explored the potential link between toxic metal exposure and thyroid disorders. Lead, in particular, has been reported to alter thyroid hormone levels by disrupting iodine transport and binding to thyroid hormone-binding proteins, affecting the thyroid axis.[11]

The literature on the impact of lead on thyroid function is inconclusive. Studies by Gharaibeh et al and Memon et al have demonstrated hypothyroid-like patterns, such as elevated TSH and decreased fT4, suggesting central hypothyroidism or peripheral hormone disruption.[12,13] In contrast, other reports by Hanif et al and Stojsavljević et al have shown hyperthyroid features (suppressed TSH, elevated fT3/fT4), potentially due to oxidative stress-induced stimulation of hormone synthesis or altered deiodinase activity.[2,14,15] Still, some researchers observed no statistically significant association between lead levels and thyroid hormone profiles, attributing variability to confounding factors such as nutritional status and exposure duration.[16,17]

Recent regional studies from North India have raised concerns over increasing lead exposure, particularly in industrial belts such as Rajasthan, Uttar Pradesh and Delhi. Studies from Aligarh and Amritsar found elevated blood lead levels in 44.2% of children in Aligarh and higher concentrations in industrial zones of Amritsar. Children aged 3 months to 6 years near factories or with old wall paint were most affected.[18,19] Lead levels increased with age and malnutrition, yet most cases were asymptomatic, indicating hidden but highlighting the silent nature of this public health threat. Another environmental survey from Varanasi highlighted significant environmental exposure of lead in this region.[20] These findings underscore the need to explore the health impact of chronic lead exposure among residents of North India, particularly on endocrine organs like the thyroid.

Despite North India's high industrial density, there are still few systematic studies evaluating the level of lead exposure and its consequences on health, especially on endocrine systems. Considering the significant exposure burden throughout North India, it is imperative to assess its effects on vital organ systems, especially the thyroid gland, which is crucial for metabolic regulation, and is particularly susceptible to disturbance by heavy metals.

Based on the conflicting evidence from existing literature, we hypothesized that increased blood lead concentration (BLC) is associated with alterations in thyroid function. Specifically, we proposed that lead exposure may result in elevated levels of free thyroxine (fT4) and decreased levels of thyroid-stimulating hormone (TSH), indicating a possible disruption of the hypothalamic-pituitary-thyroid axis among exposed individuals.

Hence, this study was planned to analyse the demographic pattern of patients of North India who are suffering from lead poisoning and assess their thyroid function compared to the healthy group. The primary objective of this study was to compare the serum concentrations of free triiodothyronine (fT3), free thyroxine (fT4), and TSH between individuals with lead poisoning and healthy controls in North

India. Additionally, the study aimed to assess the correlation between BLC and thyroid hormone levels to understand better the endocrine effects of chronic lead exposure in this population.

METHODOLOGY

Study Design: This was a retrospective observational study collaboratively designed by the Departments of Biochemistry and Endocrinology at our institution. Institutional Ethics Committee approval was obtained before the commencement of data collection. Since it was a retrospective analysis of anonymized patient information, the need for informed consent was waived according to institutional guidelines and the Declaration of Helsinki.

Inclusion and Exclusion Criteria: To be included in the study, patients were required to have concurrent measurements of BLC and thyroid hormones. Patients were excluded if they had a previously diagnosed thyroid disorder or were undergoing treatment for thyroid dysfunction. Exclusion was also applied to individuals taking medications known to interfere with thyroid function, such as corticosteroids, amiodarone, lithium, interferon-alpha, dopamine, phenytoin, carbamazepine, antipsychotics, beta-blockers, or antidepressants. Additionally, pregnant or lactating women, individuals with autoimmune thyroid disease or other autoimmune conditions, and those with acute or chronic renal failure were also excluded from the study.

Data Collection and Sampling: Patient data were retrieved from the hospital's electronic medical record system for the period between January 2022 and December 2023. A consecutive sampling method was employed, and all eligible patients during this time who had undergone in-house estimation of blood lead levels (BLC) were screened. From this group, patients were included if they also had a thyroid profile (fT3, fT4, and TSH) performed during the same clinical visit and if complete demographic and clinical information was available.

Group Stratification: Included patients were stratified into three groups based on their blood lead concentration: Group 1 comprised patients with BLC less than 10 µg/dL; Group 2 included those with BLC between 10.1 and 25 µg/dL; and Group 3 consisted of individuals with BLC greater than 25 µg/dL. These thresholds were selected based on guidelines from the Centers for Disease Control and Prevention (CDC) and the U.S. Department of Health and Human Services. Although the World Health Organization does not specify cutoffs for adults, the ≥10 µg/dL level is widely recognized in clinical and epidemiological studies as indicative of toxicologically relevant lead exposure, including in the Indian context.[2,21]

Laboratory Analysis: Blood lead levels were measured using the LeadCare II Analyzer (Magellan Diagnostics Inc. 101 Billerica Ave, Building 4 N. Billerica, Massachusetts 01862-1271 USA) which is the only CLIA-waived point-of-care instrument for blood lead based on the principle of Anodic stripping voltammetry (ASV).[22] Its validity and reliability have been well established and it is used worldwide for blood lead screening.[23] The LeadCare II analyzer demonstrated high accuracy and reliability, with 97.9% of results falling within OSHA-defined Allowable Total Error limits and a strong correlation with GFAAS (r^2 = 0.992). The average bias was minimal, with only 4.7–5.0% deviation in higher lead ranges, confirming its suitability for clinical lead screening.[24]

Thyroid hormone levels, including free triiodothyronine (fT3), free thyroxine (fT4), and thyroid-stimulating hormone (TSH), were estimated using the Roche Elecsys immunoassay system on the Cobas 8000 platform. The reference ranges used were: fT3, 3.1–6.8 pmol/L; fT4, 12.0–21.9 pmol/L; and TSH, 0.27–4.2 microIU/L. All test results were validated by internal quality controls and external quality assurance procedures routinely implemented in our clinical biochemistry laboratory.[25]

Statistical Analysis: Data analysis was carried out using Microsoft Excel and Jamovi software (Version 2.4). Continuous variables were described as means with standard deviations or medians with interquartile ranges, whereas categorical variables were frequencies and percentages. Data normality was tested using the Shapiro-Wilk test. As needed, the unpaired t-test or one-way ANOVA was used to compare groups, and Tukey's HSD post-hoc test was used for significant ANOVA results. Depending on the data normality, Pearson or Spearman correlation coefficients were used to investigate the correlation between BLC and thyroid hormone. The connection between BLC and thyroid markers was examined using linear regression models with age and sex adjustments. A p-value under 0.05 was significant.

RESULTS

A total of 237 patients were included, with 132 patients in group 1 (BLC <10 µg/dL), 47 patients in group 2 (BLC 10 – 25 µg/dL) and 58 patients in group 3 (BLC >25 µg/dL). The Mean age was 45.85 ± 18.45 years in group 1, 43.02 ± 15.56 years in group 2 and 39.9 ± 12.43 years in group 3. There were 86 (65%) males and 46 (35%) females, 35 (74.5%) males and 12 (25.5%) females and 53 (91.4%) males and 5 (8.6%) females in first, second and third group respectively. The mean fT4 levels were 16.26±6.65 pmol/L, 15.37±3.12 pmol/L and 19.26±4.95 pmol/L in the three groups respectively. The serum TSH levels were 3.60±4.59 µIU/L, 2.75±1.84 µIU/L and 2.19±1.77 µIU/L in the three groups respectively. The mean blood lead concentrations were 5.23±1.63 µg/dL (median was 1.63 µg/dL), 15.80±4.53 µg/dL (median was 14.90 µg/dL) and 50.72±16.55 µg/dL (median was 62.20 µg/dL) in all 3 groups respective-

ly. One-way ANOVA shows that serum fT4 levels and blood lead levels were significantly higher in patients of group 3 (p=0.001, p=0.0001 respectively) and serum TSH was significantly lower in group 3 patients (p=0.047). In contrast, serum fT3 showed no significant difference among the three groups (table 1).

The pattern of thyroid hormones and blood lead concentrations in all patients cumulatively (n=237) are shown in Fig. 1 (a, b and c). Only fT4 showed a mild linear pattern with changes in blood lead concentrations.

Tukey's HSD test showed that TSH levels were significantly lower in the >25 µg/dL BLC group than in the <10 µg/dL group (p = 0.0265), with no significant differences among the other pairs. For fT4, levels were significantly higher in the >25 µg/dL group compared to the 10.1–25 µg/dL (p = 0.0018) and <10 µg/dL groups (p = 0.0028), with no difference found between the two lower exposure groups. These findings suggest that lead exposure's endocrine effects are most pronounced at blood lead levels exceeding 25 µg/dL.

Fig. 2 shows the change in the thyroid hormone pattern in different groups. As shown in Fig. 2a, fT3 and fT4 had a positive linear correlation in both group 1 and group 2. In group 1 the level of fT4 abruptly increased at a higher concentration of fT3 (>8 pmol/L), whereas the rise in fT4 concentration with fT3 concentration in group 2 was very subtle. In group 3, no such relation was present and fT4 remained almost unchanged with the increase in fT3 concentration except in the initial part.

In Fig. 2b, TSH and fT3 showed a non-linear relationship, where TSH showed a positive correlation with fT3 at lower concentration (<4 pmol/L) but showed a negative correlation at high fT3 levels in patients of both group 1 and group 3. Patients of group 2 showed a wavy pattern, where alternate positive and negative correlations were seen.

Table 1: Comparison of fT3, fT4, TSH and blood lead concentration (BLC) between all three groups

Variable	Group 1 (n=132)		Group 2 (n=47)		Group 3 (n=58)		F	p-value
	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)	Mean ± SD	Median (IQR)		
fT3 (pmol/L)	4.38 ± 1.83	1.83 (1.71)	4.08 ± 1.37	4.03 (2.0)	4.41 ± 1.36	4.37 (1.64)	0.675	0.513
fT4 (pmol/L)	16.26 ± 6.65	6.65 (4.3)	15.37 ± 3.12	15.31 (3.81)	19.26 ± 4.95	18.04 (7.8)	7.438	<0.0001*
TSH (µIU/L)	3.60 ± 4.59	2.72 (3.34)	2.75 ± 1.84	2.69 (2.33)	2.19 ± 1.77	1.79 (2.1)	2.766	0.039*
BLC (µg/dl)	5.23 ± 1.63	1.63 (2.33)	15.80 ± 4.53	14.90 (7.6)	50.72 ± 16.55	62.20 (32.75)	579	<0.0001*

*p<0.05 is statistically significant

Table 2: Post-Hoc Tukey HSD Comparison of TSH and fT4 Levels Between Blood Lead Concentration (BLC) Groups

Hormone	Group1	Group2	Mean diff	p-adj	Lower	Upper	Reject
TSH	10.1 - 25	<10	0.8437	0.3542	-0.6006	2.2879	FALSE
TSH	10.1 - 25	>25	-0.6346	0.6427	-2.3033	1.0341	FALSE
TSH	<10	>25	-1.4782	0.0265	-2.8177	-0.1388	TRUE
fT4	10.1 - 25	<10	0.8868	0.6318	-1.401	3.1746	FALSE
fT4	10.1 - 25	>25	3.8886	0.0018	1.2453	6.532	TRUE
fT4	<10	>25	3.0018	0.0028	0.88	5.1236	TRUE

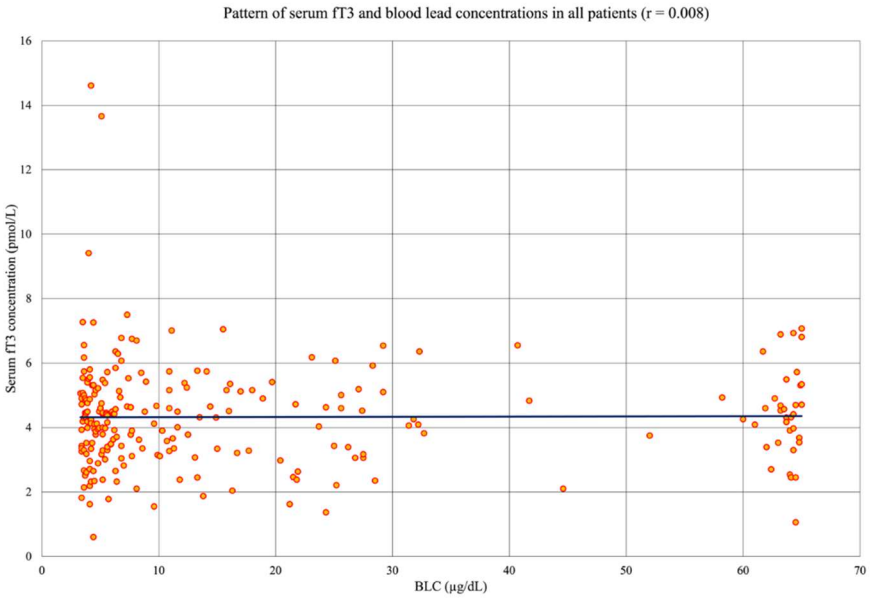

Figure 1a: Scatter plot showing fT3 vs. BLC; no significant correlation observed (r = 0.008)

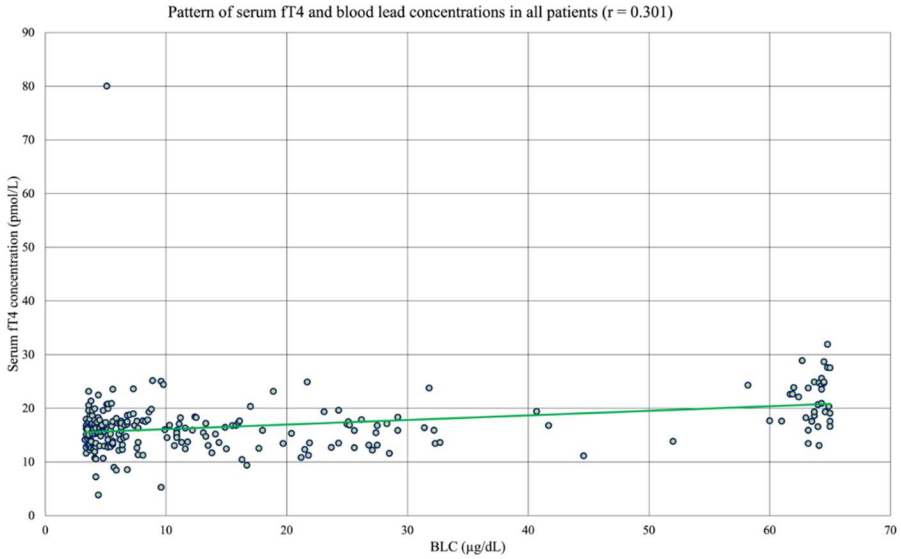

Figure 1b: Scatter plot showing fT4 vs. BLC; weak positive correlation (r = 0.301, p < 0.001)

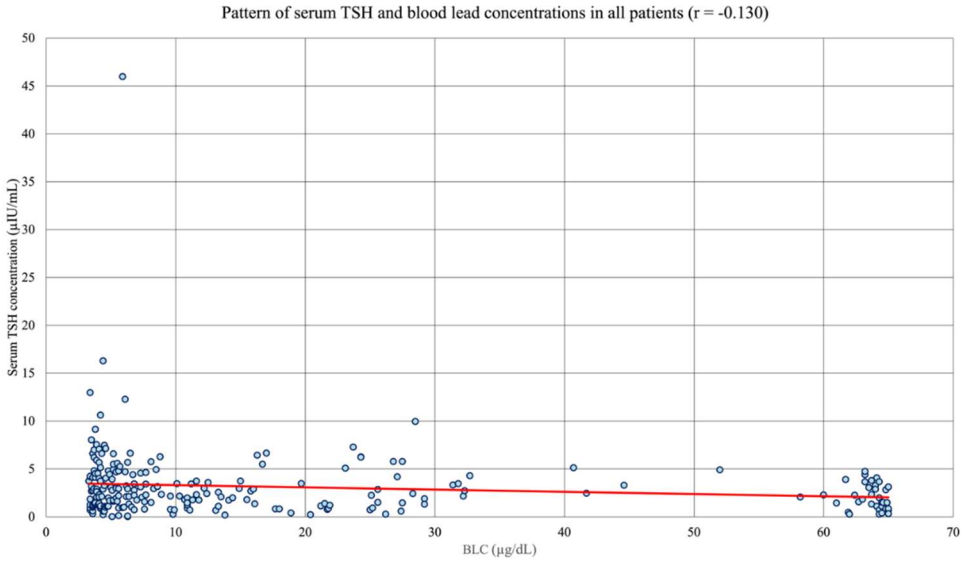

Figure 1c: Scatter plot showing TSH vs. BLC; weak negative correlation (r = –0.130, p = 0.029)

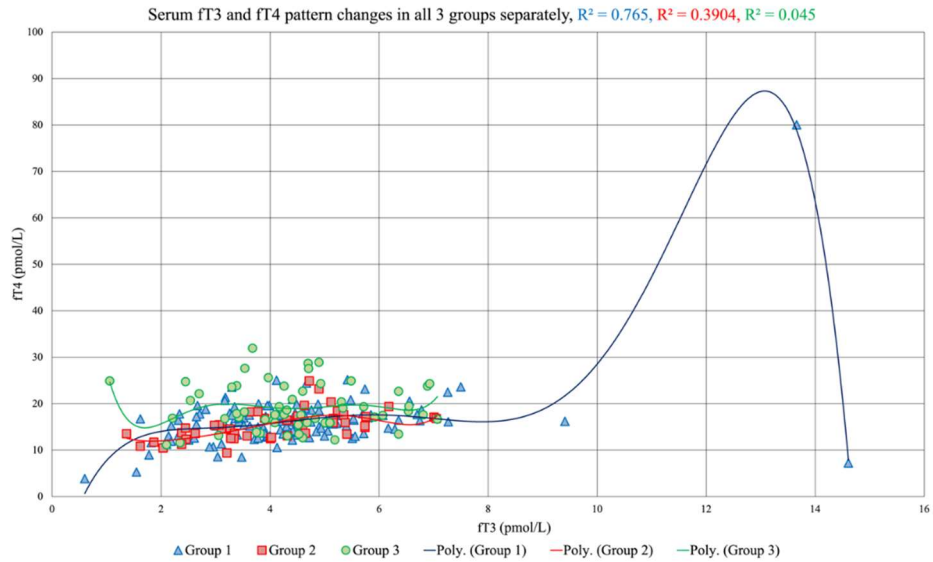

Figure 2a: Scatter plot depicting correlations between fT3 and fT4

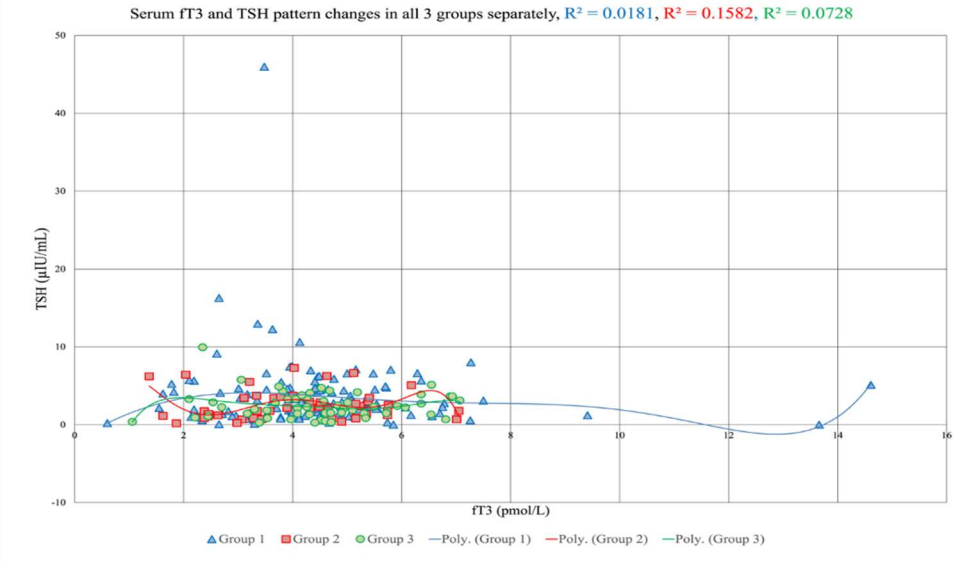

Figure 2b: Scatter plot showing correlations between fT3 and TSH

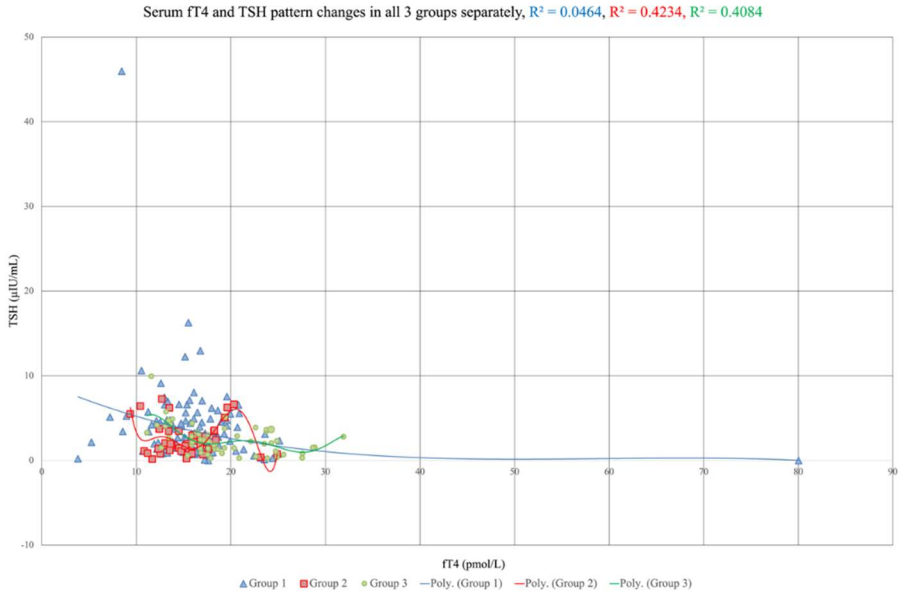

Figure 2c: Scatter plot showing correlations between fT4 and TSH

In Fig. 2c, TSH showed a negative correlation with fT4 in both group 1 and group 3 patients. Group 2 patients showed a gradual decrease of TSH concentration at lower levels of fT4 (<15 pmol/L) and then increased until fT4 levels reached 20 pmol/L. TSH levels again showed a negative correlation with fT4 levels after that.

Linear regression revealed a weak negative correlation between TSH and BLC ($r = -0.130$, $p = 0.029$), and a modest positive correlation between fT4 and BLC ($r = 0.301$, $p < 0.001$). No significant correlation was found between fT3 and BLC ($r = 0.008$, $p = 0.913$).

To quantify the strength of association between blood lead concentration (BLC) and thyroid parameters, effect size calculations were performed. The linear regression model for serum free thyroxine (fT4) yielded an R^2 value of 0.091, corresponding to a Cohen's f^2 of 0.10, indicating a small to moderate effect size. For thyroid-stimulating hormone (TSH), the model showed an R^2 of 0.031 and a Cohen's f^2 of 0.03, reflecting a small effect size. These results imply that BLC has a modest but measurable impact on thyroid function, particularly on fT4 levels.

The mean fT4 in Group 3 was 19.26 pmol/L, exceeding the reference range's upper limit (21.9 pmol/L) but still within the euthyroid range. Mean TSH levels across groups remained normal (0.27–4.2 µIU/mL), although the decreasing trend may indicate subclinical suppression from high BLC exposure. While statistically significant, these changes do not indicate overt thyroid dysfunction but may suggest early or subclinical endocrine alterations from lead toxicity.

Table 3: Linear Regression Model Outcomes Evaluating the Impact of Different Blood Lead Level Groups on T3, T4, and TSH

Response	Covariate	Estimate	SE	t-value	p-value
Group 1					
fT3	Lead	-0.0369	0.09500	-0.389	0.698
	Sex (Female)	-0.2970	0.32463	-0.915	0.362
	Age	-0.0310	0.00831	-3.728	<0.001*
fT4	Lead	0.2708	0.3580	0.757	0.451
	Sex (Female)	-0.8983	1.2233	-0.734	0.464
	Age	-0.0579	0.0313	-1.850	0.067
TSH	Lead	-0.06852	0.2487	-0.275	0.783
	Sex (Female)	1.39210	0.8500	1.638	0.104
	Age	0.00291	0.0218	0.134	0.894
Group 2					
fT3	Lead	-0.05929	0.0453	-1.310	0.197
	Sex (Female)	-0.19194	0.4662	-0.412	0.683
	Age	-0.00636	0.0132	-0.481	0.633
fT4	Lead	0.0470	0.1047	0.4486	0.656
	Sex (Female)	-0.0908	1.0783	-0.0842	0.933
	Age	0.0218	0.0306	0.7110	0.481
TSH	Lead	0.09186	0.0606	1.515	0.137
	Sex (Female)	0.61249	0.6245	0.981	0.332
	Age	-0.00179	0.0177	-0.101	0.920
Group 3					
fT3	Lead	0.00212	0.0112	0.1889	0.851
	Sex (Female)	-0.04935	0.6577	-0.0750	0.940
	Age	-0.01253	0.0149	-0.8421	0.403
fT4	Lead	0.1702	0.0317	5.362	<0.001*
	Sex (Female)	-1.5519	1.8618	-0.834	0.408
	Age	-0.0875	0.0421	-2.076	0.043*
TSH	Lead	-0.0269	0.0132	-2.0454	0.046*
	Sex (Female)	0.0728	0.7723	0.0943	0.925
	Age	0.0504	0.0175	2.8864	0.006*

*p<0.05 is statistically significant

DISCUSSION

Lead, a significant environmental contaminant, can damage cell membranes and negatively impact cellular oxido-reductive processes. Its effects are evident at the sub-cellular level, ranging from enzyme inhibition to pronounced morphological changes.[26] Due to the ongoing preventive measures against occupational and environmental lead (Pb) exposure, the health consequences of acute poisoning have diminished. However, attention has shifted to the harmful effects of lower doses, whether from acute or chronic exposure. Evidence suggests lead can be harmful at any concentration.[27] Some studies indicate that lead levels above a certain threshold may disrupt thyroid gland function by causing structural changes, potentially contributing to various thyroid disorders, including cancers.[28]

A total of 237 patients were studied and divided into 3 groups according to their blood lead concentration. A significant difference was found in blood lead concentrations between the three groups (table 1). Analysis showed that there were significant differences in fT4 and TSH levels among the three groups. The fT4 levels were significantly higher and TSH levels were significantly lower in patients of group 3 (table 1). There was no difference in fT3 levels in patients across the 3 groups.

Previous studies on the effect of lead on thyroid gland physiology have produced non-consensus and contradictory results. The results of this study were supported by a similar study by Nakhaee et al, which reported a similar pattern of changes in T4 and TSH levels in patients with high blood lead and reported an opposite pattern in the case of T3 concentration.[2] Nouri et al, in their study to assess the thyroid hormone levels in patients of lead poisoning (BLC>25 µg/dl) compared to healthy individuals, reported an increase in T4 levels and a decrease in TSH levels in lead-poisoned patients.[29] The report from Dursun et al also supported the findings of this study that high lead levels affect thyroid function, reduce TSH, and increase fT4 levels.[30]

A study by Kassy et al. reported a negative correlation between TSH and higher blood lead levels, consistent with our findings. However, their results differed in terms of fT4 levels, which showed a negative correlation in their study. A study from Michigan also supported the findings of this study reporting lower TSH levels in patients with higher blood lead concentrations.[31]

Several studies in the literature report findings that differ from this study. Studies by Ji Yoon Choi et al, Baljinder Singh et al, Magdi et al and Pekcici et al reported that high blood levels caused a rise in serum TSH levels in lead-exposed patients.[26,32–34] On the

other hand, studies by Rahimpour et al, Krieg et al, Jose Estefano et al etc reported no relation between thyroid gland activity and blood lead concentration in a different group of patients.[7,28,35]

Conflicting findings on lead's impact on thyroid function stem from several factors. Population iodine status is a key determinant, as deficiency or excess can alter hormone levels and influence lead exposure effects.[36] Assay methodology differences such as chemiluminescence immunoassay (CLIA) versus radioimmunoassay (RIA) also create inconsistencies.[37] Moreover, study design (cross-sectional vs. longitudinal), sources of lead exposure (occupational vs. environmental), co-exposure to other heavy metals (e.g., cadmium, arsenic), and genetic variations in hormone metabolism can affect outcomes.[38] Our study reduced these confounders with strict exclusion criteria and validated assay platforms.

The effects of lead on thyroid function have been under investigation since the mid-1950s. While a study by Slingerland provided evidence of decreased iodine uptake by the thyroid gland, Sandstead's study confirmed that. Another survey by Tuppurainen et al reported that lead imparts its effect both on the thyroid gland and thyroid-pituitary axis.[39–41]

Researchers have proposed several theories about lead's effects on the thyroid gland, but consensus remains elusive. The significantly high fT4 and low TSH levels found in patients with elevated blood lead concentrations can be attributed to various hypotheses. These include oxidative stress, interference with catecholaminergic neurotransmitter transmission particularly dopamine and immune system dysregulation. It is well established that lead induces oxidative stress by generating reactive oxygen species (ROS), thereby altering immune responses. Chronic lead exposure can result in cellular damage and inflammation, which may lead to the release of thyroid follicle contents, resulting in early-stage hyperthyroidism.[13,15] Moreover, lead inhibits type I 5′-deiodinase activity, the enzyme that converts thyroxine (T4) to its active form, triiodothyronine (T3), potentially explaining why fT3 levels remain stable despite increased fT4 levels.[2] Additionally, it is suggested that lead exposure can trigger the release of synaptosomal catecholamines, especially dopamine, in the cerebellum, hippocampus, and cerebral cortex. This surplus of dopamine may inhibit TSH release from the pituitary gland.[42]

Though studies and cases have indicated that lead poisoning is associated with altered thyroid physiology. However, researched have failed to establish the usual cause-effect relationship. Some studies showed a negative correlation between blood lead levels and TSH, where blood lead levels were raised due to secondary hyperthyroidism. Bones are the primary sites where the majority of the lead is deposited. Hyperthyroidism causes increased bone turnover due to an imbalance between bone formation and resorption, which leads to the release of the deposited lead into the bloodstream.[7,43]

Similarly in this study, group 3 patients showed an increase in fT4 levels with an increase in blood level and a decrease in age, whereas advancing age caused an increase in TSH levels (table 3). Age modulates blood lead levels and thyroid function due to dynamic bone turnover, with bone tissue holding 90–95% of total body lead. Increased osteoclastic activity, often from osteopenia or thyroid-induced remodelling, mobilizes lead into the bloodstream.[7,43] This elevation in blood lead concentration (BLC) may impact thyroid physiology. In hyperthyroid states, accelerated bone turnover can worsen lead release. Interestingly, younger patients in our study had higher BLC, while older age correlated with increased TSH levels, suggesting a compensatory mechanism or late-onset thyroid resistance. This highlights the importance of considering skeletal lead stores when interpreting blood lead levels in endocrine studies.[44]

This study highlights significant public health implications for industrial areas in North India. Changes in thyroid hormone levels among individuals with high blood lead levels suggest that even subclinical lead toxicity may impact endocrine health. Regular screening for thyroid dysfunction in populations chronically exposed to lead especially workers in battery, paint, and smelting industries could enable early detection of thyroid issues. Moreover, improving environmental monitoring, enhancing workplace safety, and enforcing stricter lead exposure regulations are crucial to reduce long-term endocrine risks. Incorporating thyroid function tests into lead exposure management may help reduce undiagnosed thyroid disorders in at-risk groups.

Strengths

This study has several methodological strengths that enhance its findings' credibility. First, it uses a large sample size (n = 237), strengthening statistical power and generalizability. Second, all biochemical measurements were conducted with validated assays: blood lead levels were analyzed using the accurate LeadCare II analyzer; thyroid hormones (fT3, fT4, TSH) were measured with Roche Elecsys kits on the Cobas 8000 platform, ensuring assay precision. Third, stringent exclusion criteria were applied patients with thyroid disorders, pregnancy, or medications affecting thyroid function were excluded. This careful design minimized confounding and improved internal validity.

Limitations

Despite its strengths, this study has certain limitations. First, being retrospective in nature, it relied on existing medical records, which may be prone to documentation errors and lacked detailed clinical follow-up. Second, although care was taken to exclude patients on thyroid-altering medications, unreported over-the-counter drug use or environmen-

tal co-exposures (e.g., to cadmium or arsenic) could not be fully ruled out. Third, the study did not assess urinary iodine status, which is a key modulator of thyroid function and could have acted as an effect modifier. Fourth, because the analysis was hospital-based, it may not reflect the true exposure patterns or thyroid status of the general population. Lastly, although subgroup analysis by region or occupation was considered, the available sample distribution limited its feasibility.

Conclusion

This study identified a significant association between elevated blood lead concentrations and altered thyroid hormone levels specifically, higher fT4 and lower TSH suggesting a potential disruption of thyroid homeostasis in lead-exposed individuals. While mechanistic hypotheses such as oxidative stress and neurotransmitter interference offer possible explanations, the relationship remains complex and likely influenced by factors such as age-related bone turnover. Future longitudinal studies should evaluate the role of lead exposure duration, iodine status, genetic susceptibility, and bone lead burden in modulating thyroid function across diverse populations.

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Availability of Data: Available in excel sheet. Detailed data is kept at MRD of DMCH, Ludhiana. Accessible upon request and with administration clearance.

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