ISSN- O: 2458 - 868X, ISSN–P: 2458 – 8687
National Library of Medicine - ID: 101731606

International Journal of Medical Science and Innovative Research (IJMSIR)
IJMSIR : A Medical Publication Hub
Available Online at: www.ijmsir.com
Volume – 10, Issue – 5, September – 2025, Page No. : 81 – 87

Study To Assess Serum Homocysteine Levels in Patients with Hypothyroidism

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Citation this Article: Ananya Tripathi, Mahendra Pratap Singh, Shivendra Verma, Richa Giri, "Study To Assess Serum Homocysteine Levels in Patients with Hypothyroidism", IJMSIR - September – 2025, Vol – 10, Issue - 5, P. No. 81 – 87.
Type of Publication: Original Research Article
Conflicts of Interest: Nil

Abstract

Introduction: Hypothyroidism is a common endocrine disorder characterized by insufficient thyroid hormone production, resulting in the slowing of metabolic processes. Elevated homocysteine levels have been observed in patients with hypothyroidism and are recognized as an independent risk factor for cardiovascular disease.

Objective: To assess serum homocysteine levels in patients with hypothyroidism

Material and Methods: This cross-sectional study was conducted at K.P.S. Post Graduate Institute of Medicine, GSVM Medical College, Kanpur. A total of 280 newly diagnosed hypothyroid patients aged 18 years and above were enrolled. Inclusion criteria required TSH levels above 5 mU/L. Patients with conditions affecting homocysteine metabolism, such as diabetes mellitus, chronic liver disease, chronic kidney disease, or those with a history of stroke, were excluded. Serum homocysteine levels were measured using photometry). Data were analyzed using SPSS v26.0, with results presented through tables and graphs.

Results: The mean age of study participants was 40.57 ± 13.26 years, with a female predominance (86.4%). Serum homocysteine levels were found to be elevated in 58.2% of participants. Homocysteine levels did not show significant age-dependent variations ($p = 0.08$), nor were there significant gender-based differences ($p = 0.50$) A moderate positive correlation ($r = 0.3084$, $p < 0.00001$) was observed between serum TSH and serum homocysteine levels, indicating that increased TSH levels were associated with higher homocysteine levels.

Conclusion: The study demonstrates a significant association between elevated homocysteine levels and hypothyroidism, suggesting that hypothyroid patients are at increased risk for cardiovascular complications.

Keywords: Homocysteine, Hypothyroidism, TSH, Metabolism, Cardiovascular risk

Introduction

Hypothyroidism, characterized by insufficient production of thyroid hormones, disrupts several physiological processes, including metabolism, cardiovascular regulation, lipid metabolism, and renal clearance. Classified into primary, secondary, and tertiary forms based on origin, hypothyroidism manifests in various

clinical forms: overt, subclinical, congenital, and iatrogenic. Globally, it affects approximately 5% of the population, with a higher prevalence in women and in iodine-deficient regions. In India, the prevalence is estimated at 10–11%.

One consequence of hypothyroidism is hyperhomocysteinemia. Homocysteine, a sulfur-containing amino acid derived from methionine metabolism, is usually converted to methionine or cysteine via pathways requiring vitamins B12 (methylcobalamin), B6, and folate. Disruption in these metabolic pathways, especially due to hypothyroidism, can lead to elevated Homocysteine levels—an independent risk factor for cardiovascular disease. People with high homocysteine levels may also experience neurological symptoms such as memory problems, difficulty concentrating, and cognitive decline. In more severe cases, elevated homocysteine has been associated with peripheral neuropathy, which can impair balance and coordination and cause tingling, numbness, or weakness in the hands and feet. Hyper homocysteinemia, or elevated blood homocysteine levels, is believed to be a risk factor for cardiovascular diseases (CVD), such as atherosclerosis, stroke, and coronary artery disease (CAD).

The pathophysiological mechanisms contributing to hyperhomocysteinemia in hypothyroidism include impaired renal clearance, altered hepatic metabolism, and nutritional deficiencies. The global prevalence of hyper homocysteinemia varies depending on factors like age, diet, genetics, and country-specific health factors. It is estimated that 5-10% of the global population have elevated levels of homocysteine India shows a notable prevalence of hyper homocysteinemia, with studies estimating around 20-30% of the adult population having elevated homocysteine levels, depending on the region and population group

This study focuses on evaluating serum homocysteine levels in hypothyroid patients to understand their interrelation and cardiovascular implications.

Materials and Methods

Study Design: A cross-sectional observational study was conducted at the K.P.S. Post Graduate Institute of Medicine, G.S.V.M. Medical College, Kanpur from February 2024 to February 2025.

Sample Size: 280 patients diagnosed with hypothyroidism (TSH > 5 mU/L) were recruited. In a pilot study of 20 patients Homocysteine levels were elevated in patients having serum TSH levels between 5-10 mIU/L. The sample size was calculated to be 280 at power 80 % and level of significance of 5 %.

Inclusion Criteria: Adults (>18 years) of Both sexes that are Newly diagnosed with hypothyroidism (TSH > 5 mU/L).

Exclusion Criteria

Patients with conditions that may interfere with homocysteine metabolism were excluded: Diabetes mellitus, Chronic liver/kidney disease, History of stroke, Chronic alcoholism, Coronary artery disease, Genetic enzyme deficiencies (MTHFR, CBS, methionine synthase), Pernicious anemia, Inflammatory bowel disease or celiac disease, Long-term use of Metformin, PPIs, chloramphenicol and Strict vegetarians

Data Collection:

Serum homocysteine was measured using photometry and TSH levels were measured to confirm hypothyroidism.

Data analysis was done using SPSS v26.0.

Results

Age Group Wise distribution of Cases (n=280)

The study showed that the highest number of cases in the 41-50 age range (27.5%), followed by the 31-40 group (26.8%). With a standard deviation of 13.26 and an overall mean age of 40.57 years, the sample's ages were moderately distributed.

Table 1: Distribution according to Age

Age group	No. of cases	Percentage
<18	1	0.4%
18-30	69	24.6%
31-40	75	26.8%
41-50	77	27.5%
51-60	28	10.0%
>61	30	10.7%
Mean ± SD	40.57 ± 13.26	

Gender Wise distribution of Cases {n =280}

The study showed that the gender distribution of cases, with females representing the majority at 86.4% (242 cases), while males accounted for 13.6% (38 cases). In total, there were 280 cases.

Table 2: Distribution according to Gender

Gender	No. of cases	Percentage
Female	242	86.4%
Male	38	13.6%
Total	280	100.0%

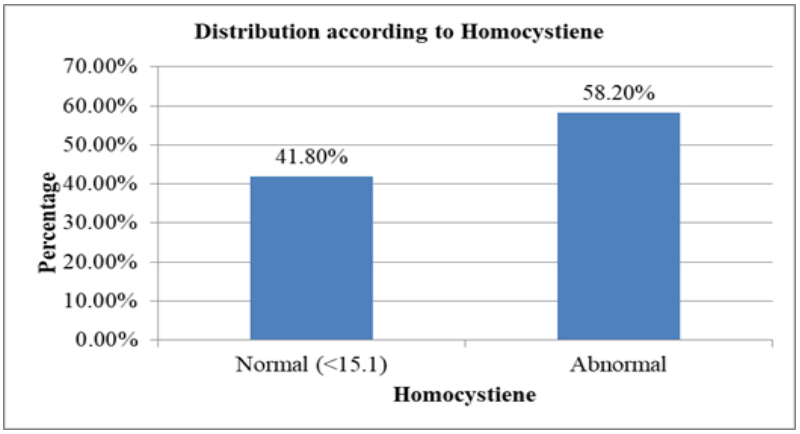
Distribution of Cases {n=280} According To Homocystiene Levels

Table 3: Distribution according to Homocystiene

Homocystiene	No. of cases	%
Normal (<15.1)	117	41.8%
Abnormal	163	58.2%

Graph 1: Distribution according to Homocystiene

The study showed that the 41.8% of cases had normal levels (less than 15.1), while 58.2% had abnormal levels.



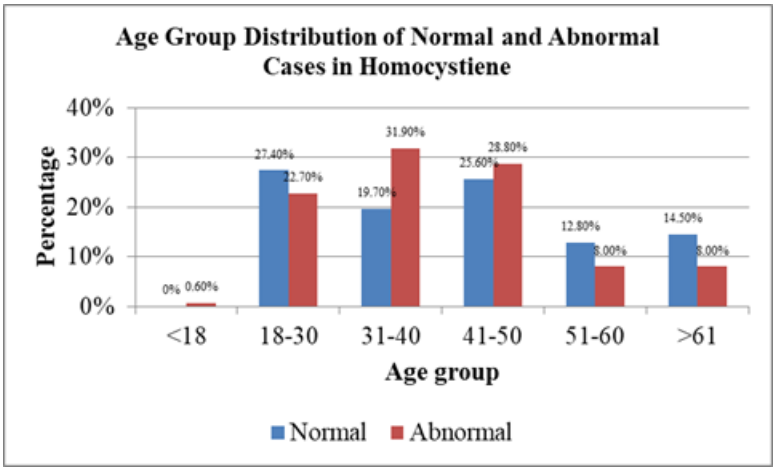
Age Group Wise Distribution of Normal Cases {n=117} and Abnormal Cases {n=163} of Homocystiene Levels

The chi-square value of 9.71 and p-value of 0.08 in the above table show that there is no statistically significant difference between the age groups in terms of normal or abnormal instances because the p-value is greater than the 0.05 limit.

Table 4: Age Group Distribution of Normal and Abnormal Cases in Homocystiene

Age group	Normal		Abnormal		Chi-sq	P-value
	No. of cases	%	No. of cases	%		
<18	0		1	0.6%	9.71	0.08
18-30	32	27.4%	37	22.7%		
31-40	23	19.7%	52	31.9%		
41-50	30	25.6%	47	28.8%		
51-60	15	12.8%	13	8.0%		
>61	17	14.5%	13	8.0%		

Graph 2: Age Group Distribution of Normal and Abnormal Cases in Homocystiene



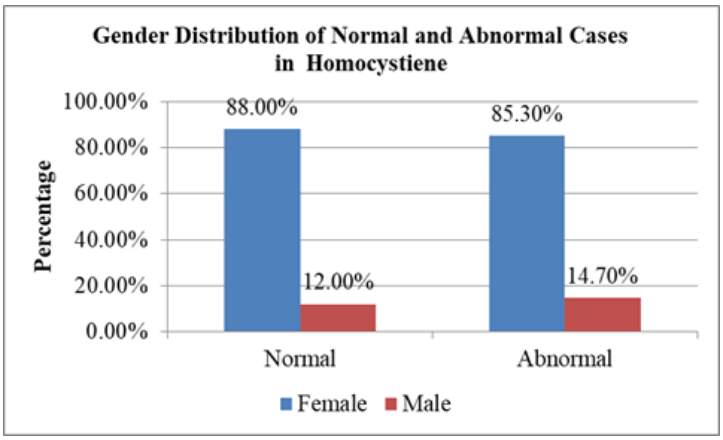
Gender Wise Distribution of Normal Cases {n=117} and Abnormal Cases {n=163} of Homocystiene Levels

The study shows that 88.0% of the females were normal and 85.3% were aberrant. Of the males, 12.0% were normal and 14.7% were abnormal. The chi-square value of 0.44 and the p-value of 0.50 indicate that there is no statistically significant difference between the genders in terms of normal or atypical cases.

Table 5: Gender Distribution of Normal and Abnormal Cases in Homocystiene

Gender	Normal		Abnormal		Chi-sq	P-value
	No. of cases	%	No. of cases	%		
Female	103	88.0%	139	85.3%	0.44	0.50
Male	14	12.0%	24	14.7%		

Graph 3: Gender Distribution of Normal and Abnormal Cases in Homocystiene

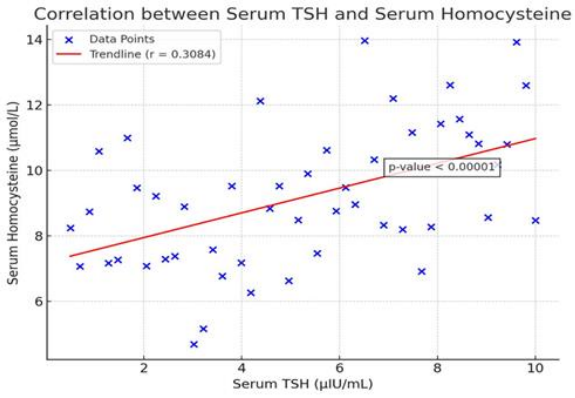


Correlation of Serum TSH Values with Serum Homocystiene Levels

The correlation between Serum TSH and Serum Homocysteine showed a correlation coefficient (r) of 0.3084, indicating a moderate positive correlation. The p-value of < 0.00001 suggests that this correlation is statistically significant, meaning there is a reliable relationship between Serum TSH and Serum Homocysteine levels in this case.

Table 6: correlation of Serum TSH with Serum Homocystiene

Correlation of Serum TSH with Serum Homocystien	
correlation coefficient (r)	0.3084
p-value	< .00001



Graph 6: correlation of Serum TSH with Serum Homocystiene

Discussion

Results of B. Catargi et al.'s study when contrasted with the current study, which examined 280 participants, the age distribution of the subjects showed that the largest percentage of instances occurred in the 41–50 age range (27.5%), followed by the 31–40 age group (26.8%). The average age in this study was 40.57 ± 13.26 years, which is less than the age of hypothyroid patients in the study by B. Catargi et al.

The present study showed a predominance of female participants, comprising 86.4% (242 cases), while males accounted for 13.6% (38 cases). This gender distribution is consistent with previous findings, including those by B. Catargi et al. The current study's results are in good agreement with those published by Garmendia Madariaga et al.

The present study when compared with Mufida Begum Ifthikhar et al. which analyzed gender distribution across different age groups, it was observed that females accounted for a higher number of cases in most age categories, with the highest percentage in the 31–40 age group (27.7%). Males exhibited higher representation in the 18–30 and 41–50 age groups, both at 28.9%.

A study conducted by Anna Orzechowska-Pawilojc et al. reported that women with hypothyroidism exhibited a

mean total homocysteine (tHcy) level that was 1.92 µmol/L higher than that of the control group; however, this difference was not statistically significant. Similarly, research conducted by Ranran Xu et al. demonstrated that homocysteine levels were significantly higher in males than in females across all age ranges. Homocysteine concentrations initially declined before subsequently increasing, with the lowest levels observed in individuals aged 30–50 years, followed by a significant rise beyond the age of 50 years.

In comparison, the present study evaluated the distribution of homocysteine levels among participants and found that 41.8% of cases exhibited normal homocysteine levels (<15.1 µmol/L), while a majority (58.2%) demonstrated abnormal levels.

A Chi-square value of 9.71 and a p-value of 0.08 from an examination of the age group distribution showed that there was no statistically significant variation in homocysteine levels between age groups. The age group aged 31–40 years had the largest percentage of those with abnormal homocysteine levels (31.9%), followed by those aged 41–50 years (28.8%) and 18–30 years (22.7%). The 18–30 age group had the highest distribution of normal homocysteine levels (27.4%), followed by the 41–50 age group (25.6%) and the 31–40 age group (19.7%).

Furthermore, gender-wise distribution analysis indicated no statistically significant difference in homocysteine levels between males and females, as evidenced by a Chi-square value of 0.44 and a *p*-value of 0.50. Among females, 88.0% exhibited normal homocysteine levels, while 85.3% had abnormal levels. In contrast, 12.0% of males had normal homocysteine levels, whereas 14.7% demonstrated abnormal levels.

When comparing these results to prior studies, the present study similarly observed higher homocysteine levels in a substantial proportion of participants, aligning with the findings of Ranran Xu et al. regarding increased homocysteine levels beyond the age of 50 years.

Anna Orzechowska-Pawilojc et al. results showed that hypothyroid individuals had higher tHcy levels than the control group, but this difference was not statistically significant. Similarly, Nedrebo et al. demonstrated that Homocysteine levels were significantly elevated in hypothyroid patients compared to hyperthyroid individuals. Diekman et al. further corroborated these findings, reporting elevated Homocysteine levels in hypothyroid patients, with a mean reduction of approximately 4.6 µmol/L following treatment.

In comparison, the present study analyzed the correlation between serum TSH and serum homocysteine, revealing a correlation coefficient (r) of 0.3084, indicating a moderate positive correlation. The statistically substantial p-value of <0.00001 implies a robust and dependable association between serum TSH and homocysteine levels. These findings accord with earlier research that have consistently showed a connection between thyroid dysfunction and variations in homocysteine metabolism. The magnitude of change in tHcy levels observed in the current study was comparatively smaller than that reported in prior research. This discrepancy may be attributed to the mild nature of hypothyroidism in the present cohort, with 60% of participants exhibiting TSH levels between 5–10 mU/L. These results highlight the intricate relationship between thyroid function and homocysteine metabolism, as well as the possible influence of thyroid hormone replacement treatment on regulating homocysteine levels in patients with hypothyroidism.

Conclusion

The present study aimed to evaluate the relationship between homocysteine and levels in hypothyroid

patients, particularly in correlation with serum thyroid-stimulating hormone (TSH) levels. The current investigation was conducted at K.P.S. Post Graduate Institute of Medicine, GSVM Medical College, Kanpur, it included 280 patients, predominantly female (86.4%), with a mean age of 40.57 ± 13.26 years. 58.2% of patients had abnormally high levels (>15.1 µmol/L) of homocystiene whereas 41.8% had normal levels. Homocysteine levels did not show significant age-dependent variations ($p = 0.08$), nor were there significant gender-based differences ($p = 0.50$). However, a statistically significant moderate positive correlation was found between serum TSH and homocysteine levels ($r = 0.3084$, $p < 0.00001$), indicating that elevated TSH is associated with increased homocysteine levels. These findings suggest that while hypothyroidism is linked to elevated homocysteine levels, potentially increasing cardiovascular risks. The study highlights need of monitoring homocysteine levels in hypothyroid patients and underscores the need for routine monitoring of homocysteine levels in hypothyroid patients, given its potential role in cardiovascular disease. Further research is needed to explore the mechanisms underlying these biochemical interactions.

References

1. B. Catargi, D. Parrot-Roulaud, P. Cochet, B. Ducassou, & J. Roger. (1999). Homocysteine, hypothyroidism, and effect of thyroid hormone replacement. Thyroid, 9(12), 1163–1166. https:// doi. org/10.1089/thy.1999.9.1163
2. Garmendia Madariaga, A., Santos Palacios, S., Guillén-Grima, F., & Galofré, J. C. (2014). The incidence and prevalence of thyroid dysfunction in Europe: A meta-analysis. Journal of Clinical Endocrinology & Metabolism,99(3),923–931. https:// doi.org/10.1210/jc.2013-2409
3. Ifthikhar, M. B., Waqar, S. H., Shaikh, A. S., & Bukhari, M. H. (2021). Homocysteine and hypothyroidism: An emerging cardiovascular risk factor in South Asians. Pakistan Journal of Medical Sciences,37(5),1408–1413.https://doi.org/ 10. 12669/ pjms.37.5.3913
4. Orzechowska-Pawilojc, A., Łopatynski, J., & Bieńkiewicz, M. (2005). Total homocysteine and folate levels in hypothyroid patients. Endocrine Journal, 52(5), 537–543. https://doi.org/ 10.1507/ endocrj.52.537
5. Xu, R., Zhang, Y., Ye, H., & Yu, X. (2017). Serum homocysteine levels are associated with thyroid function: A cross-sectional study in a large cohort. Scientific Reports, 7, 43443. https://doi.org/ 10.1038/ srep43443
6. Nedrebo, B. G., Ericsson, U. B., Nygård, O., Refsum, H., Ueland, P. M., Aakvaag, A., & Schneede, J. (1998). Plasma total homocysteine levels in hyperthyroid and hypothyroid patients. Metabolism, 47(1),89–93.https://doi.org/10.1016/S0026-0495 (98) 90213-5
7. Diekman, M. J. M., van der Put, N. M. J., Blom, H. J., & Tijssen, J. P. (2001). Determinants of elevated homocysteine in patients with hypothyroidism and the effect of treatment. Journal of Internal Medicine, 249(6),521–524. https://doi.org/10.1046/j.1365-2796. 2001.00833.x
8. Indian Thyroid Society. (2012). Prevalence of hypothyroidism in India: A multicenter study. Indian Journal of Endocrinology and Metabolism, 16(4), 568–570. https://doi.org/10.4103/2230-8210.98083.