|| ISSN(online): 2589-8698 || ISSN(print): 2589-868X ||

Available online on http://www.ijmbs.info

International Journal of Medical and Biomedical Studies; 2025; 9(1); 15-21

Original Research Article

# The Prevalence of Left Ventricular Diastolic Dysfunction in Subclinical Hypothyroidism Patients

**Satyabrata Sahoo[1], Rakesh Chandra Behera[2], Sunita Sethy[3], Tushar Kantee Behera[4]**

[1]Assistant Professor, Department of General Medicine, S. C. B. Medical College & Hospital, Cuttack, Odisha, India

[2]Assistant Professor, Department of General Medicine, S. C. B. Medical College & Hospital, Cuttack, Odisha, India

[3]Assistant Professor, Department of General Medicine, S. C. B. Medical College & Hospital, Cuttack, Odisha, India

[4]Assistant Professor, Department of General Medicine, S. C. B. Medical College & Hospital, Cuttack, Odisha, India

**Received: 11-10-2024 / Revised: 17-11-2024 / Accepted: 30-12-2024**
**DOI: https://doi.org/10.32553/ijmbs.v9i1.2929**
**Corresponding author: Tushar Kantee Behera**
**Conflict of interest: No conflict of interest**

**Abstract:**

**Background:** Elevated serum thyroid-stimulating hormone (TSH) levels together with normal blood levels of free thyroxine (FT4) and free triiodothyronine (FT3) are the hallmarks of subclinical hypothyroidism (SCH). SCH is common, especially in older persons and women, and it has been linked to a number of harmful cardiovascular consequences, such as left ventricular diastolic dysfunction (LVDD). The study investigated the incidence of LVDD in females with SCH and identify key predictors of this condition.

**Methods:** A total of 1,248 female patients aged 20 to 50 years with SCH were included. Inclusion criteria were elevated TSH (5-10 micro unit/L) with normal FT3 (2.77-5.27 pg/ml) and FT4 (0.78-2.19 ng/dl) levels. Patients underwent 2D Echocardiography to assess LVDD. Descriptive statistics, chi-square testing, and logistic regression analysis were used to analyse the data.

**Result:** LVDD was identified in 25% of the patients. The prevalence increased with age, being highest (28.2%) in the 40-50 age group. Significant associations were found between thyroid function and LVDD, with higher TSH and lower FT3 and FT4 levels linked to increased LVDD risk ($p<0.001$). Echocardiographic parameters showed higher LV mass and wall thickness in LVDD patients. Doppler echocardiographic parameters indicated impaired diastolic function. Logistic regression identified age, serum FT3, serum FT4, serum TSH levels, LV mass index, and E/A ratio as independent predictors of LVDD.

**Conclusion:** Female SCH patients have high rates of LVDD, which is linked to thyroid function. Older age and greater TSH were risk factors for LVDD, but higher FT3 and FT4 were protective. SCH individuals with LVDD had significant heart structural and functional abnormalities on echocardiography.

**Recommendations:** Regular cardiovascular screening and proactive management of thyroid function are recommended for patients with SCH to prevent the progression of cardiac

dysfunction. Further research should explore the benefits of early intervention and the potential role of thyroid hormone replacement therapy in reducing cardiovascular risks.

**Keywords:** Subclinical hypothyroidism, Left ventricular diastolic dysfunction, Thyroid function, Echocardiography, Cardiovascular risk



## Introduction

Elevated serum thyroid-stimulating hormone (TSH) levels with normal serum free thyroxine (FT4) and free triiodothyronine (FT3) levels are the hallmark of subclinical hypothyroidism (SCH), a common endocrine disease. About 4–10% of the general population is affected by SCH, with women and older persons having a higher frequency [1]. Despite being asymptomatic or having mild nonspecific symptoms, SCH is associated with several adverse cardiovascular outcomes, including dyslipidemia, hypertension, and increased risk of atherosclerosis.

One of the critical cardiovascular complications linked with SCH is left ventricular diastolic dysfunction (LVDD). Diastolic dysfunction, a condition where the left ventricle has impaired relaxation and filling during diastole, is a precursor to heart failure with preserved ejection fraction (HFpEF) [2]. The pathophysiological mechanisms underlying LVDD in SCH involve altered myocardial relaxation and increased left ventricular stiffness, partly mediated by the effects of thyroid hormones on cardiac myocytes and extracellular matrix remodeling.

Recent studies have highlighted the significance of early detection and management of LVDD in patients with SCH to prevent the progression to overt heart failure [3]. However, the prevalence and determinants of LVDD in this population remain underexplored. Understanding the relationship between thyroid function and cardiac diastolic function is crucial for developing effective screening and intervention strategies.

Given the increasing recognition of the cardiovascular risks associated with SCH, there is a pressing need for detailed investigations into the cardiac manifestations of this condition. Previous research has suggested that even mild thyroid dysfunction can have significant cardiovascular effects, underscoring the importance of routine cardiovascular assessment in patients with SCH [4].

This study aims to investigate the prevalence of LVDD in female patients with SCH and identify the key predictors of this condition.

## Methodology

### Study Design

A cross-sectional observational study.

*Study Setting*

This study was conducted at S. C. B. Medical College & Hospital, Cuttack, Odisha, from April 2023 to March 2024.

### Participants

The study involved 104 patients per month, totalling 1,248 patients over the study period.

### Inclusion Criteria

- Female patients aged between 20 to 50 years.

- Diagnosed with SCH.

- Patients with the following thyroid function test results:

- Serum FT3: 2.77-5.27 pg/ml

- Serum FT4: 0.78-2.19 ng/dl

- Serum TSH: 5-10 micro unit/L

- Patients who consented to undergo a 2D Echocardiography (2D Echo) test.

**Exclusion Criteria**

- younger than 20 years.

- older than 50 years.

- with a heart rate (HR) greater than 100 beats per minute.

**Sample Size**

To calculate the sample size for this study, the following formula was used for estimating a proportion in a population:

$$n = \frac{Z^2 \times p \times (1-p)}{E^2}$$

Where:

- n = sample size

- Z = Z-score corresponding to the desired level of confidence

- p = estimated proportion in the population

- E = margin of error

**Bias**

Efforts were made to minimize selection bias by strictly adhering to the inclusion and exclusion criteria. Information bias was minimized by training data collectors and ensuring standardized procedures for data collection and analysis.

**Variables**

Variables included age, serum FT3, serum FT4, serum TSH levels, presence of left ventricular diastolic dysfunction as determined by 2D Echo.

**Data Collection**

Data were collected through structured interviews and medical records. Each participant underwent a 2D Echo to assess for left ventricular diastolic dysfunction. The 2D Echo results were interpreted by a qualified cardiologist.

**Statistical Analysis**

SPSS software was used to analyse the data. The individuals' clinical and demographic features were compiled using descriptive statistics. It was determined how common left ventricular diastolic dysfunction was. The relationship between LVDD and SCH was examined using logistic regression analysis and chi-square tests. Statistical significance was attained when the p-value was less than 0.05.

**Ethical Considerations**

The study protocol was approved by the Ethics Committee and written informed consent was received from all the participants.

**Result**

The study enrolled 1,248 female patients aged between 20 to 50 years with SCH. The mean age was 35.4 ± 8.2 years.

**Table 1: Demographic and Clinical Features**

| Characteristic | Mean ± SD / n (%) |
|---|---|
| Age (years) | 35.4 ± 8.2 |
| Serum FT3 (pg/ml) | 3.45 ± 0.7 |
| Serum FT4 (ng/dl) | 1.5 ± 0.4 |
| Serum TSH (micro unit/L) | 7.5 ± 1.5 |
| Heart Rate (beats per minute) | 72 ± 10 |

Out of the 1,248 participants, 312 (25%) were found to have left ventricular diastolic dysfunction (LVDD) as determined by 2D Echo. The prevalence of LVDD in different age groups is shown in Table 2.

**Table 2: Prevalence of Left Ventricular Diastolic Dysfunction**

| Age Group (years) | Number of Patients | Patients with LVDD | Percentage (%) |
|---|---|---|---|
| 20 – 29 | 312 | 62 | 19.9 |
| 30 – 39 | 426 | 106 | 24.9 |
| 40 – 50 | 510 | 144 | 28.2 |

The study found a significant correlation between thyroid function test results and the incidence of LVDD. Patients with higher TSH levels and lower FT3 and FT4 levels were more likely to have LVDD. The statistical analysis is presented in Table 3.

**Table 3: Association Between Thyroid Function and LVDD**

| Thyroid Function Test | Patients with LVDD | Patients without LVDD | p-value |
|---|---|---|---|
| FT3 (pg/ml) | 3.2 ± 0.6 | 3.6 ± 0.7 | <0.001 |
| FT4 (ng/dl) | 1.3 ± 0.3 | 1.6 ± 0.4 | <0.001 |
| TSH (micro unit/L) | 8.3 ± 1.2 | 6.9 ± 1.4 | <0.001 |

The ECG parameters related to LV morphology in SCH patients are summarized in Table 4.

**Table 4: Echocardiographic Parameters of Left Ventricular Morphology**

| Parameter | Patients with LVDD | Patients without LVDD | p-value |
|---|---|---|---|
| Left Ventricular Mass (g) | 210 ± 35 | 190 ± 30 | <0.001 |
| Left Ventricular Mass Index (g/m²) | 105 ± 18 | 95 ± 15 | <0.001 |
| Interventricular Septal Thickness (mm) | 11.5 ± 1.5 | 10.0 ± 1.2 | <0.001 |
| Left Ventricular Posterior Wall Thickness (mm) | 10.0 ± 1.4 | 9.0 ± 1.1 | <0.001 |

The Doppler ECG parameters of LV function in SCH patients are presented in Table 5.

**Table 5: Doppler Echocardiographic Parameters of Left Ventricular Function (Diastolic Function)**

| Parameter | Patients with LVDD | Patients without LVDD | p-value |
|---|---|---|---|
| E/A Ratio | 0.8 ± 0.2 | 1.2 ± 0.3 | <0.001 |
| Deceleration Time (ms) | 240 ± 30 | 200 ± 25 | <0.001 |
| Isovolumetric Relaxation Time (IVRT) (ms) | 110 ± 15 | 90 ± 12 | <0.001 |
| E/E' Ratio | 15 ± 2 | 10 ± 1 | <0.001 |

Logistic regression analysis was accomplished to identify the independent predictors of LVDD. The results are summarized in Table 6.

**Table 6: Logistic regression analysis**

| Variable | Odd ratio (OR) | 95% confidence interval (CI) | p-value |
|---|---|---|---|
| Age (years) | 1.05 | 1.02 – 1.08 | <0.001 |

| | | | |
|---|---|---|---|
| Serum FT3 (pg/ml) | 0.75 | 0.64 – 0.89 | <0.001 |
| Serum FT4 (ng/dl) | 0.60 | 0.48 – 0.75 | <0.001 |
| Serum TSH (micro unit/L) | 1.50 | 1.28 – 1.76 | <0.001 |
| LV Mass Index (g/m²) | 1.20 | 1.10 – 1.30 | <0.001 |
| E/A Ratio | 0.50 | 0.40 – 0.60 | <0.001 |

## Discussion

The study evaluated 1,248 female patients aged 20 to 50 years with SCH to determine the prevalence and predictors of LVDD. The results revealed a significant prevalence of LVDD, with 25% of the patients exhibiting this condition. The prevalence varied across age groups, being lowest (19.9%) in the youngest age group (20-29 years) and highest (28.2%) in the oldest age group (40-50 years). This indicates a higher susceptibility to LVDD with increasing age in patients with SCH.

Further analysis displayed a strong correlation among thyroid function and the presence of LVDD. Patients with lower levels of FT3 and FT4 and higher levels of TSH were more likely to have LVDD. This finding emphasizes the role of thyroid hormones in maintaining normal cardiac function, particularly in the diastolic phase. The statistical significance of these associations ($p<0.001$) underscores the significance of regular monitoring of thyroid function in these patients to prevent or manage LVDD effectively.

Echocardiographic parameters revealed notable differences in left ventricular morphology between individuals with and without LVDD. Patients with LVDD had substantially higher left ventricular mass and wall thickness, suggesting structural remodeling of the heart associated with SCH. Additionally, Doppler ECG parameters indicated impaired diastolic function in patients with LVDD, as evidenced by lower E/A ratios, longer deceleration times, higher isovolumetric relaxation times (IVRT), and higher E/E' ratios. These findings are critical as they highlight the specific echocardiographic changes that occur in this patient population, providing a basis for targeted diagnostic and therapeutic strategies.

Logistic regression analysis identified several independent predictors of LVDD, including age, serum FT3, serum FT4, serum TSH levels, LV mass index, and E/A ratio. These predictors can be utilized to develop risk assessment tools for early identification of patients at high risk of developing LVDD. Regular cardiovascular screening and appropriate management of thyroid function could potentially mitigate these risks and improve patient outcomes.

The study underscores the high prevalence of LVDD among individuals with SCH and highlights the importance of thyroid function in maintaining cardiac health. The detailed echocardiographic evaluation provides valuable insights into the cardiac changes associated with SCH, paving the way for improved diagnostic and management approaches in this population. Regular monitoring and early intervention are crucial to prevent the progression of cardiac dysfunction and ensure better long-term cardiovascular health in these patients.

The prevalence and consequences of LVDD in individuals with SCH have been investigated in recent research. Presystolic wave (PSW) was significantly correlated with subclinical left ventricular impairment in SCH patients. The existence of PSW was found to be a reliable indicator of subclinical left ventricular dysfunction, suggesting that early identification using echocardiographic techniques may be essential for the treatment of these patients [5].

In a general population cohort, SCH was revealed to be an independent predictor of left atrial dysfunction. Significant conduit

strain and impaired LA reservoir were found in SCH patients, indicating an early effect of SCH on cardiac function even prior to the emergence of overt heart failure symptoms [6]. According to a study, LVDD was present in 72.2% of SCH patients compared to 30.5% of euthyroid controls. This significant prevalence highlights the need for routine cardiac function screening in SCH patients [7]. Levothyroxine therapy significantly improved diastolic dysfunction in SCH patients. The treatment led to significant improvements in echocardiographic indices, suggesting that early thyroid hormone replacement can ameliorate cardiac dysfunction in SCH [8].

The presence of fragmented QRS (fQRS) in ECG was higher in SCH patients, correlating with increased left ventricular dysfunction. This suggests that fQRS could be a useful non-invasive marker for identifying patients at risk of developing LVDD [9]. Using cardiac magnetic resonance (CMR) T1-mapping, diffuse myocardial injuries were detected in SCH patients, particularly those with higher TSH levels. This indicates that SCH may lead to early myocardial changes detectable through advanced imaging techniques [10].

## Conclusion

This study highlights the high prevalence of LVDD in patients with SCH and identifies key predictors of LVDD. Regular monitoring and appropriate management of thyroid function are essential to mitigate cardiovascular risks in this population. The detailed echocardiographic evaluation provides valuable insights into the cardiac changes associated with SCH.

**Limitations:** The limitations of this study include a small sample population who were included in this study. Furthermore, the lack of comparison group also poses a limitation for this study's findings.

**Recommendation:** Regular cardiovascular screening and proactive management of thyroid function are recommended for patients with SCH to prevent the progression of cardiac dysfunction. Further research should explore the benefits of early intervention and the potential role of thyroid hormone replacement therapy in reducing cardiovascular risks.

**Acknowledgement:** We are thankful to the patients; without them the study could not have been done. We are thankful to the supporting staff of our hospital who were involved in patient care of the study group.

**List of Abbreviations:**

SCH - Subclinical Hypothyroidism

TSH - Thyroid-Stimulating Hormone

FT3 - Free Triiodothyronine

FT4 - Free Thyroxine

LVDD - Left Ventricular Diastolic Dysfunction

2D Echo - 2-Dimensional Echocardiography

HFpEF - Heart Failure with Preserved Ejection Fraction

ECG - Electrocardiography

LV - Left Ventricular

IVRT - Isovolumetric Relaxation Time

E/A Ratio - Ratio of Early (E) to Late (A) Ventricular Filling Velocities

E/E' Ratio - Ratio of Early Diastolic Transmitral Flow Velocity (E) to Early Diastolic Mitral Annulus Velocity (E')

OR - Odds Ratio

CI - Confidence Interval

PSW - Presystolic Wave

LA - Left Atrial

fQRS - Fragmented QRS Complex

CMR - Cardiac Magnetic Resonance

**Source of funding:** No funding received.

**Conflict of interest:** The authors have no competing interests to declare.

## References

1. Cooper DS. Subclinical hypothyroidism. New England Journal of Medicine. 2001 Jul 26;345(4):260-5.
2. Rodondi N, Den Elzen WP, Bauer DC, Cappola AR, Razvi S, Walsh JP, Åsvold BO, Iervasi G, Imaizumi M, Collet TH, Bremner A. Subclinical hypothyroidism and the risk of coronary heart disease and mortality. Jama. 2010 Sep 22;304(12):1365-74.
3. Li B, Huang Y, Li Z. Estimation of left ventricular functions in patients with subclinical hypothyroidism: a meta-analysis. Frontiers in Endocrinology. 2023 Dec 19;14:1279570.
4. Quiñones MA, Otto CM, Stoddard M, Waggoner A, Zoghbi WA. Recommendations for quantification of Doppler echocardiography: a report from the Doppler Quantification Task Force of the Nomenclature and Standards Committee of the American Society of Echocardiography. Journal of the American Society of Echocardiography. 2002 Feb 1;15(2):167-84.
5. Saylik F, Akbulut T. The association of presystolic wave with subclinical left-ventricular dysfunction in patients with subclinical hypothyroidism. J Echocardiogr. 2021;1-9.
6. Nakanishi K, Daimon M, Yoshida Y, Sawada N, Hirose K, Iwama K, et al. Subclinical hypothyroidism as an independent determinant of left atrial dysfunction in the general population. J Clin Endocrinol Metab. 2020.
7. Kuchulakanti AS, Sharma R, Utagi B. Left Ventricular Diastolic Dysfunction in Patients with Subclinical Hypothyroidism: A Single South Indian Tertiary Care Centre Study. J Health Allied Sci NU. 2023.
8. Gholami R, Kalbasi S, Sheibani M, Davoudi Z, Sadeghi R, Meeckunickee F, et al. Efficacy of Levothyroxine Therapy on Diastolic Dysfunction in Patients with Subclinical Hypothyroidism. Novelty Biomed. 2020;8:31-35.
9. Yilmaz E, Aydin E, Camcı S. Frequency of fragmented QRS on ECG and relationship with left ventricular dysfunction in patients with subclinical hypothyroidism. Eur Rev Med Pharmacol Sci. 2022;26(10):3677-3685.
10. Yao Z, Gao X, Liu M, Chen Z, Yang N, Jia Y, et al. Diffuse Myocardial Injuries are Present in Subclinical Hypothyroidism: A Clinical Study Using Myocardial T1-mapping Quantification. Sci Rep. 2018;8.