**Original Article**

# Electrocardiographic Changes in Newly Diagnosed Primary Hypothyroidism: An Observational Study

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## ABSTRACT

**Background:** The thyroid hormones have an important role in the cardiovascular system; even minimal change in its level can cause significant alteration in the cardiac activity which can cause considerable electrocardiographic changes. We conducted this study to assess the electrocardiographic (ECG) changes in patients who were newly diagnosed with primary hypothyroidism.

**Methods:** This study is a descriptive cross-sectional study conducted among 71 newly diagnosed subclinical and overt primary hypothyroidism patients visiting the out-patient department (OPD) of Universal College of Medical Sciences, Nepal from December 2018 to June 2020 after taking ethical clearance from the institutional review committee (UCMS/IRC/212/18). ECG was obtained for each patient at the time of diagnosis of primary hypothyroidism. The data were analyzed with SPSS Version 16.

**Results:** The most common ECG changes were sinus bradycardia seen in 32.4%, followed by T wave inversion in 21.1%, low voltage QRS complex in 15.5%, and prolonged PR interval in 14.1%. ECG changes were seen in 62% of cases of newly diagnosed primary hypothyroidism. Among all patients, subclinical hypothyroidism accounted for 7%, while overt hypothyroidism accounted for 55% of the ECG findings.

**Conclusion:** Our study found ECG changes like sinus bradycardia, T wave inversion, low QRS voltage, and prolonged PR interval in newly diagnosed primary hypothyroidism. We suggest that every newly diagnosed hypothyroid patient should be evaluated for ECG changes.

**Keywords:** Electrocardiography, Hypothyroidism, Sinus Bradycardia

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## INTRODUCTION

Hypothyroidism is a clinical condition that results due to a deficiency of thyroid hormone and can affect multiple body organs because of generalized slowing down of metabolic processes[1]. It can be classified as primary hypothyroidism, a condition in which there is a defect in the thyroid gland, and secondary hypothyroidism, in which pathology in glands other than the thyroid in the endocrine axis play a part in the decrease in circulating hormone levels, like surgical or pathological alteration of the hypothalamus or pituitary gland[2].

Thyroid dysfunction is an endocrine disorder affecting about 300 million people throughout the globe, with more than half of the affected population suspected to be unsuspecting of their condition[3]. The prevalence of overt hypothyroidism ranges between 0.2% to 5.3% in European countries and 0.3% to 3.7% in USA[4,5]. Thyroid dysfunction is also a significant health problem of Nepal, with the prevalence of about 30% of the population affected only in the eastern parts of Nepal[6]. The thyroid disorders in Nepali population were about 4.32% in a study, and out of population diagnosed with thyroid disorders, subclinical hypothyroidism was seen in 72.41%, primary hypothyroidism in 13.7%, and hyperthyroidism in 13.7%[7].

The normal range for free triiodothyronine (fT3) is taken as 2.0-4.2 pg/ml, for free thyroxine (fT4) was 8.9-17.2 pg/dL, and that for thyroid-stimulating hormone (TSH) is 0.3-4.5 µIU/mL. Primary hypothyroidism is hypothyroidism with an elevated serum TSH level. Subclinical hypothyroidism has increased serum TSH level with a normal serum fT4 level. Overt hypothyroidism refers to cases in which the serum TSH concentration is elevated, and serum fT4 is below the reference range. The progression from subclinical hypothyroidism to overt hypothyroidism is estimated to be approximately 2-5% per year[8].

Hypothyroidism is associated with several cardiovascular manifestations like impaired diastolic function; reduced contractility; and less commonly, pericardial effusion and heart failure. It can lead to various ECG changes, including bradycardia, flat or inverted T wave, PR prolongation, QRS prolongation, low voltage QRS, QT prolongation, arrhythmias like ventricular arrhythmia, and torsades de pointes[9].

This study aimed to find the prevalence of various ECG changes in newly diagnosed primary hypothyroidism.

## MATERIALS AND METHODS

We conducted this cross-sectional observational study on patients with newly diagnosed primary hypothyroidism visiting the outpatient department of Internal Medicine, Universal college of medical sciences (UCMS), Nepal. We enrolled patients for one and half years from 9$^{th}$ December 2018 to 30$^{th}$ June 2020 after getting ethical clearance from the institutional review committee at UCMS (Reference number – UCMS/IRC/212/18). Sample size was calculated by using the following formula $N = (Z^2PQ)/d^2$, where Z = 1.96 for 95% CI, P= Estimated proportion 0.16 (from a previous study done by Shashikanth M[10]), Q = 1 – P = 0.84; d= Maximum tolerance error = 0.1. Thus Sample Size (N) = $(1.96^2 \times 0.16 \times 0.84)/ 0.1^2 = 51.63 = 52$ cases. Considering a 10% attrition rate, a minimum of 58 patients were required for the study.

All newly diagnosed cases of primary hypothyroidism presenting to the OPD of Internal Medicine in Universal College of Medical Sciences with age 18 years or above were included in the study. Whereas patients below 18 years of age, pregnant subjects, patients with history of substance abuse, and those refusing to participate in the study were omitted. Patients with known heart disease**,** anaemia, endocrine disorders like diabetes mellitus, and

thyroid disorders who are already on treatment were also excluded from the study. Patients under cardiovascular medications (like antihypertensive drugs, lipid-lowering agents, and amiodarone), combined oral contraceptive pills, lithium, and steroids were also excluded from the study.

Seventy-one patients were enrolled after fulfilling the inclusion and exclusion criteria; their written informed consent was taken. Detailed medical history and examination of each patient were obtained, and primary hypothyroidism was confirmed based on laboratory findings. A standard 12-leads ECG was obtained for each of the participants by a trained operator with all leads placed in correct anatomical landmarks in a semi-recumbent position of 45 degrees horizontal after allowing them to rest for about 30 minutes. Appropriate measures were taken to minimize muscle tension. ECG was recorded in auto-mode with a frequency of 150 Hz at a speed of 25mm/s and gain settings of 10mm/mV. Any deviations from the standard protocol while obtaining an ECG were reported on the ECG paper. ECG of each patient was interpreted manually by qualified physicians. The data was entered in Statistical Package for Social Sciences (SPSS) Statistics Version 16. Categorical data were expressed as frequencies and corresponding percentages.

## RESULTS

The median age was 45 years for all newly diagnosed primary hypothyroidism. Out of 71 newly diagnosed hypothyroid patients, 73.2 % were female. The male to female ratio was 1:2.74. Among 71 newly diagnosed primary hypothyroid patients, 13 (18.3%) were subclinical, and 58 (81.7%) were overt hypothyroid. The results showed that both types were most commonly seen in the age 36-45 years and were least common in 18-25 years. As represented in figure 1, the most common symptoms were constipation (50.70%), followed by weight gain (42.30%) and lethargy (39.40%). Dyspnea and cold intolerance were found in 23.90% of the patients, and menstrual irregularities in 22.50%. Dry skin was present in 19.7% of cases.

**Table 1:** Age distribution of subclinical and overt newly diagnosed primary hypothyroidism.

| | Hypothyroidism | | |
|---|---|---|---|
| Age Group | Subclinical(%) | Overt(%) | Total (%) |
| 18-25 | 1(1.4) | 5(7) | 6(8.4) |
| 26-35 | 1(1.4) | 10(14.1) | 11(15.5) |
| 36-45 | 5(7) | 15(21.1) | 20(28.2) |
| 46-55 | 2(2.8) | 14(19.7) | 16(22.5) |
| 56-65 | 2(2.8) | 8(11.3) | 10(14.1) |
| >65 | 2(2.8) | 6(8.4) | 8(11.3) |
| Total | 13(18.3) | 58(81.7) | 71(100) |

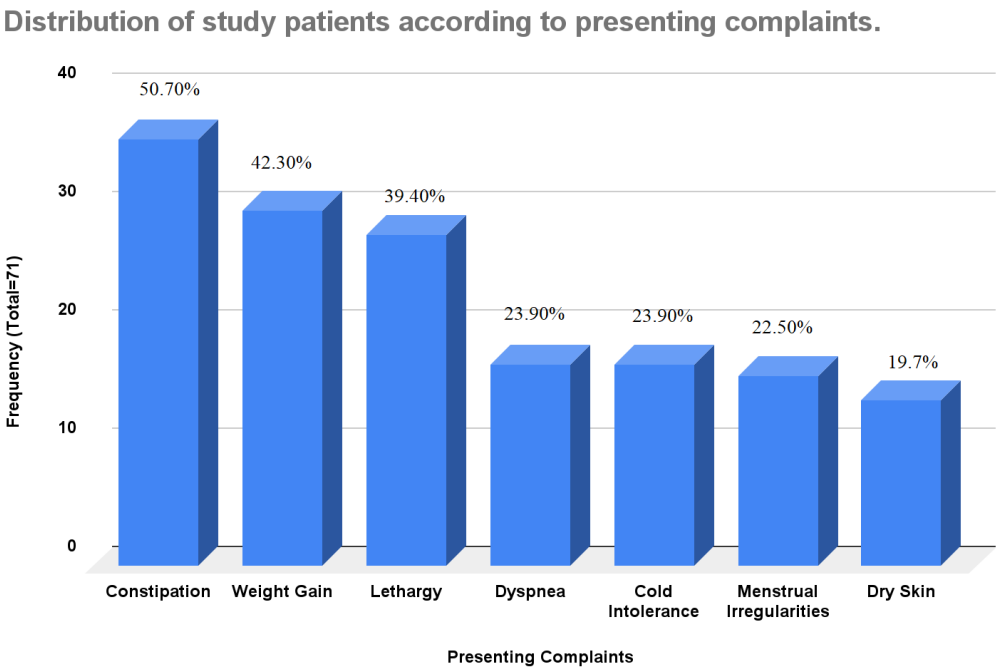


**Figure 1:** Distribution of study patients according to presenting complaints

Amongst 71 patients of newly diagnosed primary hypothyroidism, 44 (62%) had at least one abnormal ECG finding. Among them, 7% were subclinical and 55% had overt hypothyroidism. The most common ECG change was sinus bradycardia (32.4%). Likewise, 15 patients (21.1%) had T wave inversion, 11 (15.5%) had low voltage QRS, and 10 (14.1%) had prolonged PR intervals. T wave inversion was mostly noted in the precordial leads. Most of these ECG findings were seen in patients with overt primary hypothyroidism, but some patients with primary subclinical hypothyroidism also demonstrated similar ECG changes. The data has been depicted below in both tabular and graphical form in table 2 and figure 2 respectively.

**Table 2:** ECG changes in newly diagnosed primary hypothyroidism.

| ECG Changes | Subclinical (%) N=13 (18.3) | Overt (%) N=58 (81.7) | Total (%) N=71 (100) |
|---|---|---|---|
| Sinus Bradycardia | 2 (2.8) | 21 (29.6) | 23 (32.4) |
| T Wave inversion | 1 (1.4) | 14 (19.7) | 15 (21.1) |
| Low QRS Voltage | 1 (1.4) | 10 (14.1) | 11 (15.5) |
| Prolonged PR interval | 1 (1.4) | 9 (12.7) | 10 (14.1) |

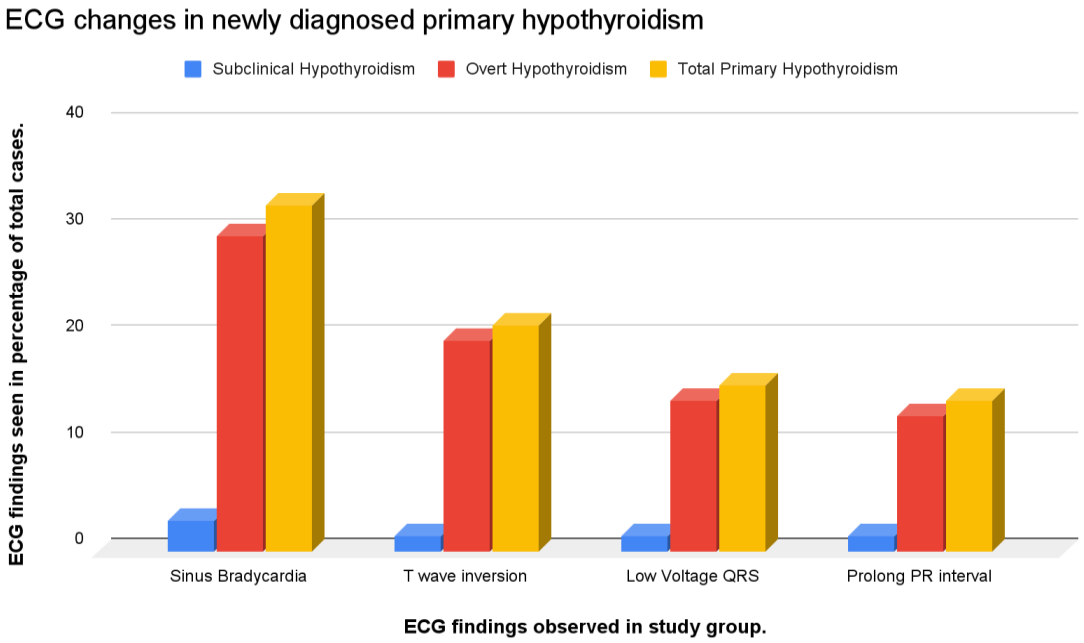


**Figure 2:** ECG changes in newly diagnosed primary hypothyroidism.

## DISCUSSION

In this study, 71 newly diagnosed primary hypothyroid patients were recruited for their evaluation of electrocardiographic changes. The median age of the study patients was 45, and most of them fall under the age group of 36-45 years. Comparable data of prevalence of hypothyroidism in the middle age group were also found in a study done by Shashikant M [11]. Overall, we found female predominance with the female population constituted 73.2%, and males. A systematic review conducted by Nygaard B. had found a much higher female preponderance, six times more common in them, affecting up to 40 in 10,000 each year (compared with 6/10,000 men) [12]. The effect of estrogen on the synthesis of hormone-binding protein, the role played by estrogen in creating an imbalance between the oxidant-antioxidant system within the thyroid gland, and the higher incidence of autoimmune disease seen in women, in general, may lead to the greater incidence of thyroid disease among women[13].

In a retrospective study done by El-Shafie, the author found fatigue as the most common symptom in 25%, followed by constipation which accounted for 20%, and 38% of patients were asymptomatic[14]. Compared to this, the most common symptom in our study was constipation (50.7%) followed by weight gain (42.3%). Fatigue was seen among 39.40% of our study population. Constipation may result from decreased gut motility, and it may worsen in patients who have a history of constipation[15]. Low thyroid hormone levels led to decreased thermogenesis and reduced metabolic rate, which can be held responsible for weight gain in hypothyroidism [16].

Hypothyroidism results in significant changes in the cardiovascular system and are very sensitive to even small changes in free thyroid hormone levels[17]. Our study identified that 62% of total patients had abnormal electrocardiographic changes. Among all patients, subclinical hypothyroidism accounted for 7%, while overt hypothyroidism accounted

for 55% of the ECG findings. Likewise, in a study conducted by Saxena P. et al. among hypothyroid patients, ECG changes were seen in 57% of patients and was normal in 43% of patients [18] In our study, we identified sinus bradycardia as the most common ECG finding present in about a third cases, followed by T wave inversion in a fifth. A different study done by Al-Farttoosi A.J.M et al. showed similar changes in ECG of patients with hypothyroidism, with sinus bradycardia being the most common finding in 47.2%, followed by inverted T waves in 27.8% [19]. In another study by Ramesh et al., 40% of patients had bradycardia on ECG [20]. Thyroid hormone directly increases the beta receptor number and sensitivity of nodes to catecholamines like norepinephrine, leading to an increase in depolarization and repolarization of nodes. This results in tachycardia, and the reverse is also true [21]. This explains the almost ubiquitous finding of sinus bradycardia in hypothyroidism and also accounts for prolonged PR interval seen in some studies, including ours.

Another study done by Behera B.K et al. in Eastern India showed the most common ECG changes as Low voltage QRS complexes (40%) followed by T wave changes (23.3%) and Right bundle branch block (6.6%) [22]. The latter was not found in our study. Sri Raveen Kandan et al.[23] have reported a rare case of severe primary hypothyroidism that presented with torsades de pointes, which was also not seen in our study. Another study by Shashikanth M. in Karnataka found ECG abnormality in 65% of cases with sinus Bradycardia (22.38%), low voltage complexes (22.38%), and ST-T changes (14.92%)[11].

The effects of Triiodothyronine (T3) on cardiac myocytes are reasonably complex, especially concerning contractility. Triiodothyronine (T3) affects the cardiac myocyte via both genomic and nongenomic mechanisms. T3 binds to its nuclear receptors and then binds to thyroid hormone response elements of the genes to regulate the transcription of various genes, directly or indirectly affecting the cardiac contractility like sarcoplasmic endoplasmic reticulum $Ca^{2+}$ ATPase (SERCA), phospholamban, beta-adrenergic receptors, cardiac muscle structural proteins like myosin, enzymes related to protein kinase A pathway, $Na^{+}$-$Ca^{2+}$ exchanger and $Na^{+}$ $K^{+}$ATPase. Additionally, it also directly stimulates membrane ion transporters, such as $Na^{+}$-$Ca^{2+}$ exchanger and $Na^{+}$-$K^{+}$ATPase. Most notable amongst these effects is the role played by phospholamban in thyroid hormone-mediated positive inotropy. When T3 is low in hypothyroidism, this could decrease the contractility of the heart and produce a low QRS voltage on ECG [24].

This study cannot be generalized as it is a single-centered study with a limited sample size, and controls with similar characteristics were not included in the study to eliminate potential confounders. In addition, further follow-up of patients was not done. A larger sample and multicenter study are needed to address these issues. Furthermore, ECG was not traced in a longitudinal model to assess its reversibility upon treatment. Also, the cardiovascular complications of the ECG changes in the patients were not studied.

## CONCLUSION

We studied electrocardiographic changes in patients with newly diagnosed primary hypothyroidism. ECG changes like sinus bradycardia, T wave inversion, low QRS voltage, and prolonged PR interval were seen among subclinical and overt hypothyroidism patients in our study. We suggest that every newly diagnosed hypothyroid patient should be evaluated for ECG changes.

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