

## Heart rate recovery to sub maximal exercise in patients with subclinical hypothyroidism – an observational study

Nagalakshmi Vijaykumar<sup>1,\*</sup>, Vivek P<sup>2</sup>, Shobha C. Nallulwar<sup>3</sup>

<sup>1</sup>Associate Professor, <sup>3</sup>Professor & HOD, SDMCMS & H, Dharwad, Karnataka, <sup>2</sup>Assistant Professor, Dept. of Physiology, Chamarajanagar Institute of Medical Sciences, Chamarajanagar, Karnataka

**\*Corresponding Author:**

Email: drlakshmi26@yahoo.com

### Abstract

**Introduction:** Exercise intolerance is typical characteristic of the subclinical hypothyroidism.

**Purpose:** Evaluation of heart rate responses to sub maximal exercise in subclinical hypothyroidism.

**Materials and Method:** Twenty three subclinical hypothyroids and thirty age, sex and BMI matched euthyroid controls were selected. Sub maximal exercise was performed using Bruce protocol using 75% target heart rate in treadmill. Heart rate recovery to sub maximal exercise was done using ECG lead II.

**Results:** Compared to Euthyroid controls, Subclinical Hypothyroidism (SCH) show a significant increase in warm up period heart rate. ( $p=0.05$ ). There is a significant increase in the heart rate during recovery period at both 1<sup>st</sup> and 2<sup>nd</sup> minute in SCH when compared to controls. ( $p=0.03, 0.01$ ), negative correlation exist between TSH level and 1<sup>st</sup> minute heart rate recovery.

**Conclusion:** We conclude that subjects with Subclinical hypothyroidism, shows a delayed heart rate recovery in response to a sub maximal exercise.

**Keywords:** Parasympathetic tones, Basal metabolic rate, Physical Exertion, Exercise tolerance, Hypothyroidism

### Introduction

Subclinical hypothyroidism (SCH) is the term used to describe patients with normal free thyroxin ( $T_4$ ) and free triiodothyronin ( $T_3$ ) and thyroid stimulating hormone (TSH) levels of more than 5 mIU/L, with generally no obvious symptoms of hypothyroidism.<sup>(1)</sup> Thyroid hormones are mandatory for various processes that are essential for human metabolism. The cardiovascular system is one of the most important targets of thyroid hormones and is very sensitive to a minimal decrease of circulating thyroid hormones.<sup>(2)</sup> There may be alterations in both myocardial function and changes in lipoprotein profile which results in increased risk of atherosclerosis, coronary heart disease, and myocardial infarction.<sup>(3)</sup> In asymptomatic patients, cardiac structure and function may remain normal at rest, but moderate to severe exercise may bring out hidden abnormalities.<sup>(4)</sup> These include reduced exercise stroke volume, reduced left ventricular ejection fraction, mild prolongation of pre ejection period, impaired exercise tolerance, lower maximum power output and maximal Oxygen consumption ( $VO_2$ ), and higher heart rates with increasing workload.<sup>(5,6)</sup> SCH may impair left ventricular diastolic function, alter endothelial function, increase the C-reactive protein level, and thus increase the risk of atherosclerosis. SCH does result in a small increase in low-density lipoprotein, cholesterol and a decrease in high-density lipoprotein, changes that enhance the risk for development of atherosclerosis and coronary artery disease.<sup>(7,8)</sup>

Flow-mediated vasodilatation, a marker of endothelial function, is significantly impaired in SCH,

and decreased heart rate variability, a marker of autonomic activity, suggests hypo functional abnormalities in the parasympathetic nervous system.<sup>(9)</sup> Heart rate recovery (HRR) which is one of the indicators of cardiovascular fitness is mainly thought to be due to parasympathetic reactivation and has been shown to be a remarkable complement to a medical assessment of an individual. Recovery of the heart rate immediately after exercise is mediated by vagal reactivation,<sup>(10)</sup> with slow heart rate recovery (HRR) being a predictor of all cause mortality and sudden death.<sup>(11)</sup> HRR  $\leq 12$  beats per minute (bpm) at 1st minute for upright position,  $\leq 18$  bpm at 1st minute for supine position and  $\leq 22$  bpm at 2 minutes for sitting position are considered abnormal.<sup>(12)</sup>

Lower exercise tolerance is an outstanding SCH characteristic. During maximal and submaximal exercises, patients with SCH showed lower efficiency of cardiopulmonary response to effort.<sup>(13,14,15)</sup> Results are conflicting during recovery.<sup>(16)</sup>

Studies have shown that HR and SBP during exercise and recovery in asymptomatic subclinical hypothyroid patients may differ from euthyroid controls.<sup>(17,18)</sup> Data on the relation between subclinical thyroid disease (SCTD) and heart rate during exercise are limited & as of our knowledge there is no work done to assess the correlation between TSH levels and HRR in hypothyroid patients.

### Materials and Method

The above study conducted in the department of physiology after obtaining the ethical clearance from the institutional ethical committee. 23 Subjects who are

diagnosed as subclinical hypothyroid with TSH more than 5.5 mIU/L with normal free T<sub>3</sub> and T<sub>4</sub> in the age group of 30-50 years of both the genders attending the medicine O.P.D selected as subjects randomly. Sample size was calculated with the help of formula based on incidence in population with the previous references.<sup>(19)</sup>

$$n = 2(Z_{\alpha} + Z_{1-\beta})^2 \sigma^2 / \Delta^2$$

With  $p < 0.05$  as acceptable and a study with 80% power; following values were:  $Z_{\alpha}$ , is 1.96.  $Z_{1-\beta}$  is 0.8416. The standard deviation would be approximately  $1.2(\sigma)$  calculated from the previous studies. The value of  $\Delta$  is 1.0

$$n = 2(1.96 + 0.8416)^2 (1.2)^2 / (1.0)^2$$

$$n = 23$$

The subjects explained regarding the procedure and written informed consent taken. 30 age and sex matched controls with normal T<sub>3</sub>, T<sub>4</sub>, and TSH, selected from general population served as controls. (n=30)

**Exclusion criteria:** Subjects with overt hypothyroidism, hypertension, ischemic or valvular heart disease, arrhythmia, previous vascular surgery, heart failure, respiratory disease, pulmonary hypertension, hepatic or renal dysfunction, diabetes mellitus, significant neurological or psychological disease and smokers were excluded.

**Study protocol:** Exercise testing

Patients were instructed not to have coffee, tea or cola 12 hours before the tests. They were asked to come to the physiology laboratory at 9.0am after having a light breakfast. Detailed history took on standard proforma about age & clinical features. Reports of investigation (T<sub>3</sub>, T<sub>4</sub>, and TSH) collected.

**Exercise protocol:** participants asked to relax for 10 minutes. At the end of 10 minutes basal HR recorded by ECG instrument in lead II. Instrument – ECG instrument with paper speed of 25mm/sec was used for above test. (BPL, Cardiart 6208 View. BPL Limited, Bannerghatta Road, Bangalore). Instrument: TREADMILL (SCHILLER, at-10 Plus, 12 Channel ECG Unit).

All the subject underwent exercise treadmill test according to Bruce protocol. A warm up period for 1 min included. Predicted peak heart rate calculated as (220-age in years). Target heart rate 70% of Predicted peak heart rate. The protocol included a graded exercise pattern on a treadmill which started at a speed of 2.7 km/hr with 10% grade, increased after 3 min to second stage at 4.0 km/hr with 12% grade. This level is

comparable to moderate submaximal exercise. HR recorded at each grade till stoppage of exercise using treadmill. Participants were, instructed to stop exercise if they achieve their target heart rate. They were also instructed to stop exercise if they experience any symptoms related to angina, light headedness, confusion, and fatigue or if there were signs of cyanosis, change in heart rhythm or failure of testing equipment. During post exercise recovery phase, HR recorded for each min for a period of 2 minute. Heart rate recovery (HRR) was taken as the difference between maximum HR and the HR at specified time period after recovery.

HRR 1<sup>st</sup> Minute = maximum Heart Rate – Heart rate at 1<sup>st</sup> minute of recovery period.

HRR 2<sup>nd</sup> Minute = maximum Heart Rate – Heart rate at 2<sup>nd</sup> minute of recovery period.

**Statistical analysis:** HRR response to submaximal exercise between hypothyroidism and euthyroid done by using unpaired T test. Intergroup analysis was done by using paired T test using SPSS software version 20.

## Results

This is a cross-sectional study done on 23 subclinical hypothyroid patients (n=23) and 30 healthy euthyroid controls (n=30). Table 1 shows the demographical characteristics of the SCH and controls. The mean age group of SCH and controls were  $34.78 \pm 5.23$  and  $36.16 \pm 7.92$  years & BMI were  $23.56 \pm 3.1$  and  $21.22 \pm 2.14 \text{ kg/m}^2$  respectively.

Table 2 shows the heart rate responses to exercise between controls and SCH. There is no significant difference in basal heart rate between SCH and controls. But there is a significant increase in warm up period heart rate in SCH when compared to controls. ( $p=0.05$ ). There is no difference in heart rate during I<sup>st</sup> stage, II<sup>nd</sup> stage of exercise between SCH and controls. There is a significant increase in the heart rate during recovery period at both 1<sup>st</sup> and 2<sup>nd</sup> minute in SCH when compared to controls. ( $p=0.03, 0.01$ ) Graph 1 demonstrates the heart rate responses to exercise between SCH and controls. Table 3 shows that HRR 1<sup>st</sup> minute and HRR 2<sup>nd</sup> minute is significantly lower in SCH when compared to controls. ( $p=0.03, 0.04$ ). Graph 2 demonstrates the correlation between TSH levels and HRR in SCH & controls.

**Table 1: Demographical characteristics of the Euthyroid and subclinical hypothyroid. (SCH)**

	Euthyroid (n=30)	SCH (n=23)	T value	P value
Mean age (Years)	36.16±7.92	34.78±5.23	0.988	0.12
Gender				
Male	12 (40%)	10(43%)		
Female	18 (60%)	13(57%)		
BMI (Kg/m <sup>2</sup> )	21.22±2.14	23.56±3.12	-1.041	0.30

BMI: Body Mass Index, values are expressed as Mean±SD.

**Table 2: Cardiovascular response to exercise between euthyroid and subclinical hypothyroid. (SCH)**

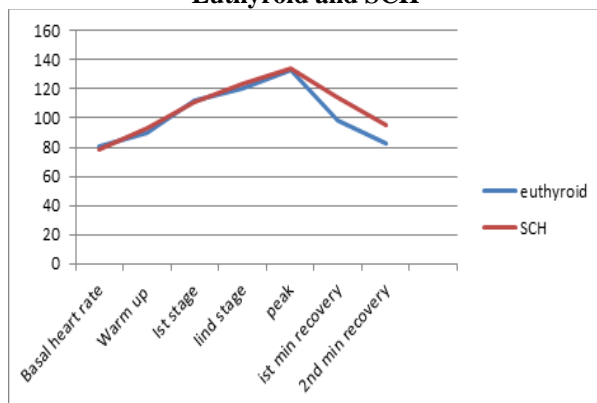
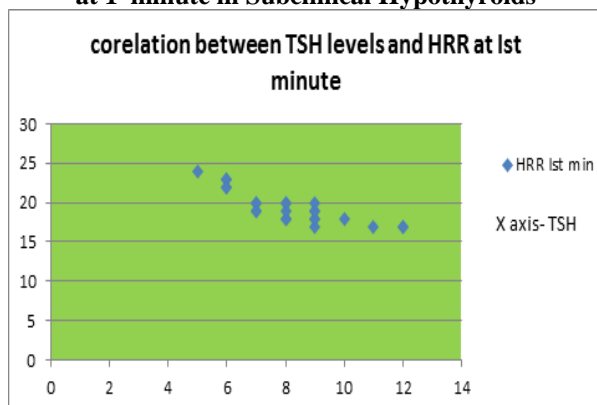
Parameter	Euthyroid (n=30)	SCH (n=23)	T value	P value
Basal heart rate	80.67±3.84	78.75±2.10	1.730	0.089
Warm up (1 min)	90.34±5.23	93.22±7.23	-1.274	0.05*
Exercise				
1. Ist stage	111.76±7.89	110.87±8.90	0.245	0.34
2. IInd stage	132.52±7.70	134.21±9.08	-0.165	0.87
Recovery				
1. Ist miute	98.90±6.56	113.65±4.53	-2.188	0.03*
2. 2 <sup>nd</sup> minute	82.44±4.22	94.76±7.66	-3.575	0.01*

Values are expressed as Mean±SD, p<0.05 considered significant \*

**Table 3: HRR in Euthyroid Vs subclinical hypothyroid. (SCH)**

	Euthyroid (n=30)	SCH (n=23)	T value	p value
HRR at 1 <sup>st</sup> minute	33.62±3.23	20.21±2.89	2.363	0.03*
HRR at 2 <sup>nd</sup> minute	50.08±6.90	40.45±4.87	1.876	0.04*

Values are expressed as Mean±SD, p< 0.05 considered significant.

**Graph 1: Heart rate responses to exercise in Euthyroid and SCH****Graph 2: correlation between TSH levels and HRR at 1<sup>st</sup> minute in Subclinical Hypothyroids**

## Discussion

This study provided a comprehensive comparison of exercise and recovery pattern between subclinical hypothyroid patients and euthyroid controls. In this study, for both groups the HR increased during exercise

and remained so, even after 2 min of recovery. Also, in comparison to controls, SCH patients had a higher HR at warm up exercise, while no difference was observed in 1<sup>st</sup> stage and II<sup>nd</sup> stage of exercise. The increased heart rate in the first minute of exercise has previously been suggested as a novel autonomic marker that helps in accurate diagnosis of high risk CAD patients.<sup>(20)</sup> In another study by Akcakoyun et al, there was no significant change in HR at rest or during exercise between groups, whereas HRR was significantly lower during exercise testing in subclinical hypothyroid patients compared to control and chronotropic incompetence was found in patients.<sup>(17)</sup> results were similar to our study, where we found no significant difference in basal HR, and also during exercise but decreased HRR in SCH. Similarly, Mainenti *et al.*, reported the lower values of HR for patients at the end of test.<sup>(16)</sup> Sunita et al showed SCH and euthyroid had normal HR and BP at rest, heart rate and BP increased with exercise and remained high even after 5 min of recovery from exercise. HR was higher in SCH at 1 min of exercise & no significant changes in HRR.<sup>(18)</sup> Our study demonstrated a significant reduction in HRR in SCH when compared to euthyroids. It has been suggested that a delayed decrease in HR during 1 and 2 min recovery of graded exercise, may be a reflection of decreased vagal activity and is a powerful predictor of overall mortality.<sup>(21)</sup>

## Conclusion

We conclude that subjects with subclinical hypothyroidism will show a delayed heart rate recovery to sub maximal exercise.

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