

## Study of Heart Rate Variability in Subclinical Hypothyroidism

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### I. Introduction

Heart Rate Variability (HRV) defined as degree of fluctuation of beat to beat differences in cardiac rhythm (1,2). It is non-invasive procedure & assess beat to beat variation in the heart. Beat to beat variation reflects time varying influence of autonomic nervous system (3). The loss of balance between sympathetic & parasympathetic system leads to cardiovascular disorders. Many hormones, including thyroid hormones (Tri-iodothyronine T3, Thyroxine T4) are thought to affect this balance. Hypothyroidism is deficiency of thyroid hormones or elevated TSH. Hypothyroidism is classified as, Overt and Subclinical hypothyroidism (SCH). SCH and cardiovascular risks are not yet correlated specifically as in that of overt. Hence in this study, we focussed on HRV in SCH.

**Aim:** To study the Heart Rate Variability in subclinical hypothyroidism.

**Objectives:** To assess and compare Heart Rate Variability among the subjects of the SCH and euthyroid subjects.

**Materials And Methods:** A cross sectional study which was carried out in patients randomly coming to Thyroid OPD in the Period of study: July 2014 to April 2016.

Institute Ethics Committee (IEC) clearance was obtained before commencement of study.

Written informed consent was taken from each subject

**Inclusion criteria for study group** (n= 30)

Newly diagnosed case of subclinical hypothyroidism of age: 20 to 50 years with no history of any significant illness and autonomic nervous disorder.

**Inclusion Criteria for Control Group:**

Age and sex matched apparently healthy individuals.

### Exclusion criteria for study & control group

Having known autonomic disorder.

Taking any drug modulating the autonomic nervous system.

Any heart disease or any other systemic diseases or factors except hypothyroidism in study group that may affect the autonomic reflexes.

Smokers and alcoholic subjects.

### Heart Rate Variability

- ECG recording for 5 minutes in supine position
- ECG recording for 5 minutes in standing position

This data was analyzed by: 1) Time domain analysis 2) Frequency domain analysis

Time domain variable	Variable Units Value	Description of statistical measures
SDNN	Ms	Standard deviation of all NN intervals
RMSSD	Ms	The square root of the mean of the sum of the squares of differences between adjacent NN interval
NN50	Count	Number of pairs of adjacent NN intervals differing by more than 50ms in the entire recording.
pNN50	%	NN50 count divided by the total number of all NN intervals.

Variable	Units	Frequency	Description
TP (total power)	ms <sup>2</sup>	<0.4	Total variance of N-N interval over the temporal segment
VLF	ms <sup>2</sup>	<0.04	Absolute power in very low frequency range
LF	ms <sup>2</sup>	0.04 to 0.15	Absolute power in low frequency range
LF norm	n.u.		LF power in normalised units [ {LF/(TP-VLF)} X100]
HF	ms <sup>2</sup>	0.15 – 0.4	Absolute power in high frequency range
HF norm	n.u.		HF power in normalised units [ {HF/(TP-VLF)} X100]
LF: HF			Ratio of LF(ms <sup>2</sup> )/HF(ms <sup>2</sup> )

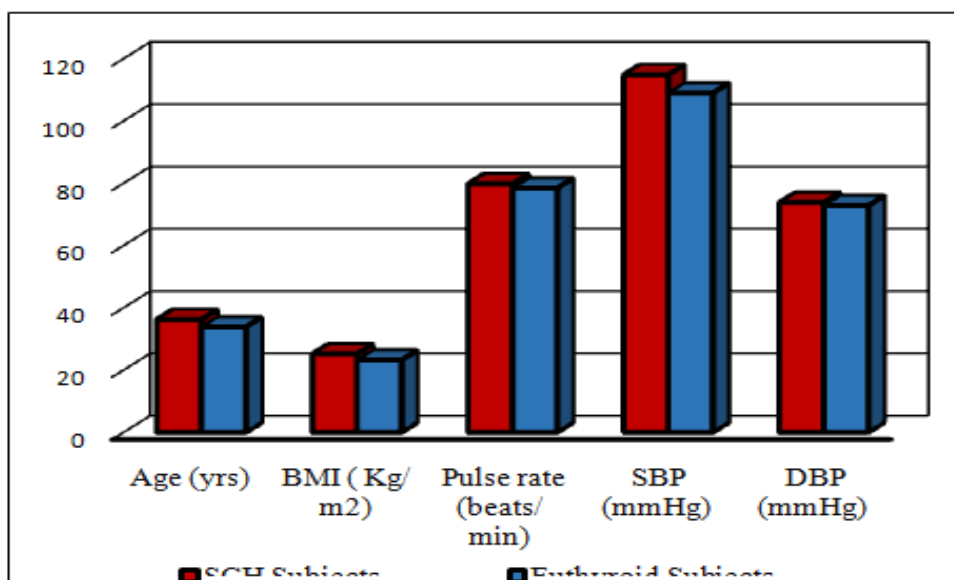
## II. Statistical Analysis

Data analysis was performed by using RMS Polyrite -D machine. Statistical analysis was done by using SPSS 17 and Microsoft Office Excel 2007 statistical software. All the data were expressed as Mean + SD. The student's t-test was used.

P-value < 0.05 was accepted as statistically significant.

### Comparison of age, anthropometric and basal cardiovascular parameters between SCH and Euthyroid subjects

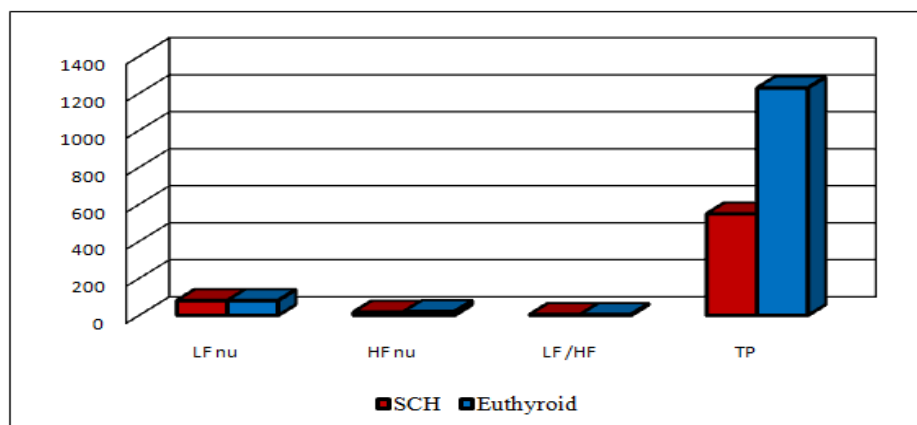
Anthropometric and basal cardiovascular parameters	SCH Subjects		Euthyroid Subjects		P Value
	Mean	SD	Mean	SD	
Age (Yrs)	36.23	8.57	33.83	7.92	0.26
BMI (Kg/ m2)	25.16	5.04	23.16	3.01	0.23
Resting pulse rate (beats/ min)	79.8	7.49	78.4	9.25	0.52
Resting SBP (mmHg)	114.8	10.88	108.93	8.73	0.02*
Resting DBP (mmHg)	73.8	5.64	72.8	4.25	0.44



Comparison of Frequency Domain parameters of HRV between SCH and Euthyroid subjects

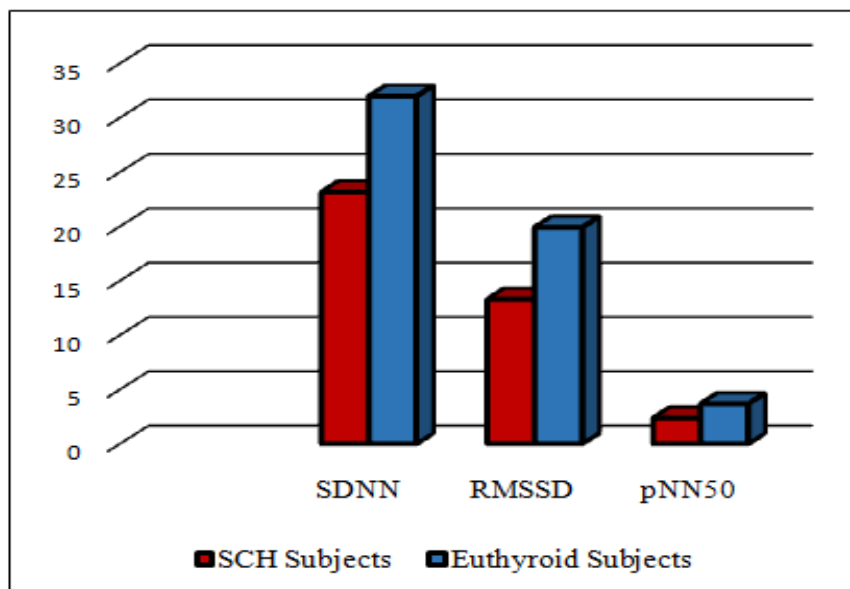
Frequency domain parameters of HRV	SCH Subjects		Euthyroid subjects		P Value
	Mean	SD	Mean	SD	
LF (nu)	79.93	8.44	79.77	9.17	0.47
HF (nu)	17.27	4.96	20.55	9.65	0.05*
LF/HF	5.37	3.71	5.31	2.72	0.47
TP	548.53	888.52	1229.30	1596.39	0.04*

Figure 2: Distribution and Comparison of Frequency Domain Parameters of HRV between Control and Study groups.



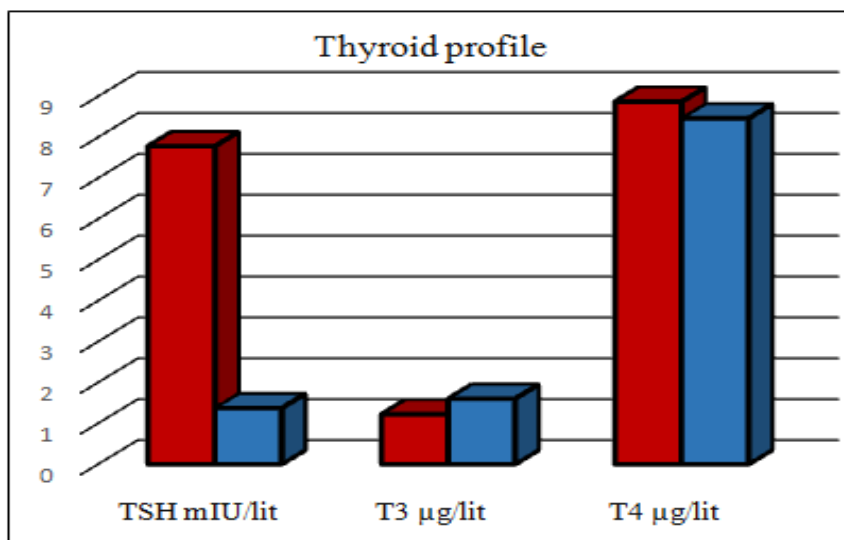
Comparison of Time Domain parameters of HRV between SCH and Euthyroid subjects

Time parameters	domain	SCH Subjects		Euthyroid Subjects		P Value
		Mean	SD	Mean	SD	
SDNN		23.15	7.32	31.96	17.41	0.01*
RMSSD		13.28	7.52	19.9	10.03	0.01*
pNN50		2.36	4.96	3.66	8.25	0.46



Comparison of Thyroid Profile parameters between SCH and Euthyroid subjects

Thyroid profile	SCH I (n=30)		EH II (n=30)		P Value
	Mean	SD	Mean	SD	
TSH mIU/lit	7.78	1.35	1.37	0.67	0.00*
T <sub>3</sub> µg/lit	1.22	0.88	1.6	0.68	0.07
T <sub>4</sub> µg/lit	8.87	2.28	8.46	1.64	0.44



### III. Discussion

The difference in pulse, SBP and DBP in SCH subjects compared to euthyroid subjects was due to symaptho-vagal imbalance. The sympathetic nervous system (SNS) and thyroid hormones regulatenumber of metabolic processes in a complementary fashion <sup>(4)</sup>. Thyroid hormones regulate the sympathetic nerve activity, and therefore, it modulates serum and tissue levels of catecholamines<sup>(5)</sup>. The hypothyroid patients have elevated plasma norepinephrine levels, to compensate for reduced adrenergic sensitivity of the receptors<sup>(6,7)</sup>. TSH level in

SCH subjects were found to be higher than euthyroid subjects. T3 and T4 levels had no significant difference which was keeping pace with definition of SCH. HRV is thought to reflect the heart's ability to adapt to changing circumstances. The normal variability in HR is due to autonomic neural regulation of the heart and the circulatory system<sup>(8)</sup>. Akselrod et al introduced power spectral analysis of heart rate fluctuations to quantitatively evaluate beat to beat cardiovascular control<sup>(9)</sup>. It consists of LF, HF, LF/HF ratio and TP. LF/HF ratio was used as an indirect index of sympathovagal imbalance<sup>(1)</sup>. Galetta *et al* had reported an increase in LF/HF frequency in heart rate variability reflecting higher sympathetic activity in subclinical hypothyroid patients<sup>(1)</sup>. Kahaly GJ et al<sup>(10)</sup> suggested Low HF value there is a reduction in vagal tone<sup>(4)</sup>. Significant reduction in TP of HRV in hypothyroid group, as TP in general indicates the vagal modulation of cardiac function<sup>(11,12)</sup>. There was reduction of RMSSD, SDNN, pNN50 in patients with SCH. Similar results were found by Matia Ahmed et al<sup>(13)</sup>. A significant decline in RMSSD and pNN50 compared to the healthy people this indicates on weakening of the parasympathetic ANS influence<sup>(14)</sup>.

#### IV. Conclusion

The increase in pulse, systolic & diastolic BP in SCH subjects compared to euthyroid subjects was suggestive of symaptho-vagal imbalance (SVI). Increase in LF nu, LF/HF and significant decrease in HF nu was suggestive of SVI with increased sympathetic tone. Significant decrease in TP was also pointing towards decreased HRV. Significant decrease in SDNN, RMSSD support SVI with increase in sympathetic tone. Increase in TSH in SCH subjects with no significant difference in T3 and T4, was keeping pace with SCH definition. SCH is associated with ANS imbalance with increased sympathetic tone, which is predisposing factor for cardiovascular risks. Hence early intervention in SCH causes prevention of cardiovascular diseases & progression to overt hypothyroidism.

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