

Hypothyroidism as an Independent Risk Factor for Cardiac Diseases: A Cross-Sectional Study

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Abstract

Background and Objectives: Hypothyroidism has significant cardiovascular manifestations. Inadequate number of studies and elusive nature of diagnosis of cardiovascular manifestations in hypothyroidism due to less prominence of symptoms and signs; attracted a great deal of investigatory endeavor. This study aims at studying the cardiovascular aftermath in hypothyroid patients by electrocardiography, lipid profile and echocardiography. The completely reversible nature of these complications, after starting treatment is well known.

Methods: 150 Subjects under the study included, out-patient and in-patient hypothyroid cases coming to Sri Siddhartha Medical College and Hospital, Tumkur. Study duration – 1st September 2012 to 31st August 2014. Patients were subjected to history, clinical examination and investigations like thyroid profile, electrocardiography, echocardiography and lipid profile. Data was analyzed using Epiinfo 7.

Results; Out of 150 cases, 97 had clinical hypothyroidism, 53 had subclinical hypothyroidism. 88.67% cases were females. 54% were in age group 21-40 yrs. Abnormal ECG in 26%, abnormal ECHO in 24%, Diastolic hypertension in 20%, Dyslipidemia in 34.67%, pericardial effusion in 14%, Ischemic heart disease in 1.33% and Anemia in 23.33% were seen in the study.

Conclusion: The hypothyroid patients present clinically with a myriad of symptoms and signs which are nonspecific. Hence a high index of suspicion is the key for the early diagnosis of hypothyroidism.

The cardiac risk factors seen in the study are in the form of diastolic hypertension, bradycardia, dyslipidemia, T wave changes in ECG, diastolic dysfunction and pericardial effusion in ECHO.

After exclusion of the other risk factors for cardiac disease; various changes seen in hypothyroid cases in this study suggest that hypothyroidism is one of the independent risk factor for cardiac disease.

As the symptoms related to hypothyroidism and cardiac disease overlap, high index of suspicion should be considered for underlying cardiac disease; and these patients should undergo complete cardiac evaluation on diagnosis of hypothyroidism; so as to prevent the catastrophic cardiac outcomes.

Early diagnosis and correction of hypothyroidism is necessary; so that adverse effects on cardiac system can be minimized.

Studies have shown that with treatment of hypothyroidism the cardiovascular risk factors improve.

Keywords: Hypothyroidism, ECG, ECHO.

I. Abbreviations

AF	Atrial fibrillation.
AV	Atrioventricular
APC	Atrial premature contraction
BMI	Body mass index
BMR	Basal metabolic rate
CAD	Coronary artery disease.
CCF	Congestive cardiac failure
CNS	Central nervous system
COPD	Chronic obstructive pulmonary disease
CVS	Cardio vascular system
ECG	Electrocardiography
ECHO	Echocardiogram
EF	Ejection fraction
ELISA	Enzyme linked immunosorbant assay
FT4	Free T4
FNAC	Fine needle aspiration cytology
GTT	Glucose tolerance test
Hb	Haemoglobin
HDL	High density lipoprotein
HOCM	Hypertrophic obstructive cardiomyopathy

IHD	Ischemic heart disease
I ¹³¹	Radioactive iodine
IVRT	Isovolumetric relaxation time
LBBB	Left bundle branch block
LDL	Low density lipoprotein
LVDD	Left ventricular diastolic dysfunction
LVEF	Left ventricular ejection fraction.
LVH	Left ventricular hypertrophy.
LVET	Left ventricle ejection time
LV	Left ventricle
MHC	Major Histocompatibility complex
mRNA	Messenger Ribonucleic acid
MPS	Mucopolysachharide
PEP	Pre ejection period
RBBB	Right bundle branch block
RBS	Random blood sugar
RIA	Radio immunoassay
RWMA	Regional wall motion abnormality
SIADH	Syndrome of inappropriate ADH production
SCH	Subclinical hypothyroidism
SD	Standard deviation
TGL	Triglyceride
TRH	Thyroid releasing hormone
TSH	Thyroid stimulating hormone
USG	Ultrasonography
VF	Ventricular fibrillation
VLDL	Very low density lipoprotein
VPC	Ventricular premature complexes
VT	Ventricular tachycardia

II. Aim And Objectives

Aim

To study cardiac manifestations in hypothyroidism.

Objectives:

1. To study the clinical profile of cardiac system in hypothyroidism.
2. To study the various ECG and echocardiographic changes in hypothyroidism.
3. To study the lipid profile in hypothyroidism.

III. Methodology

Source of data-

150 Subjects under the study included, out-patient and in-patient hypothyroid cases coming to Sri Siddhartha Medical College and Hospital, Tumkur.

Method of collection-

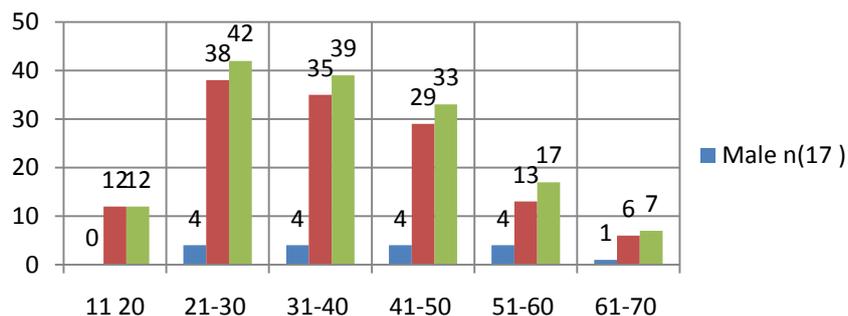
Patients with newly detected and un-controlled hypothyroidism were taken under study. Detailed history, clinical examination, cardiac system examination and investigations were done. Data was analyzed using Epiinfo 7.

Study duration –

1st September 2012 to 31st August 2014.

Inclusion criteria-

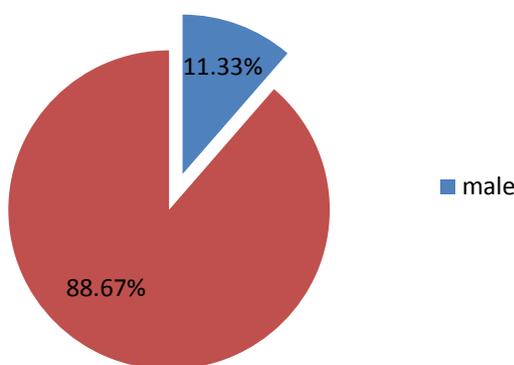
- a. Newly detected hypothyroidism.
- b. Old un-controlled hypothyroidism.



Graph 1: Age and Sex distribution

Table – 4a: Mean age and SD of the cases according to sex

Sex	Mean Age	SD
Male	43.23	11.76
Female	37.49	12.89



Graph 2: Sex distribution in Sample population

There was overall female preponderance in the study- 133 (88.67%). Males were 17 (11.67%).

Table 5: Sex distribution according to clinical and subclinical hypothyroidism

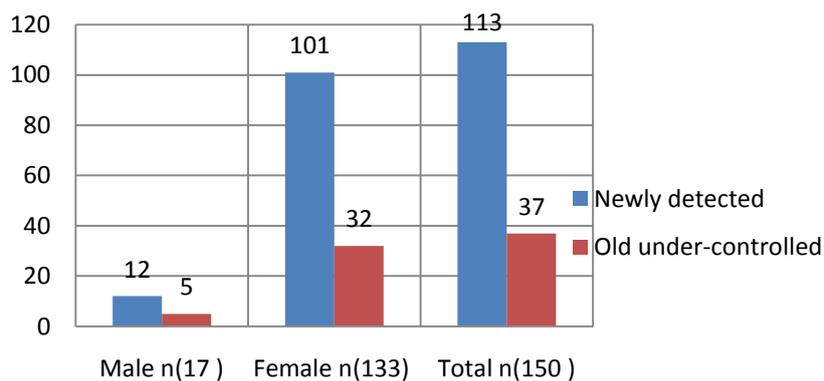
Hypothyroidism	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Clinical Hypothyroidism	15	88.24	82	61.65	97	64.67
Subclinical Hypothyroidism	2	11.76	51	38.35	53	35.33
Total	17	100	133	100	150	100

97 (64.67%) patients had clinical hypothyroidism and 53 (35.33%) had subclinical hypothyroidism. 15 (88.24%) males had clinical hypothyroidism. In females 82 (61.65%) had clinical and 51 (38.35%) had subclinical hypothyroidism.

Table 6: Sex distribution in hypothyroid cases

Hypothyroid	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Newly detected	12	70.6	101	75.93	113	75.33
Old under-controlled	5	29.4	32	24.07	37	24.67
Total	17	100	133	100	150	100

113 (75.33%) were newly detected hypothyroid cases. 37 cases (24.67%) were known hypothyroid under controlled.

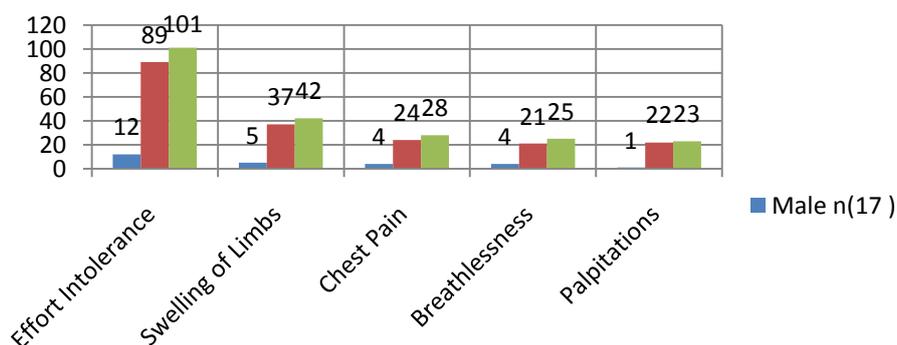


Graph 3: Sex distribution in hypothyroid cases

Symptoms at presentation:

Table 7: Cardiovascular symptoms at presentation

Cardiovascular Symptoms	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Effort Intolerance	12	70.6	89	66.91	101	67.33
Swelling of Limbs	5	29.41	37	27.82	42	28
Chest Pain	4	23.52	24	18.04	28	18.67
Breathlessness	4	23.52	21	15.8	25	16.67
Palpitations	1	5.9	22	16.54	23	15.33

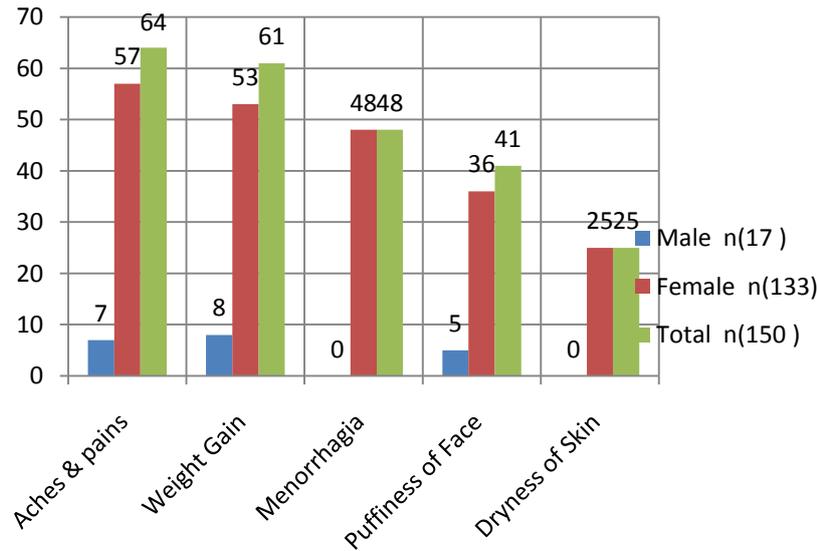


Graph 4: Cardiovascular symptoms at presentation

Most of the patients presented with multiple symptoms. The most common cardiac symptom was effort intolerance 101 (67.33%) in total, other symptoms were swelling of limbs 42 (28%), chest pain 28 (18.67%), breathlessness 25 (16.67%) and palpitations 23 (15.33%).

Table 8: Symptoms related to hypothyroidism

Hypothyroid Symptoms	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Aches & pains	7	41.18	57	42.86	64	42.67
Weight Gain	8	47.06	53	39.85	61	40.67
Menorrhagia	0	0	48	36.1	48	32
Puffiness of Face	5	29.41	36	27.06	41	27.33
Dryness of Skin	0	0	25	18.8	25	16.67



Graph 5: Symptoms related to hypothyroidism

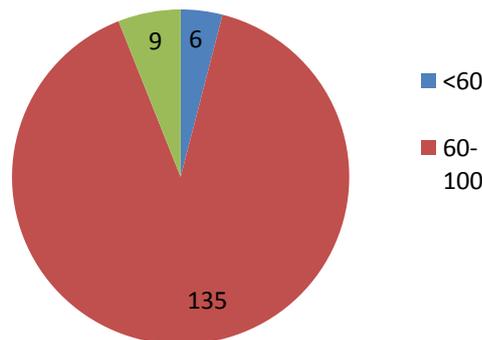
Most patients presented with multiple symptoms. Most common symptoms were aches and pains 64 (42.67%), weight gain 61 (40.67%), Menorrhagia 48 (32%), puffiness of face 41 (27.33%) and dryness of skin in 25 (16.67%). Subclinical hypothyroid patients presented with very few symptoms.

General Physical examination:

Table 9: Pulse rate in the study population

Pulse rate Per min	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
<60	2	11.76	4	3	6	4
60-100	13	76.48	122	91.73	135	90
>100	2	11.76	7	5.27	9	6

Pulse rate beats/min



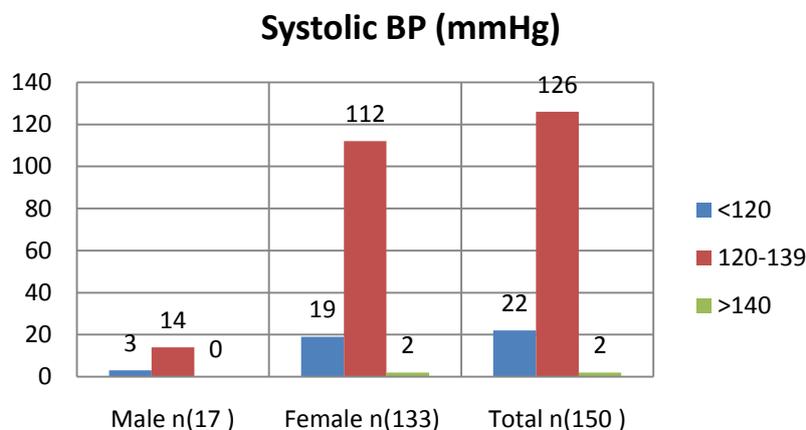
Graph 6: Pulse rate in the study population

Bradycardia (<60 beats/min) was seen in only 6 (4%) cases. Tachycardia (>100 beats/min) was seen in 9 (6%). Pulse rate was normal in 135 (90%). Mean pulse rate is 81.98. SD is 12.12 Mode is 86. Median is 83.

Table 10: Systolic blood pressure in the study population

Systolic BP mmHg	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
<120	3	17.65	19	14.29	22	14.67

120-139	14	82.35	112	84.21	126	84
>140	0	0	2	1.5	2	1.33

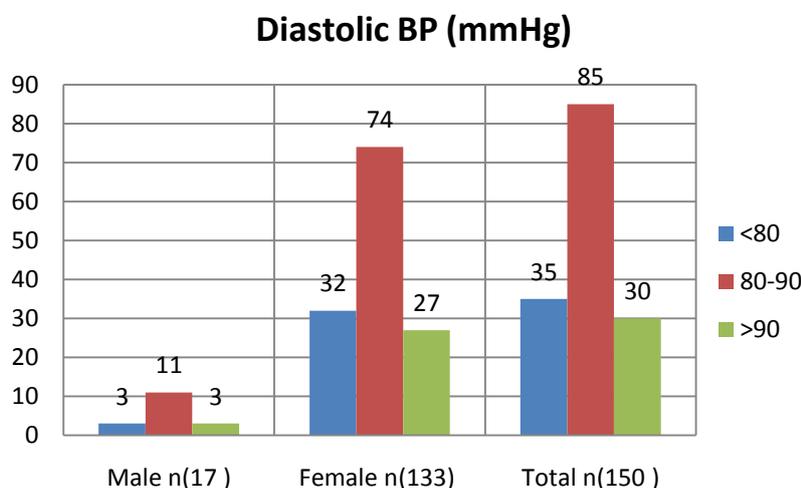


Graph 7: Systolic blood pressure in the study population

Normal systolic blood pressure in 22 (14.67%), pre hypertension in 126 (84%) cases and stage 1 hypertension in 2 (1.33%) cases on presentation according to JNC 7 criteria.³⁵

Table 11: Diastolic blood pressure in the study population

Diastolic BP mmHg	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
<80	3	17.65	32	24.06	35	23.33
80-90	11	64.7	74	55.64	85	56.67
>90	3	17.65	27	20.3	30	20

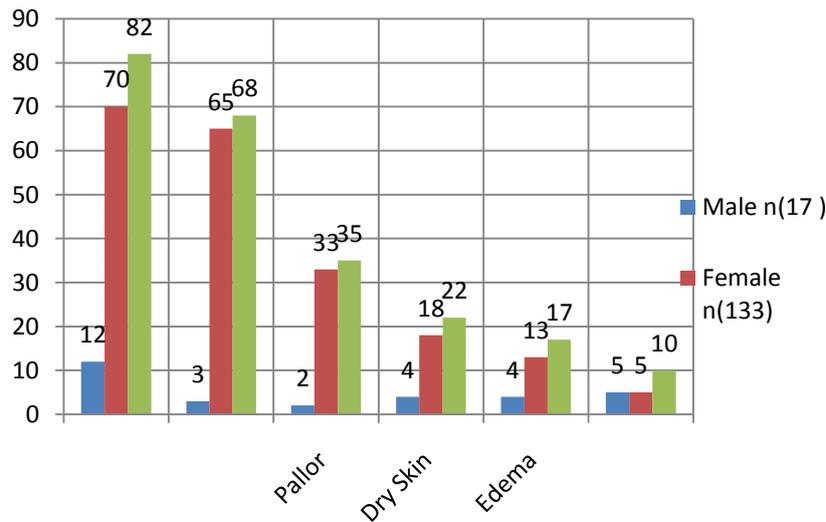


Graph 8: Diastolic blood pressure in the study population

Diastolic blood pressure >90mmHg was found in 30 (20%) of patients.

Table 12: General signs related to hypothyroidism in study population

Signs	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
BMI >25 Kg/m ²	12	70.59	70	52.63	82	54.67
Thyromegaly	3	17.65	65	48.87	68	45.34
Pallor	2	11.76	33	24.81	35	23.33
Dry Skin	4	23.53	18	13.53	22	14.67
Edema	4	23.53	13	9.77	17	11.34
Delayed ankle jerk	5	29.41	5	3.76	10	6.67



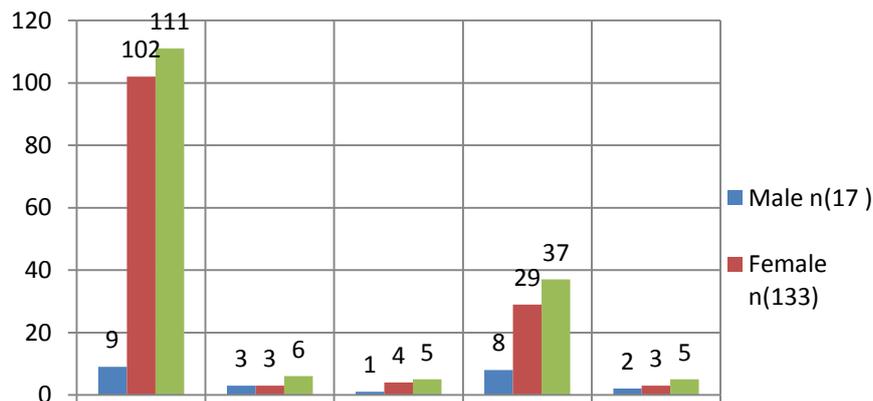
Graph 9: General signs related to hypothyroidism in study population

The most common sign was high body mass index (BMI) >25 kg/m² in 82 (54.67%). Thyromegaly was seen in 68 (45.34%) cases. Pallor in 35 (23.33%), dry skin in 22 (14.67%), edema in 17 (11.34%) and delayed ankle jerk in 10 (6.67%).

Electrocardiographic changes:

Table 13: Electrocardiographic changes in the study population

ECG changes	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Normal	9	52.94	102	76.7	111	74
Bradycardia	3	17.65	3	2.25	6	4
Low voltage complex	1	5.89	4	3	5	3.34
T wave (Flat / Inverted)	8	47.06	29	21.8	37	24.67
ST segment changes	2	11.76	3	2.25	5	3.34



Graph 10: Electrocardiographic changes in the study population

Electrocardiography was normal in 111 (74%) cases and abnormal in 39 (26%) cases. Most had multiple changes like bradycardia in 6 (4%), low voltage complex in 5 (3.34%), T wave changes in the form of flattening or inversion in 37 (24.67%) and ST segment changes in 5 (3.34%).

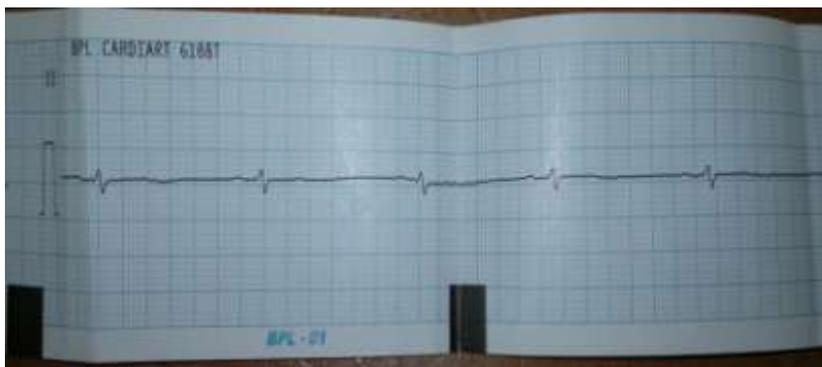


Figure 3: ECG showing Bradycardia

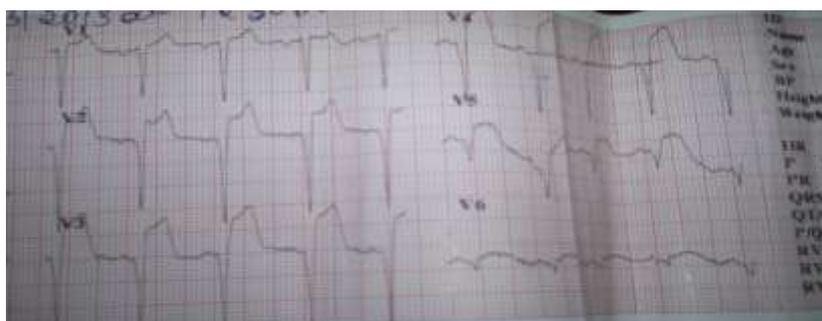


Figure 4: ECG showing anterior wall myocardial infarction in a patient

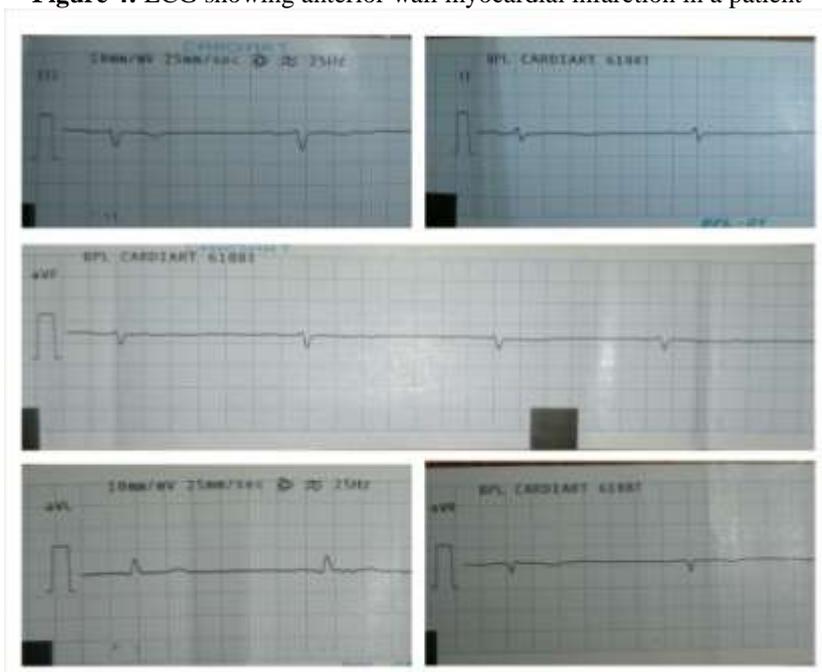
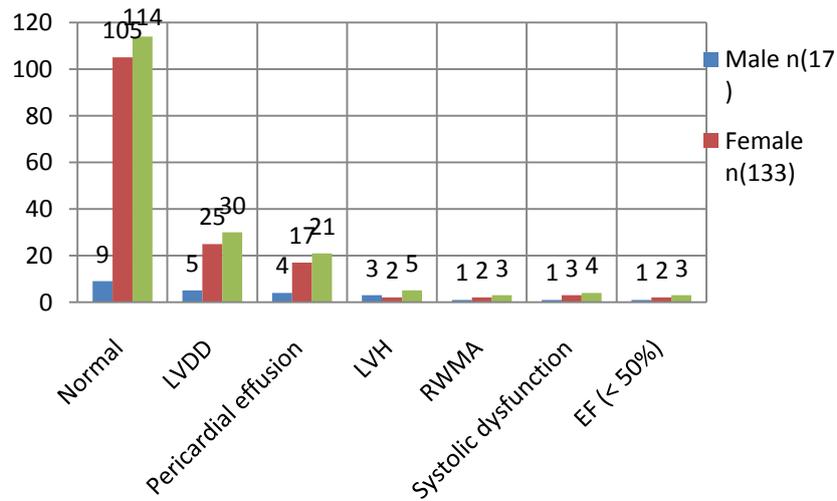


Figure 5: ECG showing low voltage complex in a patient

Echocardiographic changes:

Table 14: Echocardiographic changes in the study population

ECHO changes	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
Normal	9	52.94	105	78.94	114	76
LVDD	5	29.41	25	18.8	30	20
Pericardial effusion	4	23.53	17	12.79	21	14
LVH	3	17.65	2	1.5	5	3.34
RWMA	1	5.89	2	1.5	3	2
Systolic dysfunction	1	5.89	3	2.25	4	2.67
EF (< 50%)	1	5.89	2	1.5	3	2



Graph 11: Echocardiographic changes in the study population

Echocardiography was normal in 114 (76%) of cases and abnormal in 36 (24%) of cases; with most common finding being left ventricular diastolic dysfunction (LVDD) in 30 (20%), others are pericardial effusion in 21 (14%), left ventricular hypertrophy (LVH) in 5 (3.34%), regional wall motion abnormalities (RWMA) in 3 (2%) and systolic dysfunction in 4 (2.67%). EF<50% in 3 (2%).



Figure 6: ECHO showing pericardial effusion



Figure 7: ECHO showing Regional wall motion abnormality



Figure 8: Chest Xray of a patient with hypothyroidism showing “money bag” appearance of cardia due to pericardial effusion

Lipid profile:

Table 15: Lipid profile changes in the study

Lipid Profile (mg/dl)		Male		Female		Total	
		n(17)	%	n(133)	%	n(150)	%
Serum Cholesterol	>200	9	53	43	32.23	52	34.67
LDL	>130	8	47.05	37	27.82	45	30
TGL	>200	6	35.3	7	5.27	13	10.67
HDL	<40	3	17.65	14	10.52	17	11.34

Dyslipidemia was seen in 52 (34.67%) cases. Most patients had multiple abnormalities. Commonest being hypercholesterolemia in 52 (4.67%); others were high levels of low density lipoprotein (LDL) in 45 (30%) and hypertriglyceridemia in 13 (10.67%).

Overall changes seen during study:

Table 16a: Abnormalities seen during study according to sex

Changes	Male		Female		Total	
	n(17)	%	n(133)	%	n(150)	%
ECG Changes	8	47.06	31	23.31	39	26
ECHO Changes	8	47.06	28	21.05	36	24
Dyslipidemia	10	58.82	42	31.58	52	34.67
Diastolic Hypertension	3	17.64	27	20.30	30	20
IHD	1	5.9	1	0.75	2	1.33
CCF	1	5.9	4	3.01	5	3.34
Anemia	2	11.8	33	24.81	35	23.33

In this study; electrocardiographic changes were seen in 39 (26%), echocardiographic changes in 36 (24%), dyslipidemia in 52 (34.67%), diastolic hypertension in 30 (20%), ischemic heart disease in 2 (1.33%), congestive cardiac failure in 5 (3.34%) and anemia in 35 (23.33%).

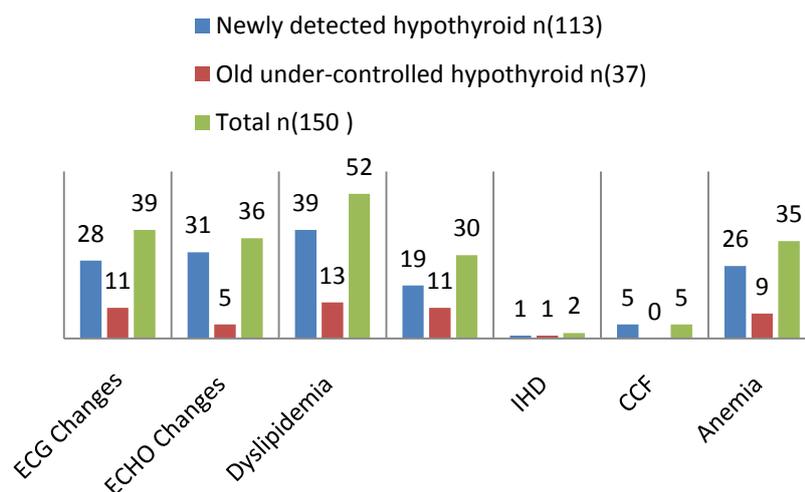
Table 16b: Abnormalities seen during study according to Serum TSH level

Serum TSH μ IU/L	Sr TSH >10 μ IU/L		Sr TSH 6-10 μ IU/L		Total	
	n(97)	%	n(52)	%	n(150)	%
ECG Changes	30	30.92	9	17.30	39	26
ECHO Changes	29	29.9	7	13.46	36	24
Dyslipidemia	37	38.14	15	28.84	52	34.67
Diastolic Hypertension	19	19.6	11	21.15	30	20
IHD	2	2.06	0	0	2	1.33
CCF	4	4.12	1	1.92	5	3.34
Anemia	26	26.80	9	17.30	35	23.33

The abnormalities seen in the study in relation to serum TSH values >10 μ IU/L (clinical hypothyroidism) were more than that for serum TSH 6-10 μ IU/L (subclinical hypothyroidism) except diastolic hypertension which was 21.15% in subclinical hypothyroid patients compared to 19.6% in clinical hypothyroid patients.

Table 16c: Abnormalities seen in hypothyroid cases during study

Changes	Newly detected hypothyroid		Old under-controlled hypothyroid		Total	
	n(113)	%	n(37)	%	n(150)	%
ECG Changes	28	24.78	11	29.73	39	26
ECHO Changes	31	27.43	5	13.51	36	24
Dyslipidemia	39	34.51	13	35.13	52	34.67
Diastolic Hypertension	19	16.81	11	29.73	30	20
IHD	1	0.9	1	2.7	2	1.33
CCF	5	4.42	0	0	5	3.34
Anemia	26	23	9	24.32	35	23.33



Graph 12: Abnormalities seen in hypothyroid cases during study

As seen from the table the changes seen in the study were more in old under-controlled hypothyroid patients compared to the newly detected hypothyroid cases.

V. Discussion

The present study was conducted at Shri Siddhartha Medical College and Hospital, Tumkur. Total numbers of patients were 150. Study period being Sept 2012 to 31st Aug 2014 (24 months).

Age and sex distribution-

Patients were in the age group of 18-70 yrs. 54% were in age group of 21-40 yrs. Out of 150, 133 were females and 17 were males.

Table 17: Comparison of percentage of females

Present Study (n=150)	Minshed AJ et al ³⁶ 2010 (n=36)	Shah SK et al ³⁷ 2013 (n=30)
88.67%	86.1%	73.33%

There was a female preponderance seen in this study- 88.67% compared to other study 86.1% Minshed AJ et al³⁶ which was almost same.

Table -18: Comparative study of Symptomatology of hypothyroidism

Symptom	Present Study (n=150) %	Watanakunakorn 1965 ³⁸ %	Shah SK et al ³⁷ 2013 (n=30) %
Aches and pains	42.67	15.25	-
Weight gain	40.67	47	76.66
Menorrhagia	32	-	59
Puffiness of face	27.33	67	-

Weight gain was 40.67% in present study and 47% in Watanakunakorn 1965³⁸.

Table -19: Comparative study of cardiovascular symptoms in hypothyroidism

Symptom	Present Study (n=150) %	Watanakunakorn 1965 ³⁸ %	Minshed AJ et al ³⁶ 2010 (n=36) %
Effort intolerance	67.34	69.75	88.9
Chest pain	18.67	8.25	-
Breathlessness	16.67	12.5	75
Swelling of limbs	28	-	11.1

Effort intolerance the most common symptom was 67.34% in present study and 69.75% in Watanakunakorn 1965³⁸.

Table -20: Comparative study of signs in hypothyroidism

SIGN	Present Study (n=150) %	Shah SK et al ³⁷ 2013 (n=30) %	Minshed AJ et al ³⁶ 2010 (n=36) %
Bradycardia	4	40	47.2
Diastolic HTN	20	23.33	19.5
BMI > 25 Kg/m ²	54.67	76.67	-
Thyromegaly	45.34	10	-
Edema	11.34	20	11.1
Pallor	23.33	26.67	-

Diastolic hypertension was 20% in present study and 19.5% in Minshed AJ et al³⁶. Edema was 11.34% in present study and 11.1% in Minshed AJ et al³⁶.

Table -21: Comparative study of ECG changes

Changes	Present Study (n=150) %	Shah SK et al ³⁷ 2013 (n=30) %	Minshed AJ et al ³⁶ 2010 (n=36) %
Bradycardia	4	40	47.2
Low voltage complex	3.34	33.3	33.3
T wave changes	24.67	-	27.8
ST segment changes	3.34	26.6	-

T wave changes were most common 24.67% in the present study compared to 27.8% in Minshed AJ et al³⁶.

Table -22: Comparative study of ECHO changes

Changes	Present Study (n=150) %	Shah SK et al ³⁷ 2013 (n=30) %	Gupta M.M. et al ³⁹ 2000 %
LVDD	20	26.67	-
Pericardial effusion	14	26.67	15
LVH	3.34	-	-
RWMA	2	-	-
Systolic dysfunction	2.67	6.67	-

Pericardial effusion was 14% in present study and 15% in Gupta MM et al³⁹.

Lipid profile

Dyslipidemia was found in 34.67%. Most common abnormalities were hypercholesterolemia in 34.67% and high LDL in 10.67%. Similar changes were in study done in NRI General Hospital, Guntur¹². Incidence of ischemic heart disease was 1.33% in present study compared to 11.75% in Watanakunakorn 1965.³⁸

VI. Summary

This study was conducted on 150 hypothyroid patients with an objective to study cardiovascular changes. Study period being Sept 2012 to 31st Aug 2014.

- Total of 113 cases were newly detected hypothyroid cases and 37 were old uncontrolled hypothyroid cases.
- Patients were in the age group of 18-70 yrs. 54% were in age group of 21-40 yrs.
- Out of 150, 133 (88.67%) were females and 17(11.33%) were males.
- 64.67% patient had clinical hypothyroidism and 35.33% had subclinical hypothyroidism in the study.
- The most common cardiac symptom was effort intolerance 67.33%, others were swelling of limbs 28%, chest pain 18.67%, breathlessness in 16.67% and palpitations in 15.33%.
- Other symptoms were aches and pains 42.67%, weight gain 40.67% and Menorrhagia 32%.
- Subclinical hypothyroid patients presented with very few symptoms.

- Diastolic blood pressure >90mmHg was found in 20% of patients. Bradycardia (<60 beats/min) was seen in only 4% cases.
- BMI >25 kg/m² in 54.67%, Thyromegaly was seen in 45.34% cases, pallor in 23.33%, dry skin in 14.67%, edema in 11.34% and delayed ankle jerk in 6.67%.
- Electrocardiography was abnormal in 26% cases. Most common finding being T wave changes in the form of flattening or inversion in 24.67%, then bradycardia in 4%, low voltage complex in 3.34% and ST segment changes in 3.34%.
- Echocardiography was abnormal in 24% of cases; with most common finding being left ventricular diastolic dysfunction (LVDD) in 20%, others are pericardial effusion in 14%, left ventricular hypertrophy (LVH) in 3.34%, regional wall motion abnormalities (RWMA) in 2% and systolic dysfunction in 2.67%. EF <50% in 2%.
- Dyslipidemia was seen in 34.67% cases. Most common being hypercholesterolemia in 34.67%; others were high levels of low density lipoprotein (LDL) in 30% and hypertriglyceridemia in 10.67%.
- In this study; Ischemic heart disease was found in 1.33%, congestive cardiac failure in 3.34% and anemia in 23.33%.
- Out of 37 known under-controlled hypothyroid cases; electrocardiographic changes were seen in 11 cases, echocardiographic changes in 5 cases, dyslipidemia in 13 cases, diastolic hypertension in 11 cases, ischemic heart disease in 1 case and anemia in 9 cases.

VII. Conclusion

- The hypothyroid patients present clinically with a myriad of symptoms and signs which are nonspecific. Hence a high index of suspicion is the key for the early diagnosis of hypothyroidism.
- Most of the symptoms like effort intolerance, lower limb swelling and breathlessness which hypothyroid patients presents with are similar to that of cardiac failure symptoms, hence the cardiac disease is masked and unrecognised.
- The cardiac risk factors seen in the study are in the form of diastolic hypertension, bradycardia, T wave changes in ECG, diastolic dysfunction and pericardial effusion in ECHO.
- Dyslipidemia seen in the study is also a risk factor for ischemic heart disease.
- After exclusion of the other risk factors for cardiac disease; various changes seen in hypothyroid cases in this study suggest that hypothyroidism is one of the independent risk factor for cardiac disease.
- As the symptoms related to hypothyroidism and cardiac disease overlap, high index of suspicion should be considered for underlying cardiac disease; and these patients should undergo complete cardiac evaluation on diagnosis of hypothyroidism; so as to prevent the catastrophic cardiac outcomes.
- Early diagnosis and correction of hypothyroidism is necessary; so that adverse effects on cardiac system can be minimized.
- Studies have shown that with treatment of hypothyroidism the cardiovascular risk factors improve.

Bibliography

- [1]. Guyton AC and Hall JE. Thyroid Metabolic Hormones. Chapter 76. In: Guyton AC and Hall JE, editors. Text book of Medical Physiology. 11th ed. Pennsylvania: Saunders Elsevier; 2006. p. 931-43.
- [2]. Brent GA, Larsen PR and Davies TF. Hypothyroidism and Thyroiditis. Chapter 12. In: Kronenberg HM, Melmed S, Polonsky AS and Larsen PR. Williams Text book of Endocrinology. 11th ed. Philadelphia: Saunders Elsevier; 2007. p. 377-387.
- [3]. Jameson LJ, Weetman AP. Disorders of thyroid gland. Chapter 341. In: Longo DL, Fauci AS, Kasper DL, Hauser SL, Jameson JL and Loscalzo J. Harrison's principles of internal medicine. 18th edition. USA: The McGraw Hill Companies; 2012. p. 2911-22.
- [4]. Menon UV, Sundaram KR, Unnikrishnan AG, Jayakumar RV, Nair V, Kumar H. High prevalence of undetected thyroid disorders in an iodine sufficient adult south Indian population. J Indian Med Assoc. 2009; 107: 72-7.
- [5]. Klein I and Danzi S. Thyroid Disease and the Heart. Circulation. 2007; 116: 1725-35.
- [6]. Boelaert K, Franklyn JA. Thyroid hormone in health and disease. J Endocrinol 2005; 187(1): 1-15.
- [7]. Reginad H, Maurice FS. Hypothyroidism: Clinical features and complications. Clinics in Endocrinology and metabolism. 1979; 8(1): 29-38.
- [8]. Caroline GP Roberts, Paul W. Ladenson. Hypothyroidism. Lancet. 2004; 363: 793-803.
- [9]. Kerber E, Richard, Barry S. Echocardiographic Evaluation of Pericardial Effusion in Myxoedema. Circulation. 1975; 52: 823-827.
- [10]. Park YJ, Lee YJ, Choi SI, Chun EJ, Jang HC and Chang HJ. Impact of subclinical hypothyroidism on the coronary artery disease in apparently healthy subjects. European Journal of Endocrinology. 2011; 165: 115-121.
- [11]. Razvi S, Weaver JU, Vanderpump MP, and Pearce SH. The Incidence of Ischemic Heart Disease and Mortality in People with Subclinical Hypothyroidism: Reanalysis of the Whickham Survey Cohort. J Clinical Endocrinology Metab. 2010; 95: 1734-1740.
- [12]. Shekhar R, Chowdary N V S, Das M C, Desai V and Siva P. Prevalence of subclinical hypothyroidism in coastal Andhra Pradesh. Biomedical Research 2011; 22 (4): 471-474.
- [13]. Sharma R, Sharma TK, Kaushik GG, Sharma S, Vardey SK and Sinha M. Subclinical hypothyroidism and its association with cardiovascular risk factors. Clin Lab. 2011; 57(9-10):719-24.
- [14]. Berlcovitv BK, Collins P. Neck-Thyroid gland. Chapter 31. In: Drake RL, Vogl W and Mitchell AW. Gray's Anatomy. 39th Edition. Philadelphia: Churchill Livingstone; 2005: p. 560-564.
- [15]. Serafino F, Emiliano A, Palmieri, et al. Effects of Thyroid Hormone on the cardio-vascular system. Recent progress in Hormone Research. 2004; 59: 31-50.

- [16]. Klein I, Ojamaa K. Thyroid Hormone and the Cardiovascular System. *N Engl J. Med.* 2001; 334(7): 501-508.
- [17]. Klein I. Endocrine disorders and cardiovascular disease. Chapter 86. In: Braunwald E, et al. *The Heart Disease - A textbook of Cardiovascular Medicine.* 9th Edition. Philadelphia: WB Saunders Company; 2012: 1833-38.
- [18]. Smith OJ, Evans LM, et al. Increased Central Arterial Stiffness in Hypothyroidism. *JCEM.* 2002; 87(10): 4662-66.
- [19]. Danzi S, Klein I. Thyroid hormone and the cardiovascular system. *Minerva Endocrinol.* 2004; 29: 139-50.
- [20]. Nikoo MH. Cardiovascular manifestations hypothyroidism. *SEMJ.* 2001; 2(1):1-14.
- [21]. Fletcher AK, Weetman AP. Hypertension and Hypothyroidism. *J Hum Hypertension.* 1998; 12: 79-82.
- [22]. Strachan MW, Walker BR. Endocrine disease. Chapter 20. In: Boon NA, et al. *Davidson's Principles and practice of Medicine.* 20th edition. Philadelphia: Churchill Livingstone Elsevier; 2002: 750-52.
- [23]. Valente M, Desanto C, De Mortine Rosenroll, Dimeos. The direct effect of the thyroid hormone on cardiac chronotropism. *Arch Int Physiol Biochem.* 1988; 97: 408-31.
- [24]. Arem R, Rockey R, Kiefe C, Escalante DA, Rodriguez A. Cardiac systolic and diastolic function at rest and exercise in sub clinical hypothyroidism: effects of thyroid hormone therapy. *Thyroid.* 1996; 6: 397-402.
- [25]. Bonow RO, Udelson JE. Left ventricular diastolic dysfunction as a cause of congestive heart failure. *Ann Intern Med.* 1992; 117: 502-10.
- [26]. Cohen MV, Scalman IC, Sperillo A, Surks ML. Effect of thyroid hormone on left ventricular function in patients treated for thyrotoxicosis. *Am j Cardiol.* 1981; 48: 33-38.
- [27]. Cuocolo A, Sax FL, Brush JE, Maron BJ, Bacharach SL, Bonow RO. Left ventricular hypertrophy and impaired diastolic filling in essential hypertension. *Circulation.* 1990; 81: 978-86.
- [28]. Sichel DB, Chilab HL, Lautensack Belsler N, Morgan HE. Faster protein and ribosome synthesis in thyroxine induced hypertrophy of rat heart. *Am J of Physiol.* 1985; 285: C309-319.
- [29]. Rohrer D, Dillmann WH. Thyroid hormone markedly increases the mRNA coding for sarcoplasmic reticulum Ca⁺⁺ ATPase in the rat heart. *J Biochem.* 1998; 213: 6941-6944.
- [30]. Duntas LH. Thyroid disease and lipids. *Thyroid.* 2002; 12(4): 287-93.
- [31]. Thompson GR, Soutar AK, Spengel FA, Jadhav A, Gavigan SJ, Myant NB. Defects of receptor-mediated low-density lipoprotein catabolism in homozygous familial hypercholesterolemia and hypothyroidism in vivo. *Proc Natl Acad Sci U S A.* 1981; 78: 2591–2595.
- [32]. Rush J, Danzi S, Klein I. Role of thyroid disease in the development of statin-induced myopathy. *The Endocrinologist.* 2006; 16: 279 –285.
- [33]. Mc Dermott MT. Serum TSH testing is necessary for primary hypothyroidism. *J Postgrad Med.* 2004; 50: 11.
- [34]. Shashank R Joshi. Hypothyroidism. *The Association of Physicians of India Medicine update.* 2005; 63(15): 307-313.
- [35]. Chobanian AV, Bakris GL, Black HR, et al. The seventh Report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure: the JNC 7 report. *JAMA.* 2003; 289: 2560-72.
- [36]. Minshed AJ, Fartoosi AI, Adil S, et al. Cardiovascular Manifestations of Primary Hypothyroidism. *The iraqi postgraduate medical journal.* 2010; 2: 113-119.
- [37]. Shah SK, Kilari M, Shah NK. Cross sectional study of cardiovascular manifestations of hypothyroidism. *Journal of Evolution of Medical and Dental Sciences.* 2013; 2(27): 5021-29.
- [38]. Watanakunakorn C, Robert EH, Titus CE. Myxoedema. *Arch Intern Med* 1965; 116: 183-89.
- [39]. Gupta MM, Doomra M, et al. Heart in hypothyroidism: an Echocardiographic study. *JAPI.* 2001; 49: 141.