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RESEARCH ARTICLE

CROSS SECTIONAL STUDY OF CARDIOVASCULAR MANIFESTATIONS OF HYPOTHYROIDISM

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Abstract

Hypothyroidism is a silent disease prevailing in the population. Careful observation and identification of patients is necessary as it is manifested lately. There are very few researches pertaining to cardiac manifestations of hypothyroidism. This study was conducted in order to identify the cardiac manifestations of hypothyroidism at a very early stage like detection itself.

Introduction: The number of persons in India who have metabolic and endocrine problems is close to 108 million. The most common on esarethyroid problems and diabetes. Women seem to experience thyroid disorders the most frequently.[1,2] Studies on people with goitre revealed a 5.4% overall frequency of hypothyroidism.[3] Both overt and subclinical forms of hypothyroidism may present with symptoms. When serum free thyroxine is below the normal limit and the serum thyroid stimulating hormone (TSH) concentration is increased, this condition is referred to as overt hypothyroidism.

Background 1656: The term 'Thyroid Gland' is taken from Greek Word "thyreoeides" means Shield shaped is coined by Thomas Wharton in his book Adenographica.[11]

Materials and Methods: Source of Data: 50 new hypothyroidism cases attending to Sri Aurobindo Medical College & PG Institute, Hospital- Indore is included in the study.

Sample Size: 50 new hypothyroidism cases

Study duration: from January 2022 to December 2023, 2 years

Study design: A Cross sectional study was conducted among 50 new cases of hypothyroidism. cardiac manifestations by ECG and ECHO were studied in the patients. Detailed history was taken with help of questionnaire and investigations were done.

Result: In our study subjects most of them belong to 31 to 40 years age group. The mean age was38.30+10.37 years. There was an overall female preponderance among all age Groups with mean age of 36.75+9.24 years. The female population were about 80% of the population. Conclusion In this study consisting of 50 new hypothyroid patient's bradycardia was commonest finding followed by low voltage complexes, STT changes observed in ECG. Pericardial effusion and Diastolic dysfunction are the commonest abnormal findings in ECHO.

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Introduction:-

The number of persons in India who have metabolic and endocrine problems is close to 108 million. The most common on esarethyroid problems and diabetes. Women seem to experience thyroid disorders the most frequently.[1,2] Studies on people with goitre revealed a 5.4% overall frequency of hypothyroidism.[3] Both overt and subclinical forms of hypothyroidism may present with symptoms. When serum free thyroxine is below the normal limit and the serum thyroid stimulating hormone (TSH) concentration is increased, this condition is referred to as overt hypothyroidism.

When serum free thyroxine (T4) is within the normal limits and thyroid stimulating hormone (TSH) is above the reference range's upper limit, it is said to be subclinically hypothyroid. About 2-5% of cases of overt hypothyroidism progress each year.[4]Most bodily tissues are directly impacted by thyroid hormones. Because of a disturbed metabolism, it leads to multi-organ dysfunction. Functional systolic/diastolic dysfunction, coronary artery diseases and overt failure are all examples of cardiac dysfunction. This is because of the illness's immediate impact. In addition to hypercholesterolemia, low- density lipoprotein and apolipoprotein B levels rise noticeably in hypothyroidism. This results from a decreased fractional clearance of low-density lipoproteins by fewer liver receptors for low-density lipoproteins.[5]

A lack of thyroid hormones causes the clinical syndrome6known as hypothyroidism, which in turn causes a widespread slowdown of metabolic activities. In terms of prevalence, hypothyroidism affects 2% of adult women and 0.1-0.2% of adult men. Almost all of the body's tissues are directly impacted by thyroid hormones at the cellular level. Because of a disturbed metabolism, it leads to multi-organ dysfunction.

Significant and repeatable findings clinically connected to thyroid dysfunction are cardiovascular complications[6]. Greater cardiovascular mortality and morbidity are linked to hypothyroidism. Functional systolic/diastolic dysfunction, coronary artery disease and overt failure are all examples of dysfunction.

The cardiovascular system is affected by hypothyroidism's most significant side effects. In such untreated hypothyroid patients, the morbidity and death rates are substantial. Systolic dysfunction, diastolic dysfunction, coronary artery disease and heart failure, are all possible.[7]

Hypothyroidism increases a person's chance of atrial fibrillation as well as a the ro sclerosis, which are both cardiovascular issues.[8] From early embryonic stages, the thyroid, heart, and circulatory system are inter connected. The thyroid hormone influences the blood vessels, the blood, and the heart. This complies with the flow law's definition.[9] Cardiac output is influenced indirectly by the tissue's metabolic requirements.

Vasoconstriction and dilatation of the arterioles of periphery, blood volume, and venous system capacity are all modulator so fit. As was previously said, hypothyroidism is known to affect all of the body's tissues' metabolic processes. Because of which, when metabolism slows down in hypothyroidism, it indirectly starts to affect cardiac output, gradually damaging the cardiovascular system.[10] Need for the study: Only a small number of researches have been conducted in our nation to evaluate the cardiovascular parameters in hypothyroid patients. Cardiovascular problems linked to hypothyroidism have drawn a lot of research attention.

Background

1656 - The term ‘Thyroid Gland’ is taken from Greek Word “thyreoeides” means Shield shaped is coined by Thomas Wharton in his book Adenographica.[11]

Embryology

The first formed endocrine gland the thyroid gland in fetus. The development of thyroid gland in the thyroglossal duct, in particular the median bud of the pharynx. It is easily identified by its position infront of the laryngeal cartilages and thyroid bone and by the presence of two distinct parietal lobes with a single median isthmus.[12]

Gross Anatomy
The thyroid gland is located in the lower neck, at the level of fifth cervical to first thoracic vertebrae, and is very vascular. It typically weighs 25gms, however this can change. Females have a somewhat larger thyroid gland. About 75%of persons have an isthmus-derived pyramidal lobe.

Arterial blood supply
Arteries named superior thyroid and inferior thyroid arteries which are two in number provide the thyroid with the majority of its blood supply. The thyroid receives approximately 4 to 6 ml per gm/min of blood. Thyroideaima arteries with origins in the internal mammary artery, aortic arch, or innominate artery are present in 12% of the population.

Venous Drainage
The superior thyroid veins located at the superior poles drain to the common facial veins or internal jugular, the middle thyroid veins drain to the internal jugular, and the inferior thyroid veins in to the brachiocephalic veins as part of the thyroid's venous plexus, which drains blood.

Lymphatic Drainage
The gland contains a vast lymphatic network. The lymph from the thyroid gland drains into lymphnodes located on the anterior surface of the trachea, nodes above the is thmus, and paratracheal nodes close to the recurrent laryngeal nerve on the isthmus. Lymph travels from these nodes to the media stinal group of nodes and cervical lymph chains as well as.

Metabolism of Thyroid Hormones
The enzymes5'- deiodinase and 5-deiodinase convert 45% and 33% of circulating T4 and T3 respectively. This process produces 95% of the RT3 circulating and 87% of the T3 circulating; the remaining 20% released from the thyroid directly. The liver, kidneys, and other organs deiodinate T4 and T3.T4 and T3 are combined inside liver to create sulphates and glucuronides, which travel through the bile to the intestine.

Functions of the thyroid hormones in the tissues
Thyroid hormones mostly boost metabolic activity throughout the majority of human tissues, with the exception of the brain, retina, testicles, spleen, uterus, anterior pituitary and lymphnodes. The basal metabolic rate can rise by up to 60%to 100% above average when high amounts of hormone are secreted. Thyroid hormones have wide spread effects that are duetothe stimulation of O2 intake; though the hormones also affect mammalian growth and development, they also aid to control metabolism of lipid and enhance carbohydrate absorption from intestine. By raising red-cell 2-3 DGP, they also accelerate the dissociation of O2 from haemoglobin.

Thyroid and the cardiovascular system
Cardiovascular manifestations are seen with hypothyroidism. The mechanisms through which the thyroid hormones, acts on cardiovascular are:
1. By sympathetic nervous system interaction
2. Direct effects on cell level
3. By alteration of the energy metabolism and peripheral circulation.

Cellular effects-thyroid hormone on the cardiovascular system[13-16]
The effects on circulation of hormone are caused by cellular mechanisms and by molecular. On, effect of thyroid hormone cardiac myocytes which may have both nongenomic and genomic effects.

The transcriptional repression or activation of particular target genes that encode both functional and structural proteins mediates the genomic effects of the hormone. Triiodothyronine (T3), is the biologically active thyroid hormone, enters the cardiac myocyte with help of certain transport proteins to start this process. T3 enters the cardiomyocyte myocyte and interacts with particularnuclear receptor -1 which is transcriptional activator orreleases (nuclearreceptor-2) particular DNA sequences (thyroid-responsive elements), which in turn change the transcription rates of particular genes by acting as cis- or trans-regulators.[13]

The proteins present in sarcoplasmic reticulum that control calcium-activated ATPase and also control its inhibitory cofactor, phospholamban, and myosin heavy chains are among many other proteins and its expression is controlled at the level of transcriptional. The ratio among the two is of orms of the heavy chains of myosin in humans exclusively depends on by thyroid hormone.

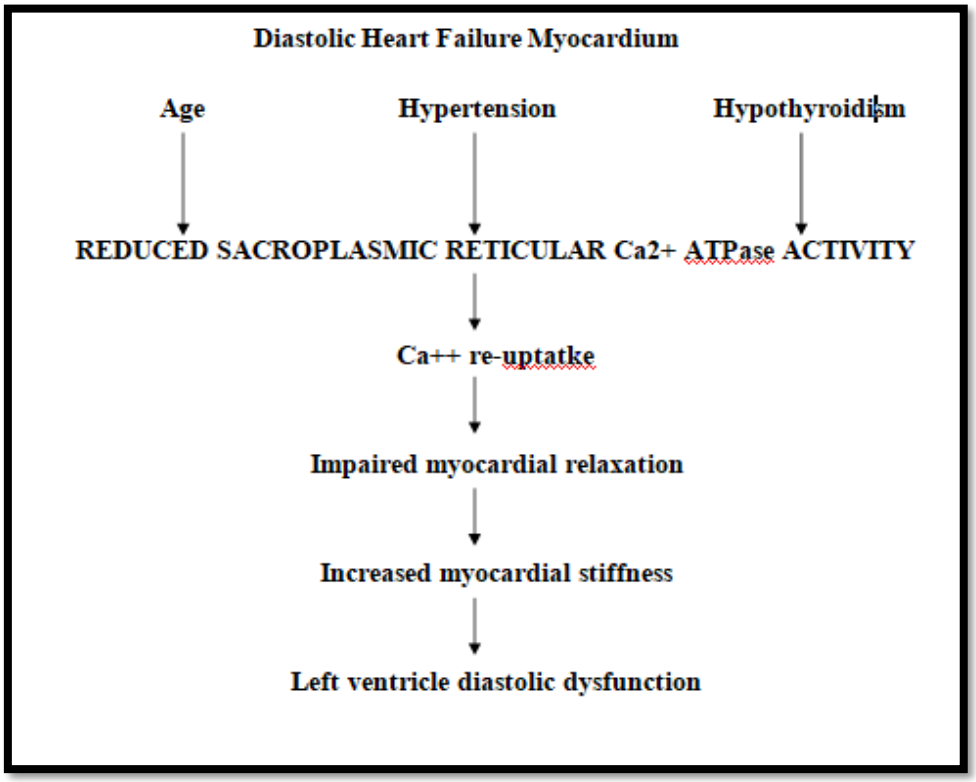
Thyroid dysfunctions and heart failure

Rarely, hypothyroid patients experience cardiac failure as a result of because of thyroid hormone on diastolic functions, left ventricular contractility, peripheral resistance, cardiac excitability and heart rates,.

Heart failure could because don by hypothyroidism. Low levels of cardiac output can be by a various factors, including a less heart rate, higher peripheral resistance, and less myocardial contractility. By having left ventricular hypertrophy, bradycardia and aberrant relaxation due to poor ventricular filling. When a sufficient cardiac output cannot keep up with peripheral metabolic demand, heart failure can result. Patients with cardiac disease experience heart failure more frequently.[24]

Monitoring of therapy

The patient should be evaluated after six weeks of treatment, and the dose should be raised gradually. Reassessment will take place in roughly 8 weeks for those who received full replacement therapy. 25 g dose changes are typically plenty. If the dose is not adjusted, a re-evaluation should be conducted in 4-6 months. It is advised to conduct a yearly evaluation once the proper dose has been established. Monitoring should be done for both clinical and biochemical indicators.



Materials and Methods:-

Source of Data:

50 new hypothyroidism cases attending to Sri Aurobindo Medical College & PG Institute, Hospital- Indore is included in the study.

Sample Size:

50 new hypothyroidism cases

Study duration:
From January 2022 to December 2023, 2 years

Study design:
A Cross sectional study was conducted among 50 new cases of hypothyroidism. cardiac manifestations by ECG and ECHO were studied in the patients. Detailed history was taken with help of questionnaire and investigations were done.

Inclusion Criteria:
1. Who are newly diagnosed hypothyroid patients
2. Hypothyroid patients who are not on treatment
3. Patients taking L-thyroxinefor<4months.

Exclusion criteria:
1. Patients with known history of cardiac disease
2. Patients with severe anemia, COPD, any endocrinal disorder and diabetes mellitus.
3. Patients on medications which change the thyroid function like lithium, beta blockers, OCP's, steroids & alcohol.

Investigations:

Hemoglobin, DC,TC,ESR
T4, T3, TSH
RBS

Blood
urea
Serum
creatinine
Lipid
profile
Urine
routine -
-albumin
- sugar

-microscopy

ECHO

12leadECG

Statistical Methods:-

Data collected will be entered in Microsoft excel. Frequencies are expressed as percentages. Continuous data will be expressed as means and standard deviation. Tests of significance used are Chisquare test. Statistical analysis will be done by using SPSS version 26. Level of significance is taken as $p<0.05$.

Results:-

Table 1:- Age Distribution With Sex.

	MALE		FEMALE		TOTAL	
	NO	%	NO	%	NO	%
21-30	2	20.0%	7	17.5%	9	18.0%
31-40	4	40.0%	22	55.0%	26	52.0%
41-50	3	30.0%	7	17.5%	10	20.0%
51-60	1	10.0%	4	10.0%	5	10.0%
TOTAL	10	100%	40	100	50	100
MEAN+SD	37.06+9.38		36.75+9.24		38.30+10.37	

In our study subjects most of them belong to 31 to 40 years age group. The mean age was38.30+10.37 years. There was an overall female preponderance among all age Groups with mean age of 36.75+9.24

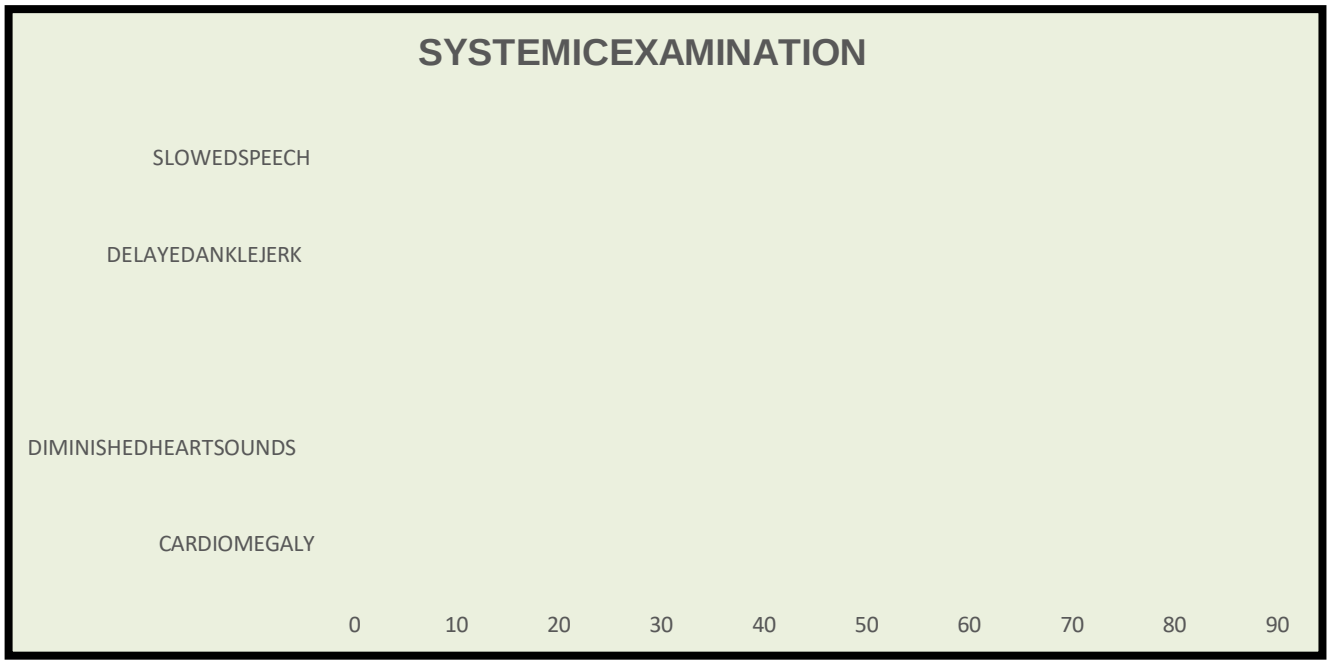
years. The female population were about 80% of the population.

Table 1:- Sex Distribution Of Study Population.

Sex	Frequency	Percentage
Male	10	20%
Female	40	80%

Table 2:- Symptomatology.

Presenting symptoms	Number	%
Lethargy	30	60
Hoarseness of voice	26	52
Dyspnea	16	32
Weight gain	33	66
Constipation	22	44
Coldintolerance	26	52
Depression	10	20
Dry skin	31	62
Menstrual symptoms	21	42



In our study group, the most common symptoms are weight gain, dryskin, lethargy, cold intolerance, constipation and hoarseness of voice. Menstrual symptoms are found in 42% of population. Depression was present among 20% individuals.

Table 3:- Blood Investigations And Hypothyroidism.

LIPID PARAMETERS	MILD(N=21)	MODERATE(N=18)	SEVERE(N=11)	Pvalue
Hb	10.6+1.14	10.3+1.52	11.2+1.42	0.282
Urea	23.3+7.47	25.3+9.49	23.9+10.36	0.789
Creatinine	0.87+0.33	1.14+0.43	1.01+0.49	0.125
RBS	98.1+23.11	105.4+17.61	113.8+31.02	0.200

There was no significant mean difference of Hb%, Blood urea, Serum creatinine and RBS levels between grades of hypothyroidism

Table 4:- Lipid Profile And Hypothyroidism.

LIPID PARAMETERS	MILD(N=21)	MODERATE(N=18)	SEVERE(N=11)	Pvalue
TOTAL CHOLESTEROL	175.8+10.86	184.3+16.13	205.8+9.49	<0.001
HDL	35.8+3.95	34.0+4.58	27.8+4.72	<0.001
LDL	132.9+15.6	131.3+18.6	148.3+16.1	0.026
VLDL	36.3+2.77	39.7+4.43	34.9+5.08	0.006
TGY	196.7+14.61	203.8+14.51	204.47+10.19	0.187

Lipid analysis showed increase in TC, VLDL, LDL, TGY levels and decrease in HDL levels were observed from mild to moderate to severe cases of hypothyroidism. There was significant mean difference of TC, HDL, LDL and VLDL levels between grades of hypothyroidism. However, no significant mean difference with Triglyceride levels.

Table 5:- Severity Of Hypothyroidism.

SEVERITY OF HYPOTHYROIDISM	TSH LEVELS	NO OF PATIENTS (%)
MILD	0.5TO20	21(42)
MODERATE	20TO50	18(36)
SEVERE	>50	11(22)
Total	50	100

Table 6:- Echo Findings.

ECHO FINDINGS	NUMBER	%
1.NORMAL	21	42
2.SYSTOLIC DYSFUNCTION	4	8
3.PERICARDIAL EFFUSION	15	30
4.DIASTOLIC DYSFUNCTION	11	22
MILD	8	16
MODERATE	3	6
SEVERE	0	0
5.IVS THICKNESS	3	6

Echo findings were normal in 42% of patients. Pericardial effusion was seen in 30%and diastolic dysfunction was seen in 22% of patients. Among diastolic dysfunction majority of them had mild dysfunction and none had severe dysfunction. IVS thickness is seen in 6% of patients.

Table 7:- Severity Of Hypothyroidism And Pericardial Effusion.

SEVERITY OF HYPOTHYROIDISM	Number	PATIENTS WITH ERICARDIAL EFFUSION			
		NOPE	MILDPE	MODPE	SEVEREPE
MILD	21	18	3	0	0
MODERATE	18	12	4	2	0
SEVERE	11	5	2	3	1

Discussion:-

In this study 50 new cases of hypothyroidism that presented to Department of Gen. Medicine, SAIMS Medical College is discussed here, and results have been analyzed and compared with other similar studies.

Age and sex distribution:
The study's age range covered people from 21 to 60 years old. Most of the patients are between the ages of 31 and 40. Overall age groups, women out numbered men. The median age was 38 years old. About 80% of the patients were female. The most of medical text books, including the Harrison text book of internal medicine, mention a similar demographic profile.[17]

However ,a study by Razvietal.[18] revealed that the most of cardiac manifestations happen in younger people, specifically in the 65 and under age group.

In their study, Maja Udovcic et al[19]demonstrated that as people get older, cardiovascular disease becomes more common.

In their study, Irwin Klein et al. [20]found that the incidence of hypothyroidism was higher among women than men and that the incidence increased with age.

Symptoms:
Weight gain, dry skin, lethargy, cold intolerance, hoarseness of voice, and constipation were the most prevalent symptoms in our study group.

Similar to our study, Levey G Sand Klein's[21] investigation revealed that bradycardia, cold intolerance, and dry skin are the most typical symptoms among hypothyroid individuals.

Similar to our study, Irwin Kleinet al.[20]found that hypothyroidism patients hadan increased incidence of bradycardia, hypertension, and cold intolerance.

Systemic examination:
The most frequent finding in our analysis was delayed ankle jerk (80%), which matches Lambert et al[22]description of the phenomenon well.

The second most frequent finding in our study, after delayed ankle jerk, was slowed speech, which was found in 60% of patients and diminished heart sounds in 30% of them, suggesting a possible pericardial effusion. Similar results were discovered in the research by Rawat B and Satyal A.[7]

Similar to our study, Maja Udovcicetal.'s study[19] revealed that hypothyroidism increases the incidence of pericardial effusion.

In their study, Khaleeli et al.[23]found that the severity of the hypothyroid state was inverselycorrelatedwiththeincidenceofpericardialeffusion.Inourstudy,wealsocame to similar conclusions.

Similar to our study, H. Vargas-Uricoechea et al.'s[24]research revealed an increased incidence of pericardial effusion, delayed ankle jerk findings, and an increase in pericardial effusion with rising TSH levels.

Cardiomegalywasfoundin3patientsinourstudy.

Severity of hypothyroidism:
There were 21 patients (42%) with mild hypothyroidism, 18 patients (36%) with moderate hypothyroidism, and 11 patients (22%) with severe hypothyroidism.

Intheirstudy, H. Vargas-Uricoecheaetal.[24]demonstrated that elevated TSH levels in the study are significantly correlated with an increased risk of coronary artery disease mortality and events.

Contrarily, a small increase in TSH levels is not linked to an increased risk of cardiovascular morbidity and

mortality, according to a study by Rodondi et al.[25]

Lipid profile:
The levels of total cholesterol, LDL, VLDL are rising, while HDL levels are falling. In our study, there is statistically significant difference between the mild, moderate, and severe cases of hypothyroidism. The triglycerides are also increasing but the difference among the groups were not statistically significant.

Maja Udovcic et al. [19]demonstrated in their study that total and LDL cholesterol incidence are both on the rise.

Similar to our work, Turm Burdge, Wing et al. [26]reported a rise in total cholesterol and LDL.

Similar to our analysis, Irwin Klein et al study's[20]revealed an increased incidence of total cholesterol and LDL. It has been demonstrated that dyslipidemia is more common in the subclinical stage of hypothyroidism, even before symptoms start to manifest. Serum lipids have increased in patients, and cholesterol levels seem to be rising concurrently with serum TSH. L-thyroxine therapy for subclinical hypothyroidism has shown improvement in cardiovascular symptoms. Similar findings were report edin Raz vietal[18]study. In their study, H. Vargas-Uricoechea et al.[24] noted that Hypercholesterolemia is the most frequent finding even before the onset of hypothyroid symptoms, and that starting patients on L-thyroxine will undoubtedly improve their cardiac hypothyroidism manifestations.

Avais jabbar et al in their study[27]showed increase in Total cholesterol and LDL levels in their study .

The connection between hypothyroidism and hyper lipidemia was les sclear in the W.J. Huestonetal. Stud[28].A Cochrane review of six RCTs came to the same conclusion as the study[29] that treating hypothyroidism had no overall impact on lowering total cholesterol but did reduce LDL cholesterol.

Echo findings:
Echo findings were normal in 42% of patients. Pericardial effusion seen similar percentage 30% in our study.

According to Rawat B and Satyal A,[7]pericardial effusion is showed that to occur in 30 to 80% of patients, which is inline withthe1995study by R. Varma19that found a prevalence of 45%.

There is relatively less pericardial effusion in our study because as we selected new hypothyroid cases.

Diastolic dysfunction was seen in 22%, most of them had mild dysfunction 16% among 8 patients and only 6% had moderate dysfunction.

Maja Udovcicetal.'s[19] investigation shown that higher diastolic dysfunction occurs as a result of a longer is ovolumetric relaxation time and a lower E/A ratio in hypothyroidism.

Serafino Fazio et al[30] in their study found the commonest cardiac abnormality LV diastolic Dysfunction in their study which is consistent with our study.

The most typical finding associated with hypothyroidism, according to Avais Jabbar et al in their study[27]found diastolic dysfunction, is consistent with our study.

In our study, 8% of individuals had systolic dysfunction. Low systolic dysfunction was highlighted by Forfar et al.[31]in their investigation of hypothyroid individuals.

However, Bough EW et al. [32]have suggested that this may be because elderly patients were included in the study. The younger individuals showed no signs of systolic dysfunction.

Forfar et al.[32]and R Varma et al.[29], who found no systolic dysfunction in hypothyroid individuals, provided additional support for this.

Both Rawat B and Satyal A[7] studies, which are similar to our investigation, failed to detect any systolic dysfunction. Only 3 patients had IVS thickness, while more IVS thickness was identified in the research mentioned above. In contrast to Rawat B and Satyal A[7], who both reported LVPW thickness in their instances, there is no LVPW thickness in our cases.

Maja Udovcicetal[19]didn't showed any IVS thickness in hypothyroidism in their study.

Although pericardial tamponade was a very uncommon occurrence in their study, H.Vargas-Uricoechea et al.[24] demonstrated that diastolic dysfunction is the commonest finding in pericardial effusion and hypothyroidism is the second most common finding.

Pericardial effusion and Diastolic dysfunction and were found to be the most frequent findings in a recent study by LillEvang Johnsen Metal[33]. These findings are consistent with those of our study.

In 1978, a study done by Edward W. Bough demonstrated that hypothyroidism causes depressed systolic time intervals, including shortened LVET, prolonged PEP, and increased PEP/LVET. [34] In their study of nine at hyrotic patients, Weishammer et al. [35]showed that the heart's decreased performance was primarily due to changes in the exercise heart rate and loading conditions.

In27.2%of cases, it has been documented, According to research done by Cuocoloin 1992 and Bonowin1990 and[36]resting left ventricular diastolic. Dysfunction is frequently the first sign of disease of heart, even coming before systolic dysfunction.

Conclusion:-

In this study consisting of 50 new hypothyroid patient's bradycardia was commonest finding followed by low voltage complexes, STT changes observed in ECG. Pericardial effusion and Diastolic dysfunction are the commonest abnormal findings in ECHO. Any pericardial effusion of unknown etiology should be screened for presence of hypothyroidism. It should be done in large no of patients.

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