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Case Report

A Pilot study on thyroid status, lipid profile creatine kinase in human cardiac patients

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Abstract

Background: The progression of Coronary Heart Disease (CHD) is linked to a multitude of comorbidities, such as thyroid dysfunction, dyslipidemia. Objectives were to determine the thyroid and serum lipid profile, cholesterol, triglycerides and creatin kinase profile of CHD patients and to establish correlation between severity of cardiac disease with these two metabolic parameters.

Methods: This was a prospective study conducted among 55 CHD patients over 1 year admitted in the department of cardiology, General Government Hospital, Bikaner.

Results: There are 66% male and 36% female patients among the 55 study cases. Majority of the patients (54/55) exhibited higher T_3 concentration, whereas one patient has low T_4 value accompanied by 14 patients with high TSH value. Three patients have higher value of cholesterol with 17 patients of higher triglycerides levels. Among the patients eleven demonstrated higher creatine kinase values.

Conclusions: The numbers of patients increasing with decreasing T3 and increasing thyroid stimulating hormone (TSH) proportionate to the severity of the cardiac failure. In addition, hypothyroidism is becoming more common in people with chronic cardiac disease. Serum triglycerides, LDL and HDL levels rise statistically significantly in CHD patients.

Keywords: Dyslipidemia, CHD, Cholesterol, triglycerides, TMB.

INTRODUCTION

Hypothyroidism is normally associated with endothelial dysfunction, mortality in addition to cardiac death. In India, Cardiovascular diseases (CVDs) have also been attributed 30% of medically certified deaths[1]. Among total cardiovascular disease, Coronary Heart Disease (CHD), has contributed to around one-third of mortality, in which 64% recorded deaths were of male population. Large number of affected population includes economic productive age group of 30-69 years[2]. Furthermore, disability due to CHD in India have been increase from 13.27 million to 22.1 million from 2000 to 2020[2]. Autonomic activity may be deranged in thyroid dysfunction and may lead to cardiovascular morbidity and mortality. Previous studies reports important risk factors for CHD in India are dyslipidemias, smoking, diabetes, hypertension, abdominal obesity, psychosocial stress, unhealthy diet, physical inactivity and genetic causes[3].

Some of the important co-morbidities are lipid dysfunction and thyroid misbalance. Hyperlipidemia i.e. high level of serum LDL, cholesterol, triglycerides is a well-known risk factor for early atherosclerosis causing various cardiovascular disease, normally seen in CHD patients[4]. In Indian prospective high level of lipid profile (hyper triglyceridemia, low HDL, high cholesterol profile) leads to stroke and CHD. In the present study relation of thyroid hormone dysfunction in relation to Coronary heart disease will be monitored.

Thyroid dysfunction may be of two types hyper or hypothyroidism. Thyroid hormones affect cardiac systolic and diastolic function, peripheral vascular resistance and arrhythmogenesis[5]. Patients with clinical hypothyroidism have sypatho-vagal imbalance and prolongation of repolarization that causes life threatening arrhythmias. Whereas, hyperthyroidism lead to cardiac complication.

Creatine phosphokinase (CPK), also known by the name creatine kinase (CK), an enzyme catalyzes the reaction of creatine and adenosine triphosphate (ATP) to phosphocreatine and adenosine diphosphate (ADP). The phosphocreatine used to supply tissues and cells the required amount of ATP, like the brain, skeletal muscles, and the heart. The normal CPK level is considered to be 20 to 200 IU/L. Many conditions such as heart disease, kidney disease, or even certain medications can cause derangement in CPK levels[6-9].

Thyroid hormone effects on the cardiac myocyte are intimately associated with cardiac function via regulation of the expression of key structural and regulatory genes. These enzyme regulates sarcoplasmic reticulum Ca^{2+}-ATPase and its inhibitor, phospholamban, regulate intracellular calcium cycling. Together they are largely responsible for enhanced contractile function and diastolic relaxation in the heart[10].

In the present study, I hypothesized the relation of cardiovascular disease with lipid profile, their thyroid status and criatine kinase level in terminally ill cardiac patients. To prove the same, in this study correlation parameters of CHD patients with CK and CK-MB in patients of hyper and hypothyroidism.

MATERIAL AND METHODS

Sera samples of 55 patients were harvested from cardiology section of General Government Hospital (**Prince Bijay Singh Memorial Hospital**), Bikaner Rajasthan. Biochemical test was done by these samples. These sera samples are treated with EDTA to prevent coagulation and stored at -20°C.

T3 HEPEIA assay

ELISA method is applied to detect the concentration of T3 hormone.

The T3 HEPEIA diagnostic kit utilizes a monoclonal anti T3 and anti T_3 HRP conjugate. The assay sample and assay buffer are incubated together with T3 antibody coated plate for 60 min. and washed. Then the diluted T3-HRP conjugate is incubated. After the incubation period the wells were decanted and washed three times. The wells is then incubated with a substrate for the enzyme. The product of enzyme substrate forms a blue color complex. Finally the stopping solution was added to stop the reaction that will turn the solution to yellow. The intensity of the color is measured spectrophotometrically at 450 nm in a microplate reader. The intensity of the color is inversely proportional to the T3 concentration.

Standard of the known T3 concentration was run concurrently with the sample been assayed and the standard curved is plotted relating the intensity of the color, optical density (O.D.) to the concentration in each sample is inter plotted from this curve.

T4 HEPEIA assay

The T3 HEPEIA diagnostic kit utilizes a monoclonal anti T3 and anti T_3 HRP conjugate. 10 µL of standard, control and patient control were administered in the corresponding wells. T4-HRP conjugate were added to the wells. The experimental plate were incubated for 40 min on the plate shaker (100±10 rpm) at room temperature. The plates were then washed with 300 µL of washing solution. 100 µL of the TMB enzyme substrate solution was added to each well. After 40 min incubation on the plate shaker (100±10 rpm) 50 µL of the stopping solution was added to the incubation plate. Absorbance was measured at 414 nm using microplate reader.

Concentration was calculated on the basis of standard curve plotted against optical density and the abscissa for the standard concentration (µg %).

TSH-ELISA

In TSH-ELISA 10 µL of standard, control and patient sample were added to corresponding wells. The plate were incubated at 22 ± 2°C on the plate shaker (100±10 rpm). After 40 min the wells were decanted and 100 µL of anti-TSH antibodies were added. After 30 min of incubation, wells were washed with 300 µL of washing solution 3 times. 100 µL of TMB enzyme substrate solution were added. The plate were kept on plate shaker (100±10 rpm at 22 ± 2°C) for about 20 min. After adding 50 µL of stopping solution absorbance was taken at 414 nm. A standard curve of optical density v/s standard concentration was prepared and values of the unknown sample were calculated.

Triglyceride measurement

Cayman's Triglycerides Colorimetric assay was used. In this method enzymatic hydrolysis of the triglycerides by lipase to glycerol and free fatty acids. The glycerol released is subsequently measured by the coupled enzymatic reaction system. The total triglycerides was measured using following equation.

$$\text{Triglycerides (mg/dL)} = A_{serum}/A_{standard} \times \text{concentration of standard}$$

Cholesterol measurement

In this enzymatic method esterified cholesterol is converted to cholesterol by cholesterol esterase. The resulting cholesterol is then acted upon by cholesterol oxidase to produce cholest-4-en-3-one and hydrogen peroxide. The hydrogen peroxide then reacts with 4-aminophenazone in the presence of peroxidase to produce a colored product that is measured at 505 nm (secondary wavelength = 700 nm). The final step is also known the Trinder reaction. This method is a single reagent, endpoint reaction that is specific for cholesterol.

Criatine Kinase estimation

The Creatine Kinase Activity Assay kit provides a simple and direct procedure for measuring CK levels in a variety of samples such as blood, serum, and plasma. In this assay, Creatine Kinase activity is determined by a coupled enzyme reaction resulting in the production of NADPH, measured at 340 nm, proportionate to the CK activity present in the sample. In this reaction, phosphocreatine and ADP are converted to creatine and ATP. The generated ATP is used by hexokinase to phosphorylate glucose resulting in glucose-6-phosphate, which is oxidized by NADP in the presence of glucose-6-phosphate dehydrogenase to produce NADPH and 6-phospho-D-gluconate. One unit of CK is the amount of enzyme that will transfer 1.0 mmole of phosphate from phosphocreatine to ADP per minute at pH 6.0. This kit has a linear range of 30–1,800 units/L CK activity.

RESULTS

The test results of 55 patients were shown below:

S. No.	T_3	T_4	TSH	Cholesterol	TG	CK	Remarks
1	8	12	1.35	185.6	100.3	90.05	High T_3, normal T_4, TSH, Chol., CK, TG value
2	6.1	9.5	3.2	-	116.3	1123.8	High T_3, CK, normal TG, CK, T_4, Chol. value
3	6.35	7.25	0.85	193.6	403.7	790.95	High T_3, CK, TG, normal T_4, TSH, Chol. value
4	5.7	9.75	2.1	133.6	173.8	49.15	High T_3, TG, low Chol., normal T_4, TSH, CK value
5	4.2	10	1.3	132.2	135.8	32.45	High T_3, low Chol., normal T_4, TSH, CK value
6	7	12	3.0	121.9	84.47	20.15	High T_3, low Chol., normal T_4, TSH, TG, CK value
7	3.7	11.75	1.7	176.0	399.3	38.60	High T_3, TG, normal Chol., T_4, TSH, CK value
8	4.05	6.5	2.5	177.9	189.6	81.40	High T_3, TG, normal Chol., T_4, TSH, CK value
9	5.15	8.6	7.4	161.3	161.5	31.35	High T_3, TSH, TG, normal Chol. T_4, CK value.

10	2.8	8.5	3.6	294.9	135.4	18.8	High T_3, Chol., normal T_4, TSH, TG, CK value
11	3.4	6.4	0.85	177.0	76.05	160.05	High T_3, normal T_4, TSH, Chol. TG, CK value
12	3.65	9.56	3.0	114.0	94.77	14.7	High T_3, low Chol., CK, normal T_4, TSH, TG value
13	4.05	11.5	6.2	250.7	103.0	36.25	High T_3, Chol., TSH, normal T_4, TG, CK value
14	6.7	10.5	4.8	155.4	89.97	21.2	High T_3, TSH, low CK, normal T_4, Chol., TG value
15	2.95	9	4.1	188.9	233.1	211.5	High T_3, TG, CK, TSH, normal T_4, Chol. value.
16	3.7	6.9	0.7	163.6	103.1	942.55	High T_3, CK normal T_4, TSH, Chol., TG value.
17	2.9	8.25	2.85	198.8	324.9	48.85	High T_3, low CK, normal T_4, TSH, Chol. value
18	2.45	8.2	0.2	131.3	83.65	228.75	High T_3, low Chol., TSH normal T_4, TG, CK value
19	2.55	6.5	1.4	144.5	147.0	23.55	High T_3, CK, low, Chol., normal TSH, T_4 value
20	7.05	8.25	3.9	254.6	338.6	688.8	High T_3, TG, Chol., low CK, normal TSH T_4 value
21	2.85	6.75	1.95	234.1	78.08	73.55	High T_3, normal TSH, T_4, TG, Chol., CK value
22	3.1	7	1.6	184.3	130.4	59.8	High T_3, normal TSH, T_4 Chol., TG, CK value
23	4.25	7.5	2.75	130.2	73.27	28.8	High T_3, low Chol., normal TSH, T_4
24	2.65	11.7	5.1	208.4	113.8	173.65	High T_3, TSH, CK, low Chol., normal T_4, TG value
25	2.05	7.5	2.8	242.0	94.18	18.45	Low CK, normal Chol., TSH, T_4, T_3, TG value
26	2.9	9.75	2.15	67.59	28.55	35.85	High T_3, normal Chol., CK, TSH, T_4, TG value
27	4.25	10.5	0.7	153.7	50.07	81.2	High T_3, normal T_4, Chol. TG, CK value.
28	6.95	10	4.2	218.8	222.3	12.4	High T_3, TSH, TG, low CK, normal T_4, Chol. value.
29	5.75	7.5	1.25	128.0	113.5	27.87	High T_3, low Chol., normal T_4, TSH, TG, CK value
30	3.4	9.75	6.1	196.4	137.7	4.4	High T_4, TSH, normal T_4, Chol., TG, CK value.
31	2.45	10	1.5	143.4	103.9	28.3	High T_3, low Chol., normal T_4, TSH, TG, CK value
32	5.5	9.75	2.3	215.2	165.0	527.5	High T_3, TG, normal T_4, TSH, Chol., CK value.
33	2.75	7.75	1.5	208.4	104.5	14.85	High T_3, low CK, normal T_4, TSH, Chol., TG value.
34	3.24	6.9	4.8	186.1	65.98	48.8	High T_3, TSH, normal T_4 Chol., TG, CK value
35	6.24	7.65	5.0	207.1	216.7	14.6	High T_3, TG, TSH, normal T_4, Chol., CK value
36	6.24	9.25	16.5	247.9	134.5	4.2	High T_3, TSH, low CK, normal T_4, Chol., TG value.
37	4.95	7.60	3.9	107.0	107.5	16.65	High T_3, low Chol., CK, normal T_4, TSH, TG value.
38	3.5	8.6	1.4	160.8	183.4	9	High T_3, TG, CK, normal T_4, Chol., TSH value.
39	3.1	7.25	1.2	151.0	171.7	1133.9	High T_3, TG, normal T_4, TSH, Chol., CK values
40	2.68	6.85	1.5	204.9	277.4	130.05	High T_3, TG, normal T_4, TSH, Chol.., CK value
41	2.55	5.0	3.15	161.3	184.3	36.95	High T_3, TG, normal T_4, TSH, Chol., CK value.
42	7.25	6.9	1.1	175.7	344.0	31.35	High T_3, TG, normal T_4, TSH, Chol., CK value
43	7.05	7.65	5.8	163.1	155.5	26.65	High T_3, TG,TSH, normal T_4, TSH, Chol., CK value
44	6.1	6.65	0.75	173.1	168.4	20.7	High T_3, TG, low CK, normal T_4, TSH, Chol.
45	4.0	8.25	4.0	172.3	86.46	35.6	High T_3, normal T_4, TSH, Chol., TG, CK value
46	3.4	2.6	5.9	113.6	91.72	67.85	High T_3, TSH, low T_4, chol., normal TG, CK value.
47	6.7	6.75	1.4	194.2	114.8	32.4	High T_3, normal T_4, TSH, Chol., TG, CK value.
48	3.4	9.0	0.15	108.7	59.90	11.20	High T_3, low Chol., TSH, CK, normal T_4, TG value
49	4.3	8.75	1.3	136.8	238.5	80.05	High T_3, TG, low Chol., normal T_4, TSH, CK value
50	2.85	6.80	4.05	140.0	77.30	7.25	High T_3, TSH, low Chol., CK, normal T_4, TG value
51	3.5	6.2	3.2	167.0	220.2	51.35	High T_3, TG low, normal T_4, TSH, Chol., CK value.
52	2.65	13.5	2.5	220.2	103.9	78.15	High T_3, normal T_4, TSH, Chol., TG, CK value
53	4.6	13.75	1.85	140.1	178.5	307.8	High T_3, T_4, TG, CK low Chol., normal TSH value
54	6.95	6.75	7.7	232.4	227.7	411.2	High T_3, TG, TSH, CK, normal T_4, Chol. value
55	5.95	9.60	0.7	138.9	57.68	13.35	High T_3, low Chol., CK, normal T_4, TSH, TG value

	T_3 (in ng/ml)	T_4 (in µg/ml)	TSH (in mU/dL)	Total Cholesterol (in mg/dL)	Triglycerides (in mg/dL)	Creatine Kinase (in U/L)
Mean±SE	4.40±0.22	8.52±0.28	3.11±0.36	175.55±23.91	148.11±12.13	339.35±20
Low-High level in patients	2.05 – 8.0	2.6 - 13.75	0.15 - 16.5	107 - 294.9	28.55 - 403.7	7.55 - 1133
Normal level	0.8-2.1	4.2- 12	0.3-4.0	150-250	≥ 150	24-170

DISCUSSION

T_3 This is not so useful for diagnosis of hyperthyroidism. Higher level may be indicated thyrotoxicosis with normal T_4 values, but TSH must be suppressed to low levels for thyroxin. Majority of the patients (54/55) exhibited T_3 concentration higher than normal. Possible condition of thyrotoxicosis are Graves disease, autonomous toxic adenomas, subacute thyroiditis, Jodbasedow disease, Thyrotoxicosis facititia, TSH hyper secretion, Struma ovarii, Hashimoto's thyroiditis, Pregnancy and trophoblastic tumors, metastatic thyroid carcinoma and Amidarone induced thyrotoxicosis[11-12].

Lack of patient history, expertise in the field is not adequate enough, but drug induced thyrotoxicosis appear to be the most probable cause of the patients related to cardiac disease.

T_4

Majority of the patients (52/55) have normal T_4 values. One patient has low T_4 value accompanied by high TSH value. This Patient may be suffering from hypothyroidism (T_4 value 2.6 µg/ml). Increased serum T_4 then 4.2-12 µg/ml confirm a clinical diagnosis of hypothyroidism[13-15].

TSH

Majority of the patients (37/55) has normal TSH concentration whereas 14 patients having high TSH values. Higher concentration of TSH is associated with Neoplastic or non-neoplastic inappropriate secretion of thyrotropin, autoimmune disease, TSH level increased due to dopamine antagonists, old age and hypothyroidism[16-18].

Screening of the values of T_3, T_4 in patients showing low or high values of TSH indicated there was no evidence of hypothyroidism except in one case, in which low T_4 value associated in the high TSH, might be due to hypothyroidism.

Cholesterol value

Majority of patients (35/55) have normal cholesterol value. Three patients have higher value of cholesterol. The main cause may be Coronary artery disease, uncontrolled diabetes mellitus, hypothyroidism, nephritic syndrome, hepatic malfunctioning[19]. Seventeen patients have decreased level of cholesterol, main causes are acute hepatitis, malnutrition, anemia, hyperthyroidism, Gaucher's disease.

Triglycerides

Majority of the patients (35/55) have normal triglyceride level. Seventeen patients have higher triglycerides levels, reason may be thickening of heart muscle, previous heart attack or stroke and obesity[20].

Creatin kinase

Majority of the patients (29/55) has normal creatin kinase level. The level of creatin kinase varies with physical activity, restraint, biopsy, age, sex. Eleven patients have higher level of creatin kinase reason may be- Intramuscular injection may also increase CK activity (local tissue necrosis). This is also indicative of rhabdomyolysis, myocardial narcosis, myositis, myocarditis, malignant hyperthermia and neuroleptic malignant syndrome. Elevated CK activity have been reported in hereditary muscular dystrophies, selenium deficiency, artterogryposis hydrocephaly syndrome[21,22]. Also seen in McLeod syndrome and hypothyroidism. The use of statin medication, which are commonly used to decrease cholesterol level, may be associated with elevation of the CPK level in about 1% of the patients taking these medications and with actual muscle damage in much smaller proportion.

15 patients have lower creatin kinase level than normal, no such effect of low creatine kinase level observed in the affected patients.

Thyroid hormone has both direct and indirect actions on the cardiovascular systems. Patients with thyroid disease, especially those with hyperthyroidism, often have symptoms and sign indicating changes in cardiovascular hemodynamics. Indeed, symptoms and signs referable to the cardiovascular system may be the only manifestation of thyroid dysfunction and thyroid function should therefore be assessed by the measurement of serum thyrotropin concentration in all the patients with cardiovascular disease. T_3 level hardly affect the cardiac health. Majority (54/55) has higher T_4 value along with higher TSH value showing person id affected with hypothyroidism.

High concentration of cholesterol in the blood, particularly the cholesterol and lipoprotein particles called low density lipoprotein (LDL) contributes to the formation of atherosclerotic plaque. Three (out of 55) patients show high cholesterol levels this suggest that cholesterol plaque (fatty acid deposits on arterial walls) are associated with heart attack and strokes.

High triglycerides expanded blood volume not only contributes to his elevated blood pressure but also put workload to heart. This increased workload will cause heart muscle to thicken and eventually fail. Triglycerides level of 22 patients are found high then 250 mg/dL indicates risk factor for future development of atherosclerosis and his consequences, such as heart attack and strokes.

Increased CK activity is due to local areas of muscle necrosis. Among all the patients studied CK of one patient is very high that gives an indication of severe muscle damage and need to be heart biopsy.

CONCLUSION

So we can conclude that 22 patients has heart disease due to higher triglycerides, three due to high cholesterol, one patient has damaged heart and only patient due to thyroid gland activity. Thyroid gland activity affects the cardiac health but its involvement in heart disease is low as compare to triglycerides and cholesterol.

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