



IJCRR

Vol 06 issue 10

Section: Healthcare

Category: Research

Received on: 11/04/14

Revised on: 28/04/14

Accepted on: 12/05/14

## APOLIPOPROTEIN B / APOLIPOPROTEIN A1 RATIO: AN IMPROVED MARKER OF CARDIOVASCULAR RISK IN HYPOTHYROIDISM

Priyanka G. Rakshasmare, P. N. Joshi

Department of Biochemistry, B J Govt. Medical College Pune, Maharashtra, India

E-mail of Corresponding Author: priyanka.rakshasmare@gmail.com

### ABSTRACT

**Introduction:** Hypothyroidism is a condition with decreased levels of thyroid hormones and elevated levels of Thyroid stimulating Hormone. Hypercholesterolemia is the characteristic feature of hypothyroidism and is also predisposing factor of atherosclerosis. Cholesterol in the body is transported through lipoproteins called Low density lipoprotein (LDL) and High density lipoprotein (HDL). The ratios, LDL/HDL and total cholesterol/HDL reflect the direction of transport of cholesterol and are conventionally used to assess risk of cardiovascular diseases. Apolipoprotein B (apo B) present in Very low density lipoprotein (VLDL), Intermediate density lipoprotein (IDL), and LDL; is considered as atherogenic whereas apolipoprotein A1 (apoA1) present in HDL, is antiatherogenic, anti-inflammatory with antioxidative properties. ApoB/apoA1 ratio represents the balance of proatherogenic and antiatherogenic lipoproteins. So the case control study was carried out to know the effectiveness of this improved ratio in hypothyroidism.

**Objective:** To find out levels of total cholesterol (TC), LDL, HDL, apoB, and apo A1 2) To find out ratios- LDL/HDL, TC/HDL and apoB/apoA1 3) To check the effectiveness of apoB/apoA1 ratio as marker of cardiovascular risk in hypothyroidism.

**Methodology:** Group A consists of 30 clinically diagnosed and biochemically confirmed cases of hypothyroidism. The levels of TC, HDL estimated using the kit, LDL using Friedewald formula, apoB and apoA1 by immuno-turbidimetric method and result were compared with Group B (n=30) age and sex matched controls.

**Results:** The levels of TC, LDL, and apoB were found to be increased highly significantly ( $p < 0.001$ ) and that of HDL and apoA1 decreased highly significantly ( $p < 0.001$ ). A highly significant increase in ratios namely LDL/HDL, TC/HDL and apoB/apoA1 was also observed.

**Conclusion:** It can be concluded from the present study that apoB/apoA1 ratio is comparable with LDL/HDL and TC/HDL ratios. ApoB/apoA1 ratio can be an improved marker for prediction of cardiovascular risk in hypothyroidism.

**Keywords:** Hypothyroidism, hypercholesterolemia, apolipoprotein B/ apolipoprotein A1 ratio, cardiovascular risk.

### INTRODUCTION

Hypothyroidism is a condition with decreased levels of thyroid hormones (T3, T4) and elevated levels of thyroid stimulating hormone (TSH)<sup>1,2</sup>. Hypothyroidism is categorized into: - Primary

hypothyroidism - a condition characterized by the failure of the thyroid gland to produce sufficient thyroid hormones. Secondary hypothyroidism (central thyroid disease) occurs as a result of pituitary or hypothalamic disease that produces a

deficiency in Thyroid stimulating hormone (TSH), thyroid releasing hormone (TRH) or both<sup>2</sup>. According to various studies on thyroid disease, it has been estimated that about 42 million people in India suffer from thyroid diseases. Recent population-based study reported the prevalence of hypothyroidism as 3.9%<sup>3</sup>. Thyroid hormones have significant effects on the synthesis and metabolism of lipids mainly cholesterol<sup>4,5,6</sup>. Thyroid hormones regulate lipid metabolism by different ways: 1) up regulation of the low density lipoprotein receptors, which results in enhanced catabolism of the low density lipoproteins (LDL) particles, 2) stimulation of the cholesteryl ester transfer protein (CETP), an enzyme which transports cholesteryl esters from HDL 2 to the very low density lipoproteins (VLDL) and intermediate density lipoproteins (IDL) and triglyceride to the opposite direction. 3) Activation of the lipoprotein lipase, which hydrolyzes the triglyceride rich lipoproteins. 4) Stimulation of hepatic lipase (HL), which catabolises HDL2 to HDL3 and IDL to LDL<sup>4,12</sup>. Hypercholesterolemia is the characteristic feature of hypothyroidism and is also predisposing factor for atherosclerosis. Cholesterol in the body is transported by low density lipoprotein (LDL) and high density lipoprotein (HDL)<sup>4,5,6,7</sup>. The ratios, LDL/HDL and TC/HDL reflect the direction of transport of cholesterol and are conventionally used to assess risk of cardiovascular diseases. Apolipoproteins are the protein moieties of lipoproteins. The various functions of apolipoproteins are 1) they can form part of the structure of the lipoprotein. 2) They are enzyme cofactors. eg A-1 for lecithin: cholesterol acyltransferase, or enzyme inhibitors. eg A-II for lipoprotein lipase. 3) They act as ligands for interaction with lipoprotein receptors in tissues. eg, Apo B for LDL receptor, apo A-1 for the HDL receptor<sup>1,2</sup>. ApoB is the major protein in VLDL, IDL and LDL, with one protein per particle of lipoprotein. ApoA-I is the major protein in HDL particles. The apoB level indicates the total number of atherogenic particles, while apoA-I

reflects the anti-atherogenic potential in HDL particles which has anti-inflammatory and anti oxidative properties.

The apoB/apoA1 ratio indicates the balance between atherogenic and anti-atherogenic particles. Thus higher the ratio, higher the cardiovascular risk in hypothyroidism<sup>8,9,10</sup>. There are some methodological advantages of using these apoB/apoA1 ratio 1) direct measurement of apo B and apo A-1 by internationally standardized methods. 2) Fasting sample is not required for the analysis. 3) Apo B and apo A-1 can be analysed on frozen samples<sup>8,9</sup>. Considering these facts, present study was conducted to find the effectiveness of this Apo B/ApoA1 ratio over conventional LDL/HDL and TC/HDL ratios in hypothyroidism.

**Objectives:** 1) To estimate levels of TC, LDL, HDL, ApoB and ApoA1. 2) To find out ratios- LDL/HDL, TC/HDL and apo B/apoA1. 3) To check the effectiveness of apoB /apoA1 ratio as a marker of cardiovascular risk in patients with hypothyroidism.

## MATERIALS AND METHODS

This study was carried out after approval from the Institutional Ethics Committee and prior consent from all participants. Study design: case control study consists of total 60 subjects they were divided in two groups.

Group A: consists of 30 clinically diagnosed and biochemically confirmed cases of hypothyroidism.

Group B: consists of 30 age and sex matched healthy controls with normal thyroid function tests.

Exclusion criteria - patients suffering from diabetes, obesity, polycystic ovarian diseases, liver, renal disease, congestive cardiac failure, taking oral contraceptive pills, statins, and other medications that alter thyroid function were excluded from this study.

**Research methods-** Venous blood samples were obtained from each participant after 12 to 14 hour fasting period. TC and HDL were measured by

enzymatic kit methods, LDL was estimated by the Friedewald equation, and apo B, apoA-1, measured by using immuno-turbidimetric method<sup>11</sup>. The assays were performed in the clinical laboratory of the institute.

### Statistical analysis

SPSS software was used to analyze all statistical data. The continuous data was expressed as Mean  $\pm$  SD and a comparison was done by using an unpaired t test. P value  $<0.01$  considered as significant,  $p < 0.001$  considered as highly significant.

### RESULTS

The data obtained was compared between group A and group B. It was found that serum levels of TC, LDL, and apo B were increased highly significantly in group A as compared to group B ( $P < 0.001$ ). Serum levels of HDL and apo A-1 were decreased. This decrease was also highly significant in group A as compared to group B ( $P < 0.001$ ). The ratios TC/HDL, LDL/HDL, apo B/apoA1 were also increased highly significantly in group A as compared to group B ( $P < 0.001$ ). see table no.1

### DISCUSSION

LDL /HDL and TC/HDL are conventionally used to know the status of cholesterol in the body. Apo B is the apoprotein of atherogenic lipoproteins VLDL, IDL, LDL while apoA1 is the apoprotein component of antiatherogenic lipoproteins HDL. The role of apoB/apoA1 ratio in predicting risk of cardiovascular diseases is well documented<sup>9,10</sup>. In the present study apoB was highly significantly increased while apoA1 was highly significantly decreased in patients with hypothyroidism. Thus apoB/apoA1 ratio was highly significantly increased, indicating levels of apoB, atherogenic component of LDL increased and levels of apoA1 antiatherogenic component of HDL decreased highly significantly (table no-1). This indicates that in patients of hypothyroidism with hypercholesterolemia, the

ratio of apoB/ apoA1 was significantly increased and they may have the risk of cardiovascular disease in the future. Treating these patients will decrease apoB to apo A1 ratio and thus may minimize risk of cardiovascular disease. Monitoring the levels of apo B, apoA1 and ratio of apo B to apoA1 will throw light on the response of the patients of hypothyroidism to the treatment.

### CONCLUSION

It can be concluded from the present study that apo B / apoA1 ratio is comparable with LDL/HDL and TC/HDL ratios, which are conventionally used for the prediction of cardiovascular risk. Considering the above advantages of apo B/apoA1 ratio over LDL/HDL and TC/HDL ratios, apoB /apoA1 ratio can be an improved marker for prediction of cardiovascular risk in hypothyroidism. It can also be used in monitoring the treatment of hypothyroid patients.

### ACKNOWLEDGEMENT

Authors acknowledge the immense help received from the scholars whose articles are cited and included in references of this manuscript. The authors are also grateful to authors / editors / publishers of all those articles, journals and books from where the literature for this article has been reviewed and discussed.

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**Table 1: Shows the levels of TC, LDL, HDL, Apo B and apoA1 and their ratios, LDL/HDL, TC/HDL, apoB/apoA1 in group A and group B**

Parameters	Group A (n=30) Mean ±SD	Group B (n=30) Mean ±SD	P value
TC (mg/dl)	198.2 ± 17	171.2 ± 14	<0.001**
LDL (mg/dl)	117.2 ± 21	104.5 ± 14	<0.009**
HDL (mg/dl)	36.3 ± 3.9	40.8 ± 3.4	<0.001**
TC/HDL	5.54 ± 0.95	4.21 ± 0.46	<0.001**
LDL/HDL	3.29 ± 0.82	2.57 ± 0.42	<0.001**
ApoB (mg/dl)	193.1 ± 35.6	106.9 ± 18.1	<0.001**
ApoA1 (mg/dl)	100.6 ± 26.5	126.5 ± 20.5	<0.001**
Apo B/Apo A1	1.97 ± 0.36	0.85 ± 0.14	<0.001**

(P<0.001\*\* highly significant)

#### Abbreviation used

- 1) TC = Total cholesterol
- 2) VLDL = Very low density lipoprotein
- 3) IDL = Intermediate density lipoprotein
- 4) LDL = Low density lipoprotein
- 5) HDL = High density lipoprotein
- 6) Apo B = Apolipoprotein B
- 7) ApoA1 = Apolipoprotein A1