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A study on lipid profile in sub clinical hypothyroidism of patients attending a tertiary care hospital

Ashwin Raj H, Ananthi N*, Sabarinathan M

Department of Biochemistry, Saveetha Medical College & Hospital, SIMATS, Chennai, Tamil Nadu, India

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ABSTRACT

Subclinical hypothyroidism is also known as mild hypothyroidism, early thyroid failure, preclinical hypothyroidism and decreased thyroid reserve. Subclinical hypothyroidism is defined as a high serum thyroid-stimulating hormone concentration and normal serum total or free thyroxine and triiodothyronine concentrations associated with few or no symptoms and signs of hypothyroidism and thus subclinical hypothyroid disease is diagnosed by laboratory findings. Subclinical hypothyroidism is far more common than overt hypothyroidism. The prevalence of subclinical hypothyroidism is relatively high and ranges from 4%-8.5% and maybe as high as 20% in women older than 60 years. Subclinical hypothyroidism is more common in elderly women than men. It is found twice as often in women as in men. Thyroid hormones have a known effect on heart rate & cardiac excitability. Cardio vascular system is the major system affected by subclinical hypothyroidism. Subclinical hypothyroidism patients have an increased risk of "atherosclerosis" & coronary artery disease. Subclinical hypothyroidism patients will have an increased level of total cholesterol, triglyceride, low-density lipoprotein and decreased level of high-density lipoprotein, leading to "atherosclerosis". Among the 110 human subjects, 55 were Euthyroid controls and 55 were subclinical hypothyroid cases. Serum total cholesterol, serum triglycerides, serum low-density lipoproteins, levels were increased in subclinical hypothyroid cases than Euthyroid controls with a high statistical significance with the P-value <0.001 and serum high-density lipoproteins levels are decreased in subclinical hypothyroid cases than Euthyroid controls with a high statistical significance with the P-value <0.001. Hence, it should be made mandatory that the estimation of lipid profile should be made as a routine investigation in all cases of subclinical hypothyroidism.

*Corresponding Author

Name: Ananthi N
Phone: +91-9381722682
Email: n_ananthi@yahoo.com

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INTRODUCTION

Endocrine diseases are increasing worldwide (Regmi *et al.*, 2010). Diseases of the thyroid gland are amongst the most abundant endocrine disorders in the world next to Diabetes Mellitus (Regmi *et al.*, 2010; Tunbridge *et al.*, 1977). Hypothyroidism is a common endocrine disorder that reduces the functional ability of life and is associated with altered lipid levels which increases the cardiovascular risk (Guntaka *et al.*, 2014; Pucci *et al.*, 2000). Hypothyroidism can

be either primary that is due to the defect in the thyroid gland (or) secondary due to the defect in the pituitary gland (Pucci *et al.*, 2000). Overt hypothyroidism is associated with dyslipidemia and hence with atherosclerosis and cardiovascular disorders (Guntaka *et al.*, 2014). The co-relation between dyslipidemia and overt hypothyroidism is well established (Guntaka *et al.*, 2014). Subclinical hypothyroidism is defined as a high serum Thyroid Stimulating Hormone(TSH) concentration and normal serum total or free thyroxine (T4) and triiodothyronine(T3) concentrations associated with few or no symptoms and signs of hypothyroidism and thus subclinical hypothyroid disease is diagnosed by laboratory findings (Desai *et al.*, 2015; Guntaka *et al.*, 2014; Singh and Singh, 2011; Pucci *et al.*, 2000). Some of the studies have documented that subclinical hypothyroidism was associated with dyslipidemia like increased serum levels of Total Cholesterol (TC), Triglycerides (TG), Low-Density Lipoprotein (LDL), and decreased levels of High-Density Lipoprotein (HDL), which potentially increases the risk of "atheroscelerosis" & "coronary artery disease", While other studies did not document any such co-relation between subclinical hypothyroidism and dyslipidemia (Baumgartner *et al.*, 2014; Rizos, 2011; Guntaka *et al.*, 2014). So dyslipidemia in subclinical hypothyroidism is still controversial (Saini *et al.*, 2012; Helfand, 2004; Hueston, 2004). Hence, the study is designed to estimate serum total cholesterol, triglycerides, low-density lipoprotein, and high-density lipoprotein in subclinical hypothyroid cases & Euthyroid controls to assess the co-relation between dyslipidemia and subclinical hypothyroidism.

MATERIALS AND METHODS

The present Case-Control study was carried out in the department of Biochemistry in Saveetha Medical College & Hospital, Chennai. The study was conducted prospectively with approval from the Institutional Ethical Committee (IEC). The Case-Control study was carried out to determine the lipid profile in subclinical hypothyroidism and the study included 110 human subjects of age group 18-60 years. Among the 110 human subjects, 55 were Euthyroid controls and 55 were subclinical hypothyroid cases. The cases and controls were selected from patients attending the outpatient department (O.P.D) and in patient department (I.P.D) of Saveetha Medical College & Hospital, satisfying the inclusion and exclusion criteria. Subclinical hypothyroid cases and Euthyroid controls of aged between 18-60 years of both sexes were included. Patients with a history of Diabetes Mellitus, Coronary Heart Disease, Obesity, Acute illness, & other disorders that affect Lipid metabolism. Patients taking any drug like Lithium, Antiepileptics-Carbamazeline, phenytoin, Beta-blockers-propanolol, Carbimazole, Propylthiouracil, Steroids, etc. which affects the thyroid & lipid metabolism were excluded. Known hypothyroid patients and Patients who were exposed to thyroid hormone therapy (or) Lipid-lowering agents are not included in this study. Informed consent was obtained from all the participants. The informed consent was taken from every patient after a full explanation of the study.

RESULTS AND DISCUSSION

In our study serum fT3, fT4, TSH, TC, LDL & HDL were estimated in 110 human subjects out of which 55 were apparently healthy Euthyroid controls and 55 were cases of subclinical hypothyroidism. These biochemical parameters were compared between Euthyroid controls and cases of subclinical hypothyroidism. The levels of the analyzed biochemical parameters namely serum fT3 pg/ml, fT4 ng/dl, TSH mIU/ml, triglycerides mg/dl, total cholesterol mg/dl, high-density lipoproteins mg/dl, low-density lipoproteins mg/dl in the 110 human subjects of age group between 18-60 years are tabulated in Table 1 & Table 2. In our study 14.5% were men and 85.4% were women in Euthyroid controls. 10.9% were men and 89.1% were women in subclinical hypothyroid cases which are tabulated in Table 3. Hence the prevalence of subclinical hypothyroidism is more in women in our study. The serum fT3 levels were low in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a p-value of <0.001 which are shown in Table 4. The serum fT4 levels of Euthyroid controls and subclinical hypothyroid cases were within the normal reference range and fT4 levels of subclinical hypothyroid cases were lower than Euthyroid controls which are shown in Table 5. The serum TSH is increased in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a P-value of <0.001 which are shown in Table 6. There was a statistically significant increase in serum TSH levels in subclinical hypothyroid cases than Euthyroid controls. The serum total cholesterol is increased in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a P-value of <0.001 which are shown in Table 7. There was a statistically significant increase in serum total cholesterol levels in subclinical hypothyroid cases than Euthyroid con-

Table 1: Euthyroid controls

Parameters	Mean	Standard deviation	Significance p-value
fT3	5.11	±0.87	<0.001
fT4	15.93	±4.01	<0.001
TSH	2.18	±1.13	<0.001
TC	156.6	±24.43	<0.001
TGL	93.51	±20.66	<0.001
HDL	44.62	±3.74	<0.001
LDL	93.16	±23.20	<0.001

*Values are expressed as mean ± SEM *p<0.05 – Significant, **p<0.01-Highly significant,***p<0.001-Extremely significant*

Table 2: Subclinical hypothyroid cases

Parameters	Mean	Standard deviation	Significance p-value
fT3	4.35	±0.89	<0.001
fT4	12.05	±3.76	<0.001
TSH	9.75	±9.21	<0.001
TC	267.02	±51.96	<0.001
TGL	179.85	±37.08	<0.001
HDL	33.91	±6.56	<0.001
LDL	197.16	±57.02	<0.001

*Values are expressed as mean ± SEM *p<0.05 – Significant, **p<0.01-Highly significant,***p<0.001-Extremely significant*

Table 3: Sex distribution in Euthyroid controls and subclinical hypothyroid cases

Groups	No. of Subjects	Males(%)	Females(%)
Controls	55	8 [14.5%]	47 [85.4%]
Cases	55	6 [10.9%]	49 [89.1%]

Table 4: Comparison of Serum fT3 levels between Euthyroid Controls and subclinical hypothyroid Cases

Group	Mean	Standard deviation
Control(n=55)	5.11	±0.87
Case(n=55)	4.35	±0.89

Table 5: Comparison of Serum fT4 levels between Euthyroid Controls and subclinical hypothyroid Cases

Group	Mean	Standard deviation
Control(n=55)	15.93	±4.01
Case(n=55)	12.05	±3.76

Table 6: Comparison of serum TSH levels between euthyroid controls and subclinical hypothyroid cases

Group	Mean	Standard deviation
Control(n=55)	2.18	±1.13
Case(n=55)	9.75	±9.21

Table 7: Comparison of serum Total Cholesterol levels between euthyroid controls and subclinical hypothyroid cases

Group	Mean	Standard deviation
Control(n=55)	156.56	±24.43
Case(n=55)	267.02	±51.96

Table 8: Comparison of serum Triglycerides levels between euthyroid Controls and subclinical hypothyroid cases

Group	Mean	Standard deviation
Control(n=55)	93.51	±20.66
Case(n=55)	179.85	±37.08

Table 9: Comparison of serum Low-Density Lipoproteins levels between euthyroid controls and subclinical hypothyroid cases

Group	Mean	Standard deviation
Control(n=55)	93.16	±23.20
Case(n=55)	197.16	±57.02

Table 10: Comparison of serum High Density Lipoproteins levels between euthyroid controls and subclinical hypothyroid cases

Group	Mean	Standard deviation
Control(n=55)	44.62	± 3.74
Case(n=55)	33.91	± 6.56

trols. The serum triglycerides is increased in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a P-value of <0.001 which are shown in Table 8. There was a statistically significant increase in serum TGL levels in subclinical hypothyroid. The serum HDL is decreased in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a P-value of <0.001 which are shown in Table 9. There was a statistically significant decrease in serum HDL levels in subclinical hypothyroid cases than Euthyroid controls. The serum LDL is increased in subclinical hypothyroid cases than Euthyroid controls. The results showed a good positive co-relation and high statistical significance with a P-value of <0.001 which are shown in Table 10.

In our study serum fT3, fT4, TSH, TC, LDL & HDL were estimated in 110 human subjects out of which

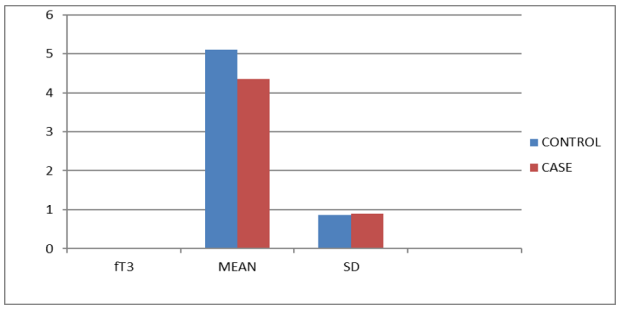

Diagram 1: Comparison of serum fT3 levels between Euthyroid controls and subclinical hypothyroid cases

55 were apparently healthy Euthyroid controls and 55 were cases of subclinical hypothyroidism. These biochemical parameters were compared between Euthyroid controls and cases of subclinical hypothyroidism. The serum fT3 levels ranged between 4.14pg/ml to 7.00pg/ml for Euthyroid controls and

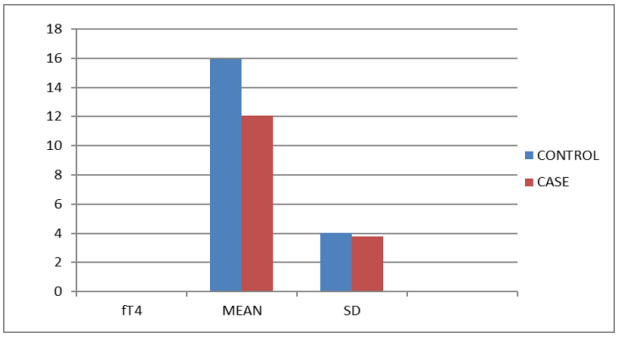

Diagram 2: Comparison of serum fT4 levels between Euthyroid controls and subclinical hypothyroid cases

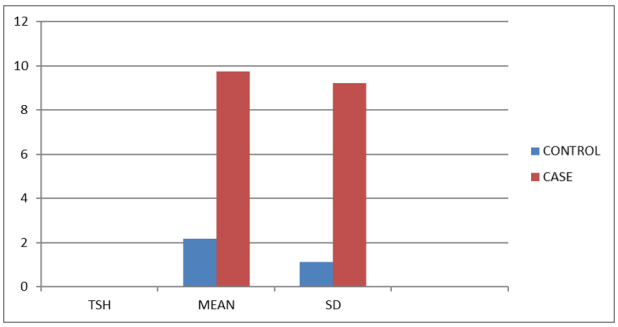

Diagram 3: Comparison of serum TSH levels between Euthyroid controls and subclinical hypothyroid cases

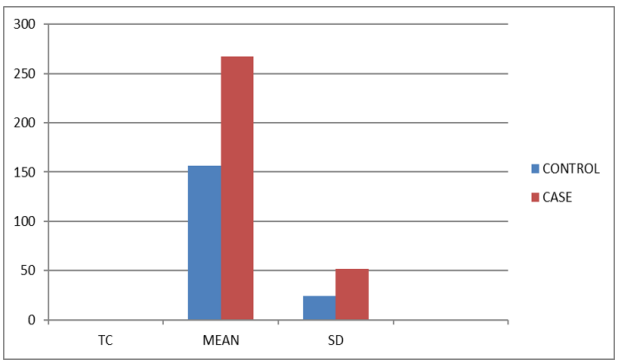

Diagram 4: Comparison of serum Total Cholesterol levels between Euthyroid controls and subclinical hypothyroid cases

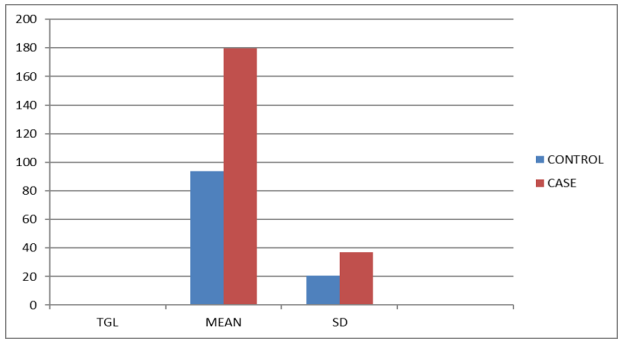

Diagram 5: Comparison of serum Triglycerides levels between Euthyroid controls and subclinical hypothyroid cases

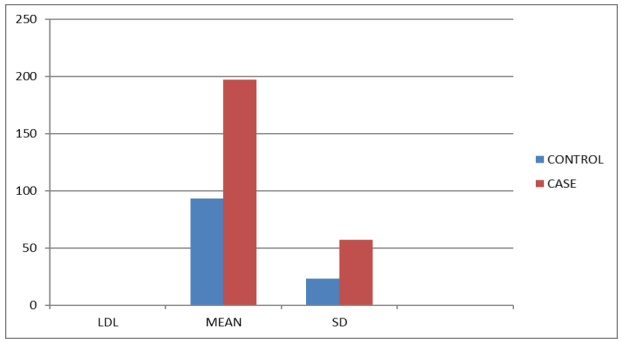

Diagram 6: Comparison of serum Low-Density Lipoproteins levels between Euthyroid controls and subclinical hypothyroid cases

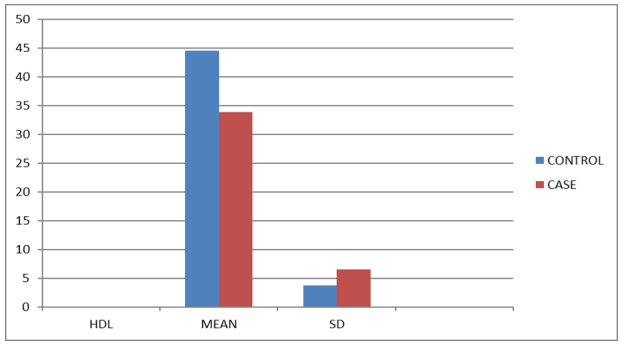

Diagram 7: Comparison of serum High Density Lipoproteins levels between Euthyroid controls and subclinical hypothyroid cases

3.93pg/ml to 6.72pg/ml for subclinical hypothyroid cases. fT3 levels of both controls & cases were well within the reference range [3.5pg/ml -7.00pg/ml] quoted in the kit methodology adopted for its analysis. The mean level of fT3 with standard deviation for controls were 5.11±0.87 and for subclinical hypothyroid cases are 4.35±0.89. Though the mean and range of serum fT3 for controls and subclinical hypothyroid cases were well within the normal reference range, the fT3 levels of cases were lesser than the controls. The serum fT4 levels ranged between 10.00ng/dl to 22.30ng/dl for Euthyroid controls and 8.03ng/dl to 19.59ng/dl for subclinical hypothyroid cases. fT3 levels of both controls & cases were well within the reference range [8.5ng/dl -22.5ng/dl] quoted in the kit methodology adopted for its analysis. Diagram 1 shows the Comparison of serum fT3 levels between Euthyroid controls and subclinical hypothyroid cases. The mean level of fT4 with standard deviation (SD) for controls were 15.93±4.01 and for subclinical hypothy-

roid cases were 12.05±3.76. Though the mean and range of serum fT4 for controls and subclinical hypothyroid cases were well within the normal reference range, the fT4 levels of cases were lesser than the controls, Diagram 2 shows the Comparison of serum fT4 levels between Euthyroid controls and subclinical hypothyroid cases. In our study there was a significant increase in serum TSH levels in subclinical hypothyroid cases when compared to Euthyroid controls. The range of serum TSH levels varied between 0.64mIU/ml – 4.82mIU/ml for Euthyroid controls and 5.5mIU/ml – 46.00mIU/ml for subclinical hypothyroid cases. The mean ± SD for Euthyroid controls & subclinical hypothyroid cases were 2.18 ± 1.13 and 9.75 ± 9.21, respectively. The increase in serum TSH in subclinical hypothyroid cases showed a high statistical significance with a P-value of <0.001. In our study there was a significant increase in serum triglycerides levels in subclinical hypothyroid cases when compared to Euthyroid controls. Diagram 3 shows the Comparison of serum TSH levels between Euthyroid controls and subclinical hypothyroid cases. In our study there was a significant increase in serum total cholesterol levels in subclinical hypothyroid cases when compared to Euthyroid controls. The range of serum total cholesterol levels varied between 119mg/dl – 197mg/dl for Euthyroid controls and 202mg/dl – 453mg/dl for subclinical hypothyroid cases. The mean ± SD for Euthyroid controls & subclinical hypothyroid cases were 156.56 ± 24.43 and 267.02 ± 51.96 respectively. The increase in serum total cholesterol in subclinical hypothyroid cases showed a high statistical significance with a p-value of <0.001. Diagram 4 shows the Comparison of serum Total Cholesterol levels between Euthyroid controls and subclinical hypothyroid cases. The range of serum Triglycerides levels varied between 64mg/dl – 142mg/dl for Euthyroid controls and 151mg/dl – 322mg/dl for subclinical hypothyroid cases. The mean ± SD for Euthyroid controls & subclinical hypothyroid cases were 93.51 ± 20.66 and 179.85 ± 37.08 respectively. The increase in serum triglycerides in subclinical hypothyroid cases showed a high statistical significance with a P-value of <0.001. Diagram 5 shows the Comparison of serum triglycerides levels between Euthyroid controls and subclinical hypothyroid cases. In our study there was a significant increase in serum low density lipoproteins levels in subclinical hypothyroid cases when compared to Euthyroid controls. The range of serum low-density lipoproteins levels varied between 57mg/dl – 130mg/dl for Euthyroid controls and 152mg/dl – 389mg/dl for subclinical hypothyroid cases. The mean ± SD for Euthyroid controls & subclinical hypothyroid cases were 93.16 ± 23.20 and 197.16 ± 57.02 respectively. Diagram 6 shows the Comparison of serum Low-Density Lipoproteins levels between Euthyroid controls and subclinical hypothyroid cases. The increase in serum low density lipoproteins in subclinical hypothyroid cases showed a high statistical significance with a P-value of <0.001. Desai *et al.* (2015) in their various studies, observed a significant increase in serum triglycerides, total cholesterol & low density lipoproteins in subclinical hypothyroid cases than Euthyroid controls, which is consistent with our study. However, studies by (Hueston, 2004) did not find any such positive co-relation between subclinical hypothyroid cases and Euthyroid controls, which is not consistent with our study. In our study there was a significant decrease in serum HDL levels in subclinical hypothyroid cases when compared to Euthyroid controls. The range of serum HDL levels varied between 35mg/dl – 50mg/dl for Euthyroid controls and 23mg/dl – 47mg/dl for subclinical hypothyroid cases. The mean ± SD for Euthyroid controls & subclinical hypothyroid cases were 44.62 ± 3.74 and 33.91 ± 6.56 respectively. Diagram 7 shows the Comparison of serum High Density Lipoproteins levels between Euthyroid controls and subclinical hypothyroid cases. The decrease in serum HDL in subclinical hypothyroid cases showed a high statistical significance with a P-value of <0.001. (Kaviprasanna *et al.*, 2015) in their various studies observed a significant decrease in serum HDL in subclinical hypothyroid cases than Euthyroid controls, which is consistent with our study. However, studies by (Kaviprasanna *et al.*, 2015) in their studies did not observe any co-relation between subclinical hypothyroid cases and Euthyroid controls, which is not consistent with our study.

CONCLUSION

From the results and discussion held so far and by comparison of total serum cholesterol, low density lipoprotein, triglycerides & high-density lipoprotein between Euthyroid controls & subclinical hypothyroid cases, the following are concluded. TSH levels are increased in subclinical hypothyroidism. The prevalence of subclinical hypothyroidism is more in women (89.1%). Serum total cholesterol levels are increased in subclinical hypothyroid cases than Euthyroid controls with a high statistical significance of P-value <0.001. Serum triglycerides levels are increased in subclinical hypothyroid cases than Euthyroid controls with a high statistical significance of P-value <0.001. Serum low density lipoproteins levels are increased in subclinical hypothy-

roid cases than Euthyroid controls with a high statistical significance of P-value <0.001. Serum high-density lipoproteins levels are decreased in subclinical hypothyroid cases than Euthyroid controls with a high statistical significance of P-value <0.001. In conclusion, in our study, subclinical hypothyroidism is more prevalent in women (89.1%) than men (10.9%) and subclinical hypothyroidism is associated with dyslipidemia and hence, a risk factor for Atherosclerosis. Hence, it should be made mandatory that the estimation of lipid profile should be made as a routine investigation in all cases of subclinical hypothyroidism. Subclinical hypothyroid patients may be treated with Levo-Thyroxine and followed up for a decrease in lipid profile so that cardio vascular diseases and atherosclerosis can be prevented.

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