## Correspondence:

# Novel cardiovascular risk markers in hypothyroidism patients

Hypothyroidism is associated with increased risk for cardiovascular disease (CVD) and accelerated atherosclerosis as indicated by hypertension and dyslipidaemia.[1,2] Not all patients with hypothyroidism have these conventional risk factors for CVD,[3] suggesting that other factors may also be involved. Elevated homocysteine levels have been reported in overt hypothyroidism and have been proposed as an independent risk factor for CVD.[4,5] Decreased thyroid function not only increases the number of low density lipoprotein (LDL) particles but also promotes LDL *oxidability*[6] as thyroxine (T4) has three specific binding sites on apolipoprotein B (ApoB) and inhibits LDL oxidation *in vitro*. Hypothyroidsm is also associated with an increase in plasma homocysteine levels,[7] arterial hypertension and a hypercoagulable state all of which predispose to CVD. Among the novel risk markers, lipoprotein (a) [Lp(a)] levels, which are an independent CVD risk factor are also elevated in hypothyroid patients. Ethnic variations are known to affect some of the predictors of CVD like homocysteine and Lp(a). The present study was designed to compare serum Lp(a) and homocysteine levels in newly diagnosed patients with hypothyroidism and normal control subjects. We studied 25 newly diagnosed patients with hypothyroidism [thyroid stimulating hormone (TSH) levels >8 μU/ml] and 25 age and gender-matched healthy control subjects. The study was approved by the Institutional Ethical Committee. All participants gave written informed consent to participate in the study. Patients already on treatment for hypothyroidism, patients with cardiovascular disease, diabetes mellitus, were excluded from the study. Five mL of peripheral venous blood sample was collected in heparinized tubes after an overnight fast, plasma was separated and stored at 80 °C until analysis. Lp(a) was estimated using Beckman CX9 fully Automated Analyzer (Synchron Cx9 Beckman Coulter, Inc. Galway, Ireland) using commercially available kits. Plasma homocysteine was measured using a commercial kit (Biorad) by enzyme linked immunosorbent assay. All values obtained were expressed as mean (± standard error of mean). Unpaired t-test (two-tailed) was performed to compare the difference in the means between controls and study group. A p-value less than 0.05 was considered as statistically significant.

Hypothyroid patients had significantly elevated levels of homocysteine compared to controls ($p<0.05$) (Table 1). This observation is in agreement with previous reports [9,10] which reported a higher plasma concentration of total homocysteine, in patients with hypothyroidism than in healthy controls. In one study, elevated

**Table: 1 Comparison of TSH homocysteine and Lp(a) levels**

| Parameter | Cases (n=25) | Controls (n=25) | p-value |
|---|---|---|---|
| TSH (mIU/mL) | 48.5±6.6 | 3.3±0.42 | <0.001 |
| Homocysteine (μmol/L) | 16.54±1.1 | 12.4±0.82 | <0.05 |
| Lp(a) (mg/dL) | 25.4±3.2 | 17.1±2.3 | <0.05 |

TSH = thyroid stimulating hormone; Lp(a) = lipoprotein A

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levels of total homocysteine were strongly associated with changes in serum folate suggesting an altered folate status to be the cause for hyperhomocysteinemia. However, either no change[11] or lower plasma homocysteine level[12] has also been described.

In the present study a higher mean levels of Lp(a) were found in patients with hypothyroidism (Table 1). This observation is in agreement with previous reports.[13] Thyroid hormones influence on Lp (a), may be at least partially modulated by thyroid hormone-dependent mechanisms, thus increasing the risk of developing premature atherosclerosis in hypothyroid state. However, another study[14] reported that serum C-reactive protein and Lp(a) levels, were not significantly affected by the degree of thyroid dysfunction.

The results of the present study show that novel risk factors like Lp(a) and homocysteine may increase CVD risk in hypothyroid patients and call for planning appropriate therapeutic interventions.

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**E. Jayanthi,[1]**
**Aparna R. Bitla,[1]**
**Alok Sachan,[2]**
**G. Shivakrishna,[1]**
**PVLN Srinivasa Rao.[1]**
*Departments of [1]Biochemistry,*
*[2]Endocrinology and Metabolism,*
*Sri Venkateswara Institute of Medical Sciences, Tirupati*