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STUDY OF SERUM CYSTATIN C LEVELS IN SUBCLINICAL HYPOTHYROIDISM

Biochemistry

KEYWORDS: subclinical hypothyroidism; Cystatin C; Thyroid stimulating hormone

Dr Chandrakanth K H — Professor, Dept. of Biochemistry, Subbaiah Institute of Medical sciences, Purle , SHIMOGA-577222.

Dr Mamatha B V — Assisstant Professor, Dept. of Biochemistry, Subbaiah Institute of Medical sciences, Purle , SHIMOGA-577222.

Dr Leela P — Assisstant Professor, Dept. of Biochemistry, Subbaiah Institute of Medical sciences, Purle , SHIMOGA-577222.

ABSTRACT

Background: Cystatin C is a low molecular weight (12.8 kDa) protein synthesized by all nucleated cells whose physiological role is that of a cysteine protease inhibitor. Compared to serum creatinine, Cystatin C has a lower interindividual variability and is not correlated to lean tissue mass, gender, and age. Cystatin C has been proposed as a good marker of GFR, particularly in patients with moderate to severe renal impairment. Hence, this study was undertaken to evaluate the serum Cystatin C levels in subclinical hypothyroidism.

Materials and methods: Patients with newly diagnosed subclinical hypothyroidism were included in the study. Subclinical hypothyroidism was defined as free thyroxine (fT4) within normal range and Thyroid stimulating hormone(TSH) above normal range. Total of 22 patients with subclinical hypothyroidism were included in the study. Serum Cystatin C levels were decreased in cases when compared to control, which is highly significant (<0.001).

Conclusion: Our study has shown the impact of subclinical hypothyroidism of Cystatin C levels, which was significant. So, it is advisable to know the thyroid status of on individual when Cystatin C is measured to know the GFR.

Introduction

Cystatin C is a low molecular weight (12.8 kDa) protein synthesized by all nucleated cells whose physiological role is that of a cysteine protease inhibitor. With regard to renal function, its most important attributes are its small size and high isoelectric point (pI=9.2), which enable it to be more freely filtered than other proteins at the glomerulus[1]. The structure of its gene is of the housekeeping type and the production of Cystatin C is not influenced by inflammatory states[2]. The protein is freely filtered at the glomerulus and practically completely reabsorbed and catabolized by tubular cells[3]. Compared to serum creatinine, Cystatin C has a lower interindividual variability and is not correlated to lean tissue mass, gender, and age[4,5]. Cystatin C was found to be an estimator of the GRF at least as well as serum creatinine in the population at large and likely even superior in specific patient populations[6]. Cystatin C has been proposed as a good marker of glomerular filteration rate (GFR), particularly in patients with moderate to severe renal impairment[7].

There are studies showing decreased Cystatin C levels in overt hypothyroidism. To the best of our knowledge, there are very few studies on serum cystatin C levels in subclinical hypothyroidism. Hence, this study was undertaken to evaluate the serum Cystatin C levels in subclinical hypothyroidism.

Patients and methods

Patients with newly diagnosed subclinical hypothyroidism were included in the study, attending medicine outpatient department of Subbaiah Institute of Medical Sciences, shimoga, Karnataka. For the study, institutional ethical committee clearance was obtained. Study was done between Febraury 2016 to November 2016. Subclinical hypothyroidism was defined as free thyroxine (fT4) within normal range and TSH above normal range.

This study included patients with untreated subclinical hypothyroidism in the age group of 22 to 60 years diagnosed based on the symptoms and laboratory data. Cases with altered kidney function were excluded from the study. Oral informed consent was taken from all patients. Blood samples were centrifuged immediately and analyzed. Serum fT3, fT4 & TSH levels were measured by electrochemo-luminescence-immunoassay (Cobas E411, Roche). Cystatin C was measured by Turbidimetric immunoassay (Turbodyne SC,Tulip) with a reference range from 0.50 to 1.16 mg/L.

Statistical analysis

SPSS 16.0 was used for data analysis. Variables were presented as mean ±SD. Independent sample t-test was used to determine the statistical significance. A P-value of <0.05 was accepted as statistical significance and P-value of <0.01 was considered as highly significant.

results

Total of 22 patients with subclinical hypothyroidism were included in the study. Mean TSH in patients with subclinical hypothyroidism was 20±12.00 at diagnosis. Serum Cystatin C levels were decreased in cases when compared to control, which is highly significant(<0.001).

Table 1: Showing age in cases and control.

VARIABLE	CASES (subclinical hypothyroid)	CONTROL	P-VALUE
AGE (years)	36.91±12.84	39.64±7.76	0.40

Table 2: Serum Thyroid hormone levels in cases and control.

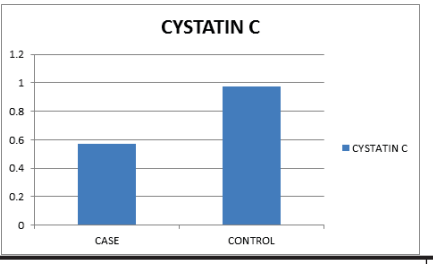
PARAMETER	CASES (subclinical hypothyroid)	CONTROL	P-VALUE
fT3 (2.0-4.4 pg/ml)	2.85±0.50	3.11±0.69	0.16
fT4 (0.93-1.7 ng/dl)	1.12±0.11	1.19±0.15	0.09
TSH (0.27-4.2 µIU/ml)	20.072±17.329	2.417±1.22	<0.001**

Table 3: Serum Cystatin C levels in cases and control.

VARIABLE	CASES (subclinical hypothyroid)	CONTROL	P-VALUE
CYSTATIN C	0.56±0.04	0.97±0.06	<0.001**

****HIGHLY SIGNIFICANT AT 0.001 LEVEL**
***SIGNIFICANT AT 0.05 LEVEL**

MEAN COMPARISON OF CYSTATIN C IN CASE AND CONTROL



DISCUSSION:

Many studies have shown that Cystatin C levels are affected in overt thyroid dysfunction like hypothyroidism and hyperthyroidism. Very few studies have evaluated the Cystatin C levels in subclinical hypothyroidism. During our present evaluation on serum Cystatin C in cases have showed significantly decreased level and has indicated the magnitude of impact of thyroid hormones on Cystatin C. This is in agreement with the study by peter wiesli et al[8]. Peter wiesli et al have also demonstrated that, changes in Cystatin C levels are reversible in subclinical hypothyroidism, as Cystatin C values came to normal levels in the same patients after treating the cases to attain euthyroid state. Others have demonstrated the same effect in overt hypothyroidism also [9,10,11].

N Kotajima et al have tried to elucidate the mechanisms involved in the regulation of Cystatin C concentration in thyroid dysfunction by studying the effects of 3,5,3'-tri-iodothyronine (T3) and TGF-β1 on Cystatin C production in cultured human hepatoblastoma (Hep G2) cells[12]. These cells are known to express nuclear T3 receptor & TGF-β1 receptors[13,14]. And their results appear to be the first to note that , T3 stimulated Cystatin C production in Hep G2 cells in a dose dependent manner in vitro[12].

Until now, one of the most appealing aspects of using Cystatin C as a marker of GFR has been the apparent lack of influence of medical conditions on its clinical utility, with only debate being whether Cystatin C concentrations are influenced by some metastatic malignancies or after renal transplantation [10,15,16].

Conclusion:

Our study has shown the impact of subclinical hypothyroidism of Cystatin C levels, which was significant. So it is advisable to know the thyroid status of an individual when Cystatin C is measured to know the GFR in the absence of other specific markers. More studies are required to find the better marker than Cystatin C for kidney function or we have to evaluate the possibility of using the correction factor in calculating the GFR in thyroid dysfunction.

References:

1. Burtis CA, Ashwood ER & Bruns DE, editors. Tietz fundamental of clinical chemistry 6th ed. Missouri: Elsevier Saunders; 2008, p639.
2. Abrahamson M, Olafsson I, Palsdottir A, et al: Structure and and expression of the Human cystatinC gene. Biochem J 1990;268:287–294,.
3. Randers E, Erlandsen EJ: Serum cystatin C as an endogenous marker of the renal function–a review. Clin Chem Lab Med 1999;37:389–395.
4. Keevil BG, Kilpatrick ES, Nichols SP, Maylor PW: Biological variation of cystatin C: Implications for the assessment of glomerular filtration rate. Clin Chem 1998;44:1535–1539, .
5. Vinge E, Lindergard B, Nilsson-Ehle P, GrubbA: Relationships among serum cystatin C, serum creatinine, lean tissue mass and glomerular filtration rate in healthy adults. Scand J Clin Lab Invest 1999;59:587–592.
6. Laterza OF, Price CP, Scott MG. Cystatin C : An improved estimator of glomerular filteration rate? Clin Chem 2002; 48(5): 699-707.
7. Newman DJ. Cystatin C. Ann Clin Biochem 2002; 39(2): 89-104.
8. Peter W, Beat S, Giatgen AS, Christoph S. Serum cystatin C is sensitive to small changes in thyroid function.Clinica Chimica Acta 2003; 338: 87-90.
9. Manuel F, Peter W, Michael B, Beat S. Impact of thyroid dysfunction on serum cystatin C. Kidney International 2003;63:1944-1947.
10. Jayagopal, Brain GK, Stephen LA, Paul EJ Eric SK. Paradoxical changes in Cystatin C and serum creatinine in patients with hypo- and hyperparathyroidism.Clinical Chemistry 2003;49(4):680-681.
11. Jan G.den H, Raymond WW, Mart JM, Arie B. Is Cystatin C a marker of glomerular filteration rate in thyroid dysfunction. Clinical Chemistry 2003;49(9):1558-1559.
12. N Kotajima et al. Influence of thyroid hormones and transforming growth factor-β1 on Cystatin C concentrations. The Journal of International Medical Research 2010;38:1365-1373.
13. Ichikawa K, DeGroot LJ: Thyroid hormone receptors in a human hepatoma cell line: multiple receptor forms on isoelectric focusing.Mol Cell Endocrinol 1987; 51:135 – 143.
14. Inagaki M, Wang Z, Carr BI: Transforming growth factor β1 selectively increases gene expression of the serine/threonine kinase receptor 1 (SKR1) in human hepatoma cell lines. Cell Struct Funct 1994; 19: 305 – 313.
15. Newman D. More on cystatin C. Clin Chem 1999; 45:2556–7.
16. Bokenkamp A, Domanetzki M, Zinck R, Schumann G, Byrd D, Brodehl J.Cystatin C serum concentrations underestimate glomerular filtration rate in renal transplant patients. Clin Chem 1999;45:1866–1868.