Increased Levels of Serum Cystatin C with Body Mass Index

ABSTRACT

Obesity is a major causative factor for many metabolic disorders and premature deaths in developing countries. The risk of many diseases like diabetes mellitus, cardiovascular disease, hypertension, hyperlipidemia, and cancers increases many folds in association with obesity. Cystatin C, though considered a renal marker, is associated with obesity irrespective of gender. Cystatin C mRNA is expressed in subcutaneous and omental adipose tissue, at twice higher levels in non-adipose than in adipose cells. The present study was conducted in the Department of Biochemistry, M.M. Institute of Medical Sciences and Research, Mullana, Ambala in which the levels of serum cystatin C were estimated in 100 healthy individuals in the age range of 17 years and above of either sex. All the 100 subjects included in the study were divided further into the suitable groups according to their body mass index and age. It was observed that serum cystatin C levels increase with the increase in BMI in both the age groups. These observations suggest a role for adipose tissue as a contributor to circulating concentration of cystatin C.

KEYWORDS obesity, cystatin C, body mass index, age

INTRODUCTION

Obesity and overweight are the fifth leading risk for global deaths. It is a major causative factor for many metabolic disorders and premature deaths in developing countries, which has been attributed to changes in the lifestyle and diet. The risk of many diseases like diabetes mellitus, cardiovascular disease, hypertension, hyperlipidemia, and certain cancers increases many folds in association with obesity1. According to a global estimate by the World Health Organization (WHO), in 2014, there were 1.9 billion overweight persons aged 18 years and above. Of these overweight adults, over 600 million were obese1. Cystatin C is an important extra- and transcellular inhibitor and its monomeric form is present in all human body fluids. It is especially abundant in cerebrospinal fluid, seminal fluid, milk, synovial fluid, saliva, tears, urine, and blood plasma. The human cystatin family presently comprises of 11 identified proteins. Two of these, cystatin A and B, form the family 1 Cystatin and are mainly intracellular proteins, while cystatin C, D, E, F, S, SA and SN are mainly extracellular and/or transcellular proteins and constitute the family 2 Cystatins. The family 3 Cystatins, high- and low-molecular weight kininogen, contain three cystatin domains and are mainly intravascular proteins, which in addition to being inhibitors of cysteine proteases also are involved in the coagulation process and in the production of vasoactive peptides4. The concentration of serum cystatin C in healthy adult individuals ranges between 0.8–1.2 mg/l depending upon the analytical method used4. Serum cystatin C is elevated in obese adults and children of both genders4. Cystatin C mRNA is expressed in subcutaneous and omental adipose tissue, at twice higher levels in non-adipose than in adipose cells5.

MATERIALS AND METHODS

The present study was conducted in the Department of Biochemistry, M.M. Institute of Medical Sciences and Research, Mullana, Ambala in which the levels of serum cystatin C were estimated. 100 healthy individuals in the age range of 17 years and above of either sex were selected for the study. They were further divided equally into two age groups, i.e. 17–49 years and 50 years and above. All 100 subjects included in the study were divided into

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the suitable groups according to their BMI as per the criteria mentioned below (Table 1).

Serum obtained from 3 ml of blood drawn from ante-cubital vein under aseptic conditions was taken. Informed consent was taken from the participants included in the study. Serum Cystatin C estimation was done by enzyme-linked immunoabsorbent assay (ELISA) as described by Pergande M8.

RESULTS

Table 2 shows comparison of serum cystatin C levels in non-obese and obese subjects of both the age groups. It was found that serum cystatin C level in non-obese group was 0.507 ± 0.239 mg/l while in obese group, it was 0.780 ± 0.404 mg/l and P-value was 0.006 (very significant) in 17–49 years age group. But when comparison was made in 50 years and above age group, the serum cystatin C levels in non-obese group was 0.753 ± 0.391 mg/l, and in obese group, it was 0.978 ± 0.415 mg/l and the P-value was 0.058, which is statistically not significant.

On further comparing the serum cystatin C level in non-obese subjects of both the age groups, the P-value was 0.010 (very significant). But when the comparison of serum cystatin C level was made within obese subjects of both the age groups, P-value was 0.100, which is not significant.

Table 3 shows a comparison of BMI in non-obese and obese subjects of both the age groups. In either age groups, the P-value was <0.001, which is highly significant.

On further comparing BMI in non-obese subjects in both the age groups, the P-value was 0.858 (non-significant). Similar results were obtained when comparison of BMI was made within obese subjects of both the age groups (P = 0.851, not significant).

Table 4 shows that serum cystatin C is positively correlated with body mass index (r = 0.339, P-value < 0.05).

DISCUSSION

It was observed that serum cystatin C levels increase with the increase in BMI in both the age groups but was not significant in 50 years and above group (Fig. 1). This could be due to small sample size. These observations suggest a role for adipose tissue as a contributor to circulating concentration of cystatin C. Similar findings were observed by other researchers in their studies4,9. A moderate but biologically insignificant correlation between BMI and cystatin C has been reported10. Our results are generally in agreement with Knight et al., who have reported that serum cystatin C levels do appear to be influenced by multiple factors including greater

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Table 1: Classification of weight status as per BMI7.

<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>Underweight</th>
<th>Healthy weight</th>
<th>Overweight</th>
<th>Obesity class I</th>
<th>Obesity class II</th>
<th>Obesity class III (extreme obesity)</th>
</tr>
</thead>
<tbody>
<tr>
<td>&lt;18.5</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
<td>25</td>
</tr>
</tbody>
</table>

Table 2: Comparison of serum cystatin C level in non-obese and obese subjects of different age groups.

<table>
<thead>
<tr>
<th>Age group</th>
<th>Category according to BMI</th>
<th>N</th>
<th>Serum cystatin C range (mg/l)</th>
<th>Mean serum cystatin C (mg/l)</th>
<th>Standard deviation</th>
<th>Standard error of mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>17–49 years</td>
<td>Non-obese</td>
<td>25</td>
<td>0.214–1.20</td>
<td>0.507</td>
<td>0.239</td>
<td>0.047</td>
<td>0.006**</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>25</td>
<td>0.226–1.59</td>
<td>0.780</td>
<td>0.404</td>
<td>0.080</td>
<td>0.058</td>
</tr>
<tr>
<td>50 years and above</td>
<td>Non-obese</td>
<td>25</td>
<td>0.217–1.69</td>
<td>0.753</td>
<td>0.391</td>
<td>0.078</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>25</td>
<td>0.450–1.91</td>
<td>0.974</td>
<td>0.415</td>
<td>0.083</td>
<td></td>
</tr>
</tbody>
</table>

*P-value < 0.05: significant, **P-value < 0.01: very significant, ***P-value < 0.001: highly significant.

Table 3: Group comparison of body mass index (BMI).

<table>
<thead>
<tr>
<th>Age group</th>
<th>Category according to BMI</th>
<th>N</th>
<th>BMI (kg/m²) (Mean ± SD)</th>
<th>Standard error of mean</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>17–49 years</td>
<td>Non-obese</td>
<td>25</td>
<td>22.81 ± 1.89</td>
<td>0.378</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>25</td>
<td>32.41 ± 3.42</td>
<td>0.685</td>
<td></td>
</tr>
<tr>
<td>50 years and above</td>
<td>Non-obese</td>
<td>25</td>
<td>22.71 ± 2.13</td>
<td>0.426</td>
<td>&lt;0.001***</td>
</tr>
<tr>
<td></td>
<td>Obese</td>
<td>25</td>
<td>32.25 ± 2.38</td>
<td>0.477</td>
<td></td>
</tr>
</tbody>
</table>

*P-value < 0.05: significant, **P-value < 0.01: very significant, ***P-value < 0.001: highly significant.

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Increased levels of serum cystatin C in relation with body mass index

CONCLUSION

Therefore, cystatin C, though conventionally considered a renal biomarker, shows significant correlation with age and BMI. Cystatin C adds to the list of adipose-secreted factors with the potential to affect adipose tissue biology and obesity-linked complications, and could be a predictor of cardiovascular disease and metabolic syndrome.

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COMPETING INTERESTS

This work was a part of the MD (Biochemistry Thesis) of Dr. Pallavi Mahajan at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala. The authors declare no conflict of interest.

REFERENCES