Concentration of Plasma Sialic Acid in the Offspring of One Type II Diabetic Parent

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Abstract

Sialic acid, oral glucose and plasma lipids were determined in 70 control subjects (age range 20-60) and 150 individuals of (age range 20-60) who were offspring of one type 2 diabetic parent. The number of first degree relatives who had impaired glucose tolerance were 50. The total sialic acid concentration was significantly higher (p<0.05) in the first degree relatives when compared to the control subjects. However the total sialic acid concentration was significantly higher in the offspring with normal glucose tolerance than in those with impaired glucose tolerance. There was no significant difference in the lipids between the control subjects and the offspring with normal glucose tolerance. But the total cholesterol and triglycerides were significantly higher in the offspring with impaired glucose tolerance when compared to the control subjects and the offspring with normal glucose tolerance. Our study shows that desialylation of the vascular endothelium is an early event that precedes the expression of impaired glucose tolerance or any lipid changes in asymptomatic offspring of one type 2 diabetic parent.

Introduction

Identification of diabetic patients at risk for accelerated vascular disease is a major challenge. In the majority of populations, both genetic and environmental influences interact to determine individual risk of NIDDM
(1). Subjects with non insulin dependent (Type 2) diabetes are at increased risk for the development of both macrovascular and microvascular complications. At that time of diagnosis, the existence of atherosclerotic manifestations is already widespread, in the NIDDM patients but the prevalence of coronary artery disease shows no correlation with the duration of diabetes (2). It is widely accepted that frank clinical NIDDM is preceded by a long prediabetic stage (3). Impaired glucose tolerance (IGT) is a widely accepted entity of the prediabetic stage and this period is associated with cardiovascular risk factors and insulin resistance commonly known as metabolic syndrome X. (4). It is even possible that NIDDM and CAD may share common antecedents (5). Therefore, it is possible that the prediabetic phase could be a period of enhanced cardiovascular risk. Although IGT is commonly believed to represent the transitional stage between normal and diabetic glucose tolerance and proved to be a risk factor for cardiovascular disease it is not a homogeneous condition Therefore it is of paramount importance to identify some definitive early markers to identify the people at high risk.

A primary role has been proposed for insulin resistance both in the etiology of the clustering of the cardiovascular factors and in the pathogenesis of atherosclerotic vascular disease (6). However this hypothesis takes no account of the central role of endothelium in the atherogenic process. What then is the relationship with insulin resistance syndrome? In this article we argue that endothelial dysfunction is not simply a consequence but a root cause of most features of the insulin resistance syndrome, in addition to playing a central role in atherogenesis. The principal cause of endothelial dysfunction is dyslipoproteinaemia and hyperoxidative stress.

Recent evidence shows that NIDDM is associated with an elevated acute phase response, particularly in those with features of syndrome X (7). If this be the case then the raised concentrations of proinflammatory cytokines and the resultant acute phase response may underlie much of the metabolic clustering including glucose tolerance (8). Sialic acid is a marker for acute phase proteins In this study we have shown that the total sialic acid concentration precedes the manifestation of IGT and lipid abnormalities in people at high risk group.

Methods

Healthy control subjects were randomly chosen from Klang valley, Kuala Lumpur. The offspring of at least one type2 diabetic parent were randomly recruited through the diabetic clinic, University of Malaya Medical Center, Kuala Lumpur and through the distribution of questionnaires.

The subjects were classified as having impaired glucose tolerance if the
fasting plasma glucose level was equal to greater than \( 6\) m.mol/l, and if the two hour plasma post glucose load value was between 7.8 and 11 m.mol/l, or as having normal glucose tolerance if the fasting level was less than \( 6 \geq \) m mol/l and two hour plasma glucose load values were less than 7.8 m mol/l according to the criteria of World Health Organisation. None of the subjects received hypolidemic drug therapy, or had any renal, hepatic or thyroid disease affecting glucose and lipid metabolism.

The lipids were determined using the individual biochemical kits supplied with Dimension R clinical chemistry system (Dode Behring, France) and the low density lipoprotein was determined by Friedewald equation (9). Sialic acid was determined by the modification of the Periodate-Resorcinol method as described by Jourdian et al. (10).

### Results

#### Table 1 Sialic acid concentrations

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Total sialic acid concentration</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals</td>
<td>60</td>
<td>1.97±0.25</td>
<td>* &lt; 0.05</td>
</tr>
<tr>
<td>IGT Offspring</td>
<td>35</td>
<td>2.43±0.35</td>
<td>** &lt; 0.05</td>
</tr>
<tr>
<td>Non-IGT Offspring</td>
<td>115</td>
<td>3.34±0.6</td>
<td></td>
</tr>
</tbody>
</table>

*there was a significant difference between the normals and the offspring (P < 0.05) **there was a significant difference between the offspring IGT and offspring Non-IGT (P < 0.05)

#### Table 2 Plasma lipid levels

<table>
<thead>
<tr>
<th>Subjects</th>
<th>n</th>
<th>Total chol</th>
<th>LDL</th>
<th>HDL</th>
<th>Trig</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normals</td>
<td>60</td>
<td>5.20±0.90</td>
<td>3.22±0.91</td>
<td>1.36±0.35</td>
<td>1.04±0.5</td>
<td></td>
</tr>
<tr>
<td>Offspring Non-IGT</td>
<td>115</td>
<td>5.46±0.97</td>
<td>3.56±0.91</td>
<td>1.40±0.32</td>
<td>1.20±0.6</td>
<td></td>
</tr>
<tr>
<td>Offspring IGT</td>
<td>35</td>
<td>*6.02±1.0</td>
<td>3.85±0.98</td>
<td>1.27±0.35</td>
<td>*1.99±1.2</td>
<td>&lt; 0.05</td>
</tr>
</tbody>
</table>

*The total cholesterol and triglycerides were significantly higher in the offspring with impaired glucose tolerance as compared to the normals and the offspring with normal glucose tolerance (non-IGT).
Discussion

In this study, the plasma lipid status and the plasma sialic acid concentration were evaluated for individuals who are genetically at high risk for developing diabetes but who presently do not demonstrate overt diabetes. Of major importance in our study is the alteration in the total cholesterol and triglycerides in the subjects with mild impaired glucose tolerance. Despite the heterogeneity within type2 diabetes the offspring of one type2 diabetic parent with normal glucose tolerance revealed virtually identical lipid profiles with normal controls with no family history of diabetes.

The novel finding in this study was that the offspring from one type2 diabetic parent had significantly higher levels of sialic acid than the control subjects with no family history of diabetes. However the interesting finding is that among the offspring the plasma sialic acid concentration was significantly higher in the subjects with normal glucose tolerance than in the offspring with impaired glucose tolerance. One plausible explanation is that the LDL particles in the subjects with impaired glucose tolerance is desialylated and partly glycosialylated. The glycosialylated particles are known to have an increased catabolism as compared to the other LDL particles.

Conclusion

Our study shows that endothelial dysfunction precedes any other metabolic disturbances in the subjects who are at high risk for type2 diabetes with no overt diabetes.

Acknowledgements

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References

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