PREVALENCE OF GLUCOSE ABNORMALITIES IN HTLV-I CARRIERS IN MASHHAD, NORTHEAST IRAN

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SUMMARY

The possible role of some viral infections in the pathogenesis of type 1 diabetes (T1DM) has been postulated. There is increasing evidence for the viral etiology of type 2 diabetes mellitus (T2DM). Human T cell leukemia virus type 1 (HTLV-I) is endemic in some areas of the world. It is also endemic in Mashhad, northeast Iran. The objective of the present study was to estimate the prevalence of glucose abnormalities in HTLV-I carriers in Mashhad. A total of 177 HTLV-I carriers older than 20 years were compared with 220 sex-, age- and BMI-matched controls without the infection. Blood samples were collected in fasting state and assayed for serum glucose. We also compared the results on the prevalence of glucose abnormalities in the general population of Mashhad, obtained in a large study. The prevalence of glucose abnormalities was significantly higher in HTLV-I carriers than in controls (10.16% vs. 5% for diabetes and 25.98% vs. 6.36% for impaired fasting glucose, P<0.05). The prevalence of glucose abnormalities was also significantly higher from the prevalence recorded in a large epidemiologic study performed in Mashhad. In conclusion, the prevalence of glucose abnormalities was significantly higher in HTLV-I carriers than in controls. HTLV-I infection may increase the risk of diabetes.

INTRODUCTION

The possibility of viral-induced autoimmunity or molecular mimicry in the pathogenesis of type 1 diabetes (T1DM) has been shown in infants with the congenital rubella syndrome (1,2). In addition, other viral agents such as coxsackie virus and cytomegalovirus have been proposed as being capable of triggering the development of T1DM (3,4). There also is increasing evidence for the viral etiology of type 2 diabetes mellitus (T2DM). Recent epidemiologic studies have shown that hepatitis C virus (HCV) infection may increase the risk of T2DM. A 2- to 10-fold increase in diabetes has been reported worldwide in HCV-positive patients (5-11). Human T cell leukemia virus type 1 (HTLV-I), a human retrovirus, is the cause of adult T cell leukemia (12) and is related to HTLV-I associated
myelopathy/tropical spastic paraparesis (13,14), uveitis (15), chronic arthropathy (16), pulmonary alveolitis (17), Sjögren’s syndrome (18) and Hashimoto thyroiditis (19,20). HTLV-I is endemic in southern Japan, intertropical Africa, Melanesia, Latin America, and the Caribbean basin (21). It is also endemic in Mashhad, northeast Iran (22,23). Recently, we demonstrated the high prevalence of HTLV-I infection in diabetic patients (24). The objective of the present study was to estimate the prevalence of glucose abnormalities in HTLV-I carriers in Mashhad.

MATERIALS AND METHODS:

A total of 177 carriers of HTLV-I, older than 20 years of age were referred for evaluation from January 2007 to March 2009. All patients were Iranian living in Mashhad (HTLV-I endemic areas), northeast of Iran. The presence of HTLV-I infection in these patients was assessed by testing for serum HTLV-I specific antibodies after blood donation or in routine check up investigations and was confirmed by Western blot test. The subjects were interviewed by using a questionnaire that collected information on medical history. Anthropometric measures were calculated and body mass index (BMI) was computed as weight in kilograms divided by height in square meters (kg/m²).

Blood samples were collected in fasting state and assayed for serum glucose (Liasys, Italy).

The subjects were compared with 220 sex-, age- and BMI matched controls without infection. We also compared the results with the prevalence of glucose abnormalities in the general population of Mashhad, performed in a large sample (3778 persons) of the population (25).

According to the American Diabetic Association criteria (26), a fasting blood sugar (FBS) < 100 mg/dL was considered as normal; values between 100 and 126 mg/dL, and those > 126 mg/dL were considered as impaired fasting glucose (IFG) and diabetes mellitus, respectively. Statistical analysis was done using the Statistical Package for Social Sciences version 11.5 (SPSS Inc, Chicago, IL, USA).

RESULTS

The study included 177 patients, 125 (70.6%) male and 52 (29.4%) female, age range 20 to 70 years, 18 (10.16%) of them with diabetes mellitus (12 male and 6 female), age range 30-64; and 46 (25.98%) with IFG (33 male and 13 female), age range 21-60 (Table 1).

Table 1. Comparison between infected non infected diabetic patients

<table>
<thead>
<tr>
<th></th>
<th>Infected with HTLV-I</th>
<th>Control</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>177</td>
<td>220</td>
</tr>
<tr>
<td>Male/female</td>
<td>125/52</td>
<td>142/78</td>
</tr>
<tr>
<td>Age (yrs)</td>
<td>55±4.59</td>
<td>54.34±11.78</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>27.46±7.23</td>
<td>28.04±4.91</td>
</tr>
<tr>
<td>Diabetes</td>
<td>18</td>
<td>11</td>
</tr>
<tr>
<td>Impaired fasting</td>
<td>46</td>
<td>14</td>
</tr>
</tbody>
</table>

The prevalence of glucose abnormalities was significantly higher in HTLV-I patients than in controls (10.16% vs. 5% for diabetes and 25.98% vs. 6.36% for impaired fasting, P<0.05). The mean age was not significantly different between the subjects with and without glucose abnormalities (41 years in abnormal fasting glucose subjects and 41.39 in normal fasting glucose subjects).

On the basis of an extensive study performed in Mashhad (25), a total of 5.5% of persons aged 15 years had diabetes and 2.5% IFG. The prevalence of glucose abnormalities was also significantly higher in HTLV-I patients than in normal population.

DISCUSSION

The possible role of some viral infections in the pathogenesis of type 1 diabetes (TIDM) has been shown (1,2). Also there are an increasing number of reports that support an infectious etiology for a variety of autoimmune, neoplastic, neurologic and psychiatric conditions as well as nutritional disorders such as type
2 diabetes (T2DM) and obesity. Cross-sectional studies performed worldwide have shown that hepatitis C virus infection is linked with T2DM (5-11). Recently we showed a high prevalence of HTLV-I infection in diabetic patients (24), and in the present study we evaluated the prevalence of glucose abnormalities in HTLV-I carriers.

Although the precise mechanisms involved in the development of glucose intolerance in viral infections are not well understood, several mechanisms have been proposed for the development of diabetes. Viral encoded proteins may cause post-receptor defects in insulin receptor substrate 1 (IRS-1) or insulin signaling defects in hepatic IRS-1 tyrosine phosphorylation and phosphatidylinositol 3-kinase activation, which may contribute to the development of insulin resistance and subsequent development of T2DM following HCV infection (27). High serum levels of inflammatory cytokines like tumor necrosis factor alpha in viral infections may induce insulin resistance (28). Viruses may also induce a direct cytopathic effect at the islet cell level and this is accompanied by β-cell dysfunction (29). Viral infections may also induce antibodies that would destroy pancreatic islet cells as seen in type 1 diabetes (30).

Recently, glucose transporter 1 (GLUT-4), a member of the multimembrane-spanning facilitative nutrient transporter family, has been introduced as a receptor for both HTLV-1 and HTLV-2. It has been shown that the cell glucose metabolism alters after expression of either full-length envelope or the receptor binding domain of the virus (31). This correlation of virus entrance pathway with glucose metabolism may be a matter of future investigation.

Our major finding in the present study was that persons with HTLV-I infection had a significantly higher prevalence of diabetes and IFG than those without infection.

This study had some limitations. First, other risk factors for diabetes, such as family history and physical activity, and socioeconomic status were not studied. Second, the small sample size limited the precision of estimated prevalence and the statistical power of the tests. Additional studies are needed to clarify the relationship between viruses and diabetes.

CONCLUSION

We found an increased prevalence of diabetes and IFG among carriers of HTLV-I. Regular diabetes screening for anti- HTLV-I positive persons is indicated. Further investigation is needed to establish temporal relationship between HTLV-I infection and diabetes and to identify the biological mechanisms involved.

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