Prevalence of Candida Infection in Patients with Type 2 Diabetes Mellitus in Sari, North of Iran

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ABSTRACT

Most physicians believe that patients with type 2 diabetes mellitus are predisposed to various infections. Candidiasis is one of the most common infectious diseases that can complicate the control of the diabetes. The aim of this study was to determine the prevalence of candidiasis in patients with type 2 diabetes mellitus. A total of 88 patients with type 2 diabetes mellitus were participated in this study. Enzyme-linked immunosorbent assay was used for detection of IgG, IgM, and IgA antibodies against C. albicans in sera of participants. The serum total cholesterol, triglyceride, lipoproteins, and glucose levels were measured by an enzymatic method with standard kits made of Pars Azmun Co. Iran. Chronic candidiasis (IgG level more than 30 U/ml) and acute candidiasis (IgM level more than 10 U/ml) were seen in 63.6% and 17% of the patients, respectively. The percentage of patients with IgA level more than 10 U/ml was 2.3%. Statistically, a significant inverse relationship was observed between the levels of IgG and IgM antibodies against Candida and HDL-C level, P=0.038. The results of this study proved that a large percentage of patients with type 2 diabetes mellitus suffering from chronic candidiasis and acute candidiasis. Moreover, HDL-C may have a role in preventing candidiasis.

Key words: Antibody; candidiasis; diabetes mellitus.

INTRODUCTION

Candida species are the most important commensal yeasts on the skin and mucosal surfaces of the 20%-50% humans¹. Patients with type 2 diabetes mellitus are at an increased risk of having opportunistic infections, including oral, vaginal and urinary tract candidiasis²-⁴. In order to evaluate of candidiasis, all studies have evaluated the Candida colonization in patients with type 2 diabetes mellitus and have provided different results⁵-⁷. Candida species can colonize healthy people⁸. So isolation of Candida species alone cannot confirm candidiasis⁹. In addition, these yeasts can colonize various sites of the body and it is very difficult to evaluate all these sites⁷. Evaluation of specific antibodies against Candida can confirm candidiasis in various sites of the body in patients with type 2 diabetes mellitus. On the other hand, level of antibodies in healthy subjects and in patients with candidiasis is well known⁶. So antibody measurement in patients with type 2 diabetes mellitus is not needed to be compared with control group. Moreover, detection of specific antibodies can determine acute and chronic candidiasis. Therefore, this study was designed to investigate the production of IgM, IgG and IgA antibodies against Candida albicans in patients with type 2 diabetes mellitus.
MATERIAL AND METHOD

Patients
Eighty-eight patients with type 2 diabetes mellitus from March 2014 to January 2015 were enrolled in the cross-sectional study. All the individuals participated voluntarily and signed a consent form approved by the Human Ethics Committee of Mazandaran University of Medical Sciences, Sari, Iran. People who had diabetic nephropathy and those who had used broad spectrum antibiotics, antifungal drugs, alcohol, and steroids as well as pregnant patients and smoking patients were excluded from the study.

Detection of anti- C. albicans antibodies
In order to serological testing, after a 14 h fasting period, 5 ml of venous blood samples were taken in sterile tubes and sera were separated by centrifugation (3000 rpm for 5 min) and stored frozen at -70°C until analysis.

Enzyme-linked immunosorbent assay [ELISA] test kits [GENESIS-Diagnostic, England] were used to measure titers of IgA, IgG and IgM antibodies against C. albicans in sera of patients with type 2 diabetes mellitus. According to the manufacturer’s instructions, patients’ sera were diluted 1:200 in sample diluents. 100 µl of each standard, positive control and the diluted samples were dispensed into appropriate wells of microplate coated with purified antigens of C. albicans. After being incubated for thirty min at room temperature, the wells content were decanted and washed three times by an automatic ELISA washer [Washer MPW1, SCO Diagnostic Co, Germany]. One hundred µl of Conjugate was added to each well and incubated for thirty min at room temperature. The wells of microplate were washed four times and 100 µl of TMB [3, 3', 5, 5'-tetramethylbenzidine] substrate was dispensed into each wells before being incubated for ten min at room temperature. The reaction was stopped by addition of one hundred µl of stop solution and the absorbance at 450 nm was read using an automated plate reader [Bio-Rad 680, Bio-Rad Co., Hercules, USA]. According to the manufacturer’s instructions, patients with IgA and IgM values above 10 U/ml and IgG values above 30 U/ml are to have had a recent or current candida infection.

Evaluation of glucose and lipid profile
The serum total cholesterol, triglyceride, high density lipoprotein [HDL-C] and FBS [fasting blood sugar] were measured by an enzymatic method with standard kits made of Pars Azmun Co. Iran. Vary low density lipoprotein [VLDL-C] and low density lipoprotein [LDL-C] values were calculated according to the following formulas: VLDL-C = triglyceride/5 and LDL-C= total cholesterol – [VLDL-C+HDL-C]. Glycosylated hemoglobin [HbA1c] was quantified through the Bayer DCA-2000 method [specific monoclonal antibody methodology for the A1c fraction] (8). Results were analyzed using descriptive statistics and Pearson’s test.

RESULTS
In this study, 88 patients (15 male and 73 female; age range between 30–74 years; age mean 53.94 ± 9.09 years) were examined. The characteristics of patients are listed in Table 1. The mean levels of IgM, IgG and IgA against Candida in patients with type 2 diabetes mellitus were 5.45 U/ml, 36.1 U/ml and 2.56 U/ml, respectively. 63.6% of patients showed IgG level more than 30 U/ml. Seventeen percent of patients showed IgM level more than 10 U/ml. 2.3% of patients showed IgA level more than 10 U/ml. There were no significant relationship between the level of antibodies and levels of total cholesterol, VLDL-C, LDL-C, triglyceride, glucose and HbA1c, P> 0.05. Statistically, a significant inverse relationship was observed between the levels of IgG and IgM antibodies against Candida and HDL-C level, P=0.038

Table 1: Characteristics of patients with type 2 diabetes mellitus (n=88)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean ± SD</th>
<th>Min–Max</th>
</tr>
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<tbody>
<tr>
<td>Age</td>
<td>53.94 ± 9.09</td>
<td>30-74</td>
</tr>
<tr>
<td>Disease duration</td>
<td>4.24 ± 3.01</td>
<td>1-14</td>
</tr>
<tr>
<td>FBS</td>
<td>133.11 ± 39.71</td>
<td>69-378</td>
</tr>
<tr>
<td>HbA1c</td>
<td>1.82 ± 0.38</td>
<td>5.1-12.2</td>
</tr>
<tr>
<td>Triglyceride</td>
<td>156.31 ± 59.84</td>
<td>76-329</td>
</tr>
<tr>
<td>Total cholesterol</td>
<td>173.91 ± 31.04</td>
<td>107-274</td>
</tr>
<tr>
<td>HDL-C</td>
<td>47.92 ± 13.48</td>
<td>27-101</td>
</tr>
<tr>
<td>LDL-C</td>
<td>91.64 ± 27.57</td>
<td>44-235</td>
</tr>
<tr>
<td>VLDL-C</td>
<td>31.22 ± 11.96</td>
<td>15.2-65.8</td>
</tr>
</tbody>
</table>
DISCUSSION

In the present study, chronic candidiasis and acute candidiasis were seen in 63.6% and 17% of the patients, respectively. In Suárez et al.'s study, Martinez et al.'s study, and Pallavan et al.'s study, colonization was seen in 71%, 41.1% and 43.3% of type 2 diabetes mellitus patients, respectively. Previous studies have examined only the rate of Candida colonization in patients with type 2 diabetes mellitus. Isolation of Candida species cannot confirm candidiasis, however, since Candida species are often part of the normal mucosal flora. In addition, against other studies, we distinguished chronic candidiasis from acute candidiasis. There have been previous reports of increased total IgA concentration in diabetic patients. But in our study increased concentration of IgA specific Candida was seen only in 2.3% of patients. It seems that patients with type 2 diabetes mellitus cannot produce suitable level of IgA specific Candida. So evaluation of IgA level is not proper for candidiasis determination. In the present study, the level of antibodies were not correlated with glucose and A1c level, suggesting that there are other reasons for the candidal infections in patients with type 2 diabetes mellitus. In the present study, a significant inverse correlation was observed between the HDL-C level and levels of both IgG and IgM for the first time. This finding suggests HDL-C can prevent candidiasis. Previous studies have shown that HDL-C can prevent the viral, bacterial, and parasitic infections.

It is known that HDL-C plays critical roles in the immune system, including the modulation of complement system and the expression of pentraxin 3 as well as modulation of antigen presentation function in antigen presenting cells (APCs). Therefore reduction of HDL-C level could have a role in candidal infection in patients with type 2 diabetes mellitus.

CONCLUSION

In conclusion, this study proved that a large percentage of patients with type 2 diabetes mellitus suffering from candidiasis. Unlike other studies, the present study distinguished acute candidiasis from chronic candidiasis. In addition, the results of this study showed a significant inverse correlation between HDL-C level and levels of candida specific antibodies in the sera of patients with type 2 diabetes mellitus.

REFERENCES

8. Shephard MD, Gill JP. Results of an innovative education, training and quality assurance program for point-of-care HbA1c


