BRIEF ARTICLES

Association of hepatitis C virus infection and diabetes in central Tunisia

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Abstract

AIM: To investigate hepatitis C virus (HCV) seroprevalence in Tunisian patients with diabetes mellitus and in a control group.

METHODS: A cross-sectional study was conducted to determine the HCV seroprevalence in 1269 patients with diabetes (452 male, 817 female) and 1315 non-diabetic patients, attending health centers in Sousse, Tunisia. HCV screening was performed in both groups using a fourth-generation enzyme immunoassay.

RESULTS: In the diabetic group, 17 (1.3%) were found to be HCV-infected compared with eight (0.6%) in the control group, although the difference was not significant ($P = 0.057$). Quantitative PCR was performed in 20 patients. Eleven patients were positive and showed HCV genotype 1b in all cases.

CONCLUSION: Frequency of HCV antibodies was low in patients with diabetes and in the control group in central Tunisia, with no significant difference between the groups.

INTRODUCTION

In recent years, a positive association between hepatitis C virus (HCV) infection and diabetes mellitus (DM) had been reported in a number of clinical studies[1-4]. It is now clear that hepatitis C conveys a risk for developing DM, in particular type 2[5-7]. Moreover, several studies have found a high prevalence of anti-HCV antibodies among patients with diabetes, especially those with type 2 DM[8-13]; however, some authors have not observed an association between HCV infection and diabetes[14-16]. Since effective therapy has become available for HCV, it may be worthwhile to determine virus prevalence in patients with and without diabetes, in order to decide whether a programme for screening should also focus on type 2 diabetes. The aim of the present study was to investigate HCV seroprevalence in Tunisian patients with DM and in a control group.

MATERIALS AND METHODS

Patients

During March 2003, we conducted a cross-sectional study of all consecutive patients with diabetes aged > 16 years who were attending the Departments of Internal Medicine, Infectious Diseases and Endocrinology of Farhat Hached Hospital, and primary health care centers in the region of Sousse, Tunisia. Sample size calculation was

based on a 2% HCV seroprevalence estimation with an 80% precision rate and a 95% confidence level. The formula for sample size determination yielded a total of 1223 patients with diabetes. Types 1 and 2 diabetes were defined on the basis of a history of therapy with oral hypoglycemic agents or insulin at the date of inclusion. Patients older than 40 years of age, and treated by oral hypoglycemic agents or switched from insulin were considered to have type 2 diabetes. A control group of non-diabetic patients were recruited from the same centers at the same time. Patients who had corticosteroid-induced diabetes were excluded. Informed consent was obtained from all participants, and the study was approved by Farhat Hached Hospital ethics committee.

Data collection
Data were recorded by using a questionnaire that collected information on demographic and clinical features of DM and risk factors for HCV infection. Blood samples were collected from all patients for HCV serology. Those who were positive for anti-HCV antibodies were called, and liver function tests, glucose blood level, HCV quantitative RNA and HCV genotyping were performed.

Laboratory methods
Serological testing for anti-HCV antibodies was performed by using a fourth-generation ELISA (Murex; Abbot Laboratories, France) according to the manufacturer's instructions. HCV RNA qualitative and quantitative testing (Amplicor; Roche Molecular Systems, Branchburg, NJ, USA) and HVC genotyping were performed at Pasteur Cerba Laboratoire, Cergy Pontoise, France). HVC genotyping was performed by RT-PCR on a segment from the core region and by hybridization of this fragment with oligonucleotide-specific probes. The assay was designed to recognize the 1a, 1b, 2a, 2b, 3, 4, 5 and 6 HCV genotypes.

Statistical analysis
Data were analyzed, using SPSS version 13.0 software (Chicago, IL, USA). A descriptive analysis was followed by bivariate analysis using the χ^2 test for comparison of the two groups, with a 5% statistical significance level. A multivariate analysis with logistic regression was used to determine predictive variables associated with seroprevalence among the significant factors found by bivariate analysis. ORs and 95% CI were calculated for these variables.

RESULTS

Our study included 1269 patients with diabetes and 1315 non-diabetic patients. In patients with diabetes, 1148 (90.5%) and 121 (9.5%) had type 2 and type 1 DM respectively; 284 (22.5%) were treated by insulin. The mean duration of DM was 8.4 years (1-35 years). Furthermore, history of surgery and hospitalization, and scarification were found to be more frequent in patients

Table 1 Epidemiological features of the study population in patients with diabetes and control group *n* (%)

	Diabetes patients (*n* = 1269)	Control group (*n* = 1315)	*P*
Gender			
Female	817 (64.4)	890 (67.6)	0.06
Age			
Mean age (yr)	55.6	46.9	< 10^{-3}
Risk factors of HCV			
Transfusion	157 (12.5)	185 (14.2)	0.2
History of surgery	592 (46.8)	551 (42.1)	0.01
Drug addiction	2 (0.2)	7 (0.5)	0.17
Scarification	247 (19.8)	301 (23.1)	0.04
Endoscopic investigation	276 (21.9)	308 (23.6)	0.30
Alcoholism	164 (13)	178 (13.6)	0.65
History of hospitalization	875 (69.3)	785 (59.9)	< 10^{-3}
Anti-HCV antibodies (+)	17 (1.3)	8 (0.6)	0.057

Table 2 Epidemiological features of the study population in type 2 DM patients and control group *n* (%)

	Type 2 DM patients (*n* = 1148)	Control group (*n* = 1315)	OR	*P*
Gender				
Female	739 (65.2)	890 (67.6)	0.8 (0.73-1.2)	0.06
Age				
Mean age (yr)	57 ± 10.4	46.9		< 10^{-3}
Risk factors of HCV				
Transfusion	136 (12.1)	185 (14.2)	0.83 (0.65-1.06)	0.2
History of surgery	528 (46.7)	551 (42.1)	1.18 (1.05-1.39)	0.01
Drug addiction	2 (0.2)	7 (0.5)	0.33 (0.05-1.78)	0.17
Scarification	222 (19.8)	301 (23.1)	0.81 (0.66-0.99)	0.04
Endoscopic investigation	248 (22)	308 (23.6)	0.90 (0.74-1.09)	0.30
Alcoholism	144 (12.8)	178 (13.6)	0.92 (0.78-1.17)	0.65
History of hospitalization	758 (67.1)	785 (59.9)	1.31 (1.11-1.55)	< 10^{-3}
Anti-HCV antibodies (+)	16 (1.4)	8 (0.6)	2.31 (1.01-5.90)	0.04

with diabetes. Patients in the control group were much younger than those with diabetes; the main demographic and clinical characteristics of both groups are shown in Table 1.

Antibodies against HCV were detected in 25 patients (1%) among the entire population studied (both diabetic and non-diabetic groups). In the diabetes group, 17 (1.3%) were found to be infected with HCV compared with eight (0.6%) control patients. No significant difference was found between DM patients and the control group ($P = 0.057$) (Table 1). Moreover, anti-HCV seropositivity was detected in 16 (1.4%) of the type 2 DM sub-group, which was significantly higher than that in the control group ($P = 0.04$) (Table 2). However, in multivariate analysis, this difference between seroprevalence of HCV in type2 DM and controls was not confirmed.

Quantitative PCR was performed in 20 patients: 13 with diabetes and seven without, was and a positive result

was obtained in eight and three patients, respectively. All patients were infected by genotype 1b HCV. All non-diabetic patients who were positive for HCV antibodies underwent liver function and blood glucose testing, but no new DM was discovered.

DISCUSSION

To the best of our knowledge, this is the first study in which HCV infection prevalence was evaluated in Tunisian patients with diabetes. Similar to blood donors in whom anti-HCV antibodies were low (0.5%-1.8%)[17-21], in our study HCV infection prevalence in the diabetes, type 2 DM, and control groups was 1.3%, 1.4% and 0.6%, respectively. Despite a high frequency of scarification, history of surgery and hospitalization in patients with diabetes and the type 2 DM subgroup, circumstances which increase risk of HCV infection, prevalence of anti-HCV antibodies was not significantly more frequent in the diabetes group ($P = 0.057$). Moreover, comparing type 2 DM patients to the control group, although a significant difference in HCV infection prevalence was observed in type 2 DM patients ($P = 0.04$), this was not confirmed by logistic regression analysis. Therefore, we cannot establish the diabetic population as a group at high risk for HCV infection. Our findings did not confirm other studies that have reported increased HCV seroprevalence in patients with diabetes[10,22-26]. In a case-control study conducted in the USA, 4.2% of 594 patients in a cohort with diabetes were found to be infected with HCV compared with 1.6% of control patients (377 patients with thyroid diseases)[27]. Other studies have reported an increased HCV seroprevalence, varying from 8% to 11% in European diabetic populations compared with 1%-2% HCV seroprevalence in the general population[10,28-30]. However, in a descriptive Greek study of patients with diabetes without a control group, HCV antibodies were detected in only seven cases, and this prevalence (1.65%) was similar to that in the general population[14].

In conclusion, our study confirms a low prevalence of anti-HCV antibodies in Tunisian patients with diabetes, and may argue against diabetes as a risk factor of HCV infection in this area. Further studies, possibly multicenter, prospective and case-control, are needed to establish the temporal relationship between HCV infection and DM.

COMMENTS

Background
Several studies have found a high prevalence of anti-hepatitis C virus (HCV) antibodies among patients with diabetes mellitus (DM), especially those with type 2 DM. However, some authors have not observed an association between HCV infection and diabetes. Since effective therapy has become available for HCV, it may be worthwhile to determine the prevalence of HCV in patients with and without diabetes, to decide whether a programme for screening should also focus on type 2 diabetes patients.

Research frontiers
The literature is still contradictory about high prevalence of HCV infection in type 2 DM. The prevalence of HCV infection is still unknown in Tunisia. In this study, the authors demonstrated that this prevalence was similar in the general population.

Innovations and breakthroughs
The study confirmed a low prevalence of anti-HCV antibodies in Tunisian patients with diabetes, and may disprove diabetes as a risk factor for HCV infection in this area.

Applications
The low prevalence of HCV infection in type 2 DM in this study argues against the systematic assessment of HCV antibodies in this population.

Peer review
The present manuscript describes a comparative analysis of HCV prevalence in diabetic and non-diabetic populations in central Tunisia. Although its findings are negative, they are interesting because of the relatively large sample size. This is an interesting small epidemiological study on the association between diabetes and HCV prevalence in central Tunisia.

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