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# Prevalence of Type 2 Diabetes Mellitus and Dyslipidemia in Patients with Cryptogenic Cirrhosis: a Hospital-Based Study

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## Abstract

**Background:** Liver cirrhosis is the end stage of liver disease that is caused by various etiologies. Type 2 diabetes mellitus (T2DM), dyslipidemia and obesity are the most common situations that are seen together with non-alcoholic steatohepatitis (NASH), which is frequently asymptomatic and can silently lead to cirrhosis. There are some studies suggesting that NASH might be one of the underlying causes of cryptogenic cirrhosis (CC).**Materials and Methods:** Two hundred twenty six cirrhotic patients registered in transplantation unit of Namazi Hospital of Shiraz University of Medical Sciences from January 2006 to the last day of June 2014 were selected in two groups of CC and non-CC patients. Age, sex, weight, child class of cirrhosis and presence of T2DM, dyslipidemia and lipid profile were extracted from their records.**Results:** There was significant difference between prevalence of T2DM and FBS levels among CC and non-CC subjects ($P < 0.01$). Prevalence of T2DM in CC group (38.9%) was more than two times higher than non-CC group (18.6%). On the contrary, the differences between prevalence of dyslipidemia and its laboratory characteristics such as total cholesterol, TG, HDL and LDL were insignificant among both groups ($P > 0.05$). **Conclusion:** Results showed a higher prevalence of T2DM in subjects with CC but there are some doubts about T2DM being one of the risk factors of CC. Dyslipidemia and its components including TG, LDL, HDL and total cholesterol were not significantly different in CC and non-CC subjects.**[GMJ. 2015;4(3):112-16]**

**Keywords:** Type 2 Diabetes Mellitus; Dyslipidemia; Cryptogenic Cirrhosis

## Introduction

Liver cirrhosis is the end stage of liver disease that is caused by various etiologies. Despite recent progress in diagnosis, the underlying etiologies have not been detected in about 5-31% of cirrhotic patients being labeled as cryptogenic cirrhosis (CC) [1,2]. Although there are different explanations such as viral infections, alcohol abuse and autoimmune hepatitis as possible causes of CC, these are underlying causes of only some of the CC patients [3,4]. In recent years, with the diverse use of laboratory tests for hepatitis C virus (HCV), prevalence of CC has decreased to about 5%. Previous reports ranged from 10% to 30% [3].

Although the prevalence of silent autoimmune hepatitis in patients with CC is unknown, several studies have proposed a sig-

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nificant number of patients with CC that may have burnt-out autoimmune hepatitis [3,5]. Occult virus disease (Non-B, non-C hepatitis) is considered to be responsible for about 15% of post-transfusion hepatitis [6] and may exist in a silent form for several years [7].

The prevalence of type 2 diabetes (T2DM) is shown to be higher in patients who have certain liver diseases. There is a correlation between the presence of T2DM and the severity of liver damage. Liver diseases associated with T2DM include nonalcoholic fatty liver disease, chronic viral hepatitis, hemochromatosis, alcoholic liver disease and cirrhosis [8]. T2DM, dyslipidemia and obesity are the most common situations that are seen together with non-alcoholic steatohepatitis (NASH), which is frequently asymptomatic and can silently lead to cirrhosis [9]. There are some studies that have suggested NASH might be one of the underlying causes of CC [10,12]. Rapid lifestyle and diet changes in urban population are dramatically altering the leading causes for listing in liver transplantation from infectious causes to cryptogenic cirrhosis. There is a growing population having T2DM, dyslipidemia, obesity and at the same time patterns of liver cirrhosis etiologies that are changing to NASH [13].

This study was designed as a cross-sectional study with primary aim of assessing the prevalence of T2DM and dyslipidemia in patients with CC in comparison with non-CC and exploring the odds ratio of them.

## Materials and Methods

*Study Population and Patient Selection*

All medical records of cirrhotic patients registered in transplantation unit of Namazi Hospital of Shiraz University of Medical Sciences from January 2006 to the last day of June 2014 were examined. Cryptogenic cirrhosis was a diagnosis made by exclusion, so the patients who were labeled as cryptogenic without undergoing proper procedures and laboratory workups were excluded. Subjects between 20-80 years old were included except the ones with a metabolic disease other than T2DM and dyslipidemia. One hundred thirteen remaining records diagnosed with cryptogenic cirrhosis were selected randomly. Also, from cirrhotic patients' records, having a known etiology for the disease, 113 patients were selected randomly. None of the subjects had undergone liver transplantation because the medication that is used in post transplantation phase has a well-known effect on fasting blood sugar (FBS) levels.

*Data Collection*

After selection of subjects, records were reviewed by a physician and age, sex, weight, child class of cirrhosis and presence of T2DM (FBS>125 mg/dl), dyslipidemia (TG>150 mg/dl and/or HDL<40 mg/dl) were determined. Lipid profile consisting of low-density lipoprotein (LDL), high-density lipoprotein (HDL), triglyceride (TG) and total cholesterol and FBS were also collected from hospital charts and laboratory records.

*Statistical Analysis*

All statistical analyses were performed using the statistical package for Social Sciences version 14.0 (SPSS Inc., Chicago, IL, USA). Data was presented as mean ± standard deviation (SD). 95% confidence intervals for the means of data were calculated and the significance of differences between the study groups was assessed using independent t-tests. x2 tests were used to compare proportions. A two-sided P=0.05 was considered statistically significant.

## Results

A total number of 226 hospital records from transplant center of Namazi Hospital of Shiraz University of Medical Sciences were studied. There were 113 (50%) patients with CC and 113 cirrhotic patients as non-CC group consisting of 56 (24.8%) hepatitis B, 43 (19%) hepatitis C infection and 14 (6.2%) patients with autoimmune hepatitis. Mean age was 49.5 years old (range 20-69) in patients of both groups that 155 (68.6%) of them were male and 71 (31.4%) were female. Frequency of patients with child A, B and C cirrhosis was 45 (19.9%), 118 (52.2%) and 63 (27.9%), respectively. Table-1 has a summary of demographic and laboratory parameters.

There was significant difference between prevalence of T2DM and FBS levels among CC and non-CC subjects (P<0.01). Prevalence of T2DM in CC group (38.9%) was more than 2 times higher than non-CC group (18.6%). On the contrary, differences between prevalence of dyslipidemia and its laboratory characteristics such as total cholesterol, TG, HDL and LDL were insignificant among both groups (P>0.05).

The same results also came from cross tabulation of T2DM and dyslipidemia in CC and non-CC patients. Pearson Chi-Square, Odd's Ratio and Linear-by-Linear association of T2DM and CC were 11.680 (P<0.01), 11.968 (P<0.01) and 10.302 (P<0.01). On the other hand, Pearson Chi-Square, odd's Ratio and Linear-by-Linear association of dyslipidemia and CC 2.772 (P>0.05), 2.796 (P>0.05), 1.785 (P>0.05), respectively. A summary of the cross-tabulation results came in table-2 and -3.

## Discussion

Results showed a higher prevalence of T2DM and higher FBS levels in subjects with CC. This finding is very important because it provides further evidence to support the theory that NAFLD/NASH can progress to cirrhosis in some patients. Prevalence of T2DM in CC group (38.9%) was more than two times

**Table1.** Demographic and laboratory parameters of patients; data are expressed as mean± standard deviation.

| Variables | Cryptogenic cirrhosis n=113, % | Non-cryptogenic cirrhosis n=113 |
|---|---|---|
| Age | 49.77±11.1 | 49.11±12.03 |
| Sex (male) | 74 ,65.5% | 81,71.7% |
| Weight | 72.43±12.9 | 74.84±15.80 |
| T2DM | 44,38.9% | 21,18.6% |
| FBS | 130.87±70 | 107.59±37.95 |
| Dyslipidemia | 54,47.8% | 48,42.5% |
| Total Chol | 149.41±14.51 | 129.23±41.15 |
| TG | 96±35.36 | 94.53±41.51 |
| HDL | 38.82±13.31 | 40.93±15.15 |
| LDL | 76.46±28.47 | 74.89±36.20 |

**Table 2.** Chi-square test results of T2DM in CC and non-CC groups. P value<0.05 is considered as statistically significant.

| T2DM Cross tabulation | Value | P value |
|---|---|---|
| Pearson Chi-Square | 11.680 | .009 |
| Likelihood Ratio | 11.968 | .007 |
| Linear-by-Linear Association | 10.302 | .001 |

**Table 3.** Chi-square test results of dyslipidemia in CC and NCC group; P value<0.05 is considered as statistically significant.

| Dyslipidemia Cross tabulation | Value | P value |
|---|---|---|
| Pearson Chi-Square | 2.772(a) | .428 |
| Likelihood Ratio | 2.796 | .424 |
| Linear-by-Linear Association | 1.785 | .182 |

higher than that of non-CC group (18.6%). Pearson Chi-Square, Odd's Ratio and Linear-by-Linear association of T2DM and cryptogenic cirrhosis were 11.680, 11.968 and 10.302, respectively.

In 1999, Caldwell *et al*. [14] reported the prevalence of obesity and T2DM in 70 cases with CC and compared them with three patient groups: NASH, cirrhosis with hepatitis C and primary biliary cirrhosis (PBC). The prevalence of these risk factors (obesity and T2DM) were the same in patients with NASH and patients with CC, both of which had a higher prevalence in contrast with patients with hepatitis C and PBC.

In another study by Poonawala *et al*. [10], the prevalence of obesity and T2DM in patients with CC was compared with a control group. Various causes of cirrhosis in the control group were alcohol, chronic viral hepatitis, autoimmune hepatitis, PBC and primary sclerosing cholangitis. Similar to the results found by Caldwell *et al*. [14], the prevalence of obesity (55% vs. 24%) and T2DM (47% vs. 22%) was significantly higher in cases with CC compared with the controls. Both of these studies concluded that NASH may be an etiological factor in some of the cases with CC [10,14].

There are a lot of other reports showing higher prevalence of T2DM in CC. Kojima *et al*. [11], Siriwardana *et al*. [12] and Dassanayeke *et al*. [13] also came to the conclusion that T2DM is one of the NASH risk factors and T2DM might be one of the under-recognized reasons of CC. On the other hand, the influence of the etiology or severity of cirrhosis on the incidence of T2DM is relatively unknown. Petit and colleagues' study [15] showed that there was a significant correlation between hepatocellular carcinoma and cirrhosis etiology for the risk of DM. Cirrhosis was strongly associated with T2DM, with around 40% of diabetic cases. It can be concluded from these studies that there are some doubts about T2DM being one of the risk factors of CC and it might be the cirrhosis that causes T2DM. Studies with different designs need to be done to evaluate the causality of T2DM and CC. Until that time, there are some doubts about the causality of T2DM for CC.

Dyslipidemia and its components including TG, LDL, HDL and total cholesterol were not significantly different in CC and non-CC groups. Pearson Chi-Square, Odd's Ratio and Linear-by-Linear association of dyslipidemia and cryptogenic cirrhosis were 2.772 (P value>0.05), 2.796 (P value>0.05) and 1.785 (P value>0.05), respectively. Tellez-Avila and colleagues [16] reported that in the prevalence of each of the metabolic syndrome components of patients with and without CC, only abnormal glucose values and dyslipidemia showed statistically significant differences between the two groups. There is controversy between our study and Tellez-Avila and colleagues' [16] about the significance of different status of dyslipidemia in CC and control groups. It might be justified with the case selection in this study that patients with any other metabolic diseases except T2DM and dyslipidemia were excluded but in Tellez's study this criterion was not considered for the case selection and this might be the cause of difference.

## Conclusion

The results showed a higher prevalence of T2DM in subjects with CC but there are some doubts about T2DM as being one of the risk factors of CC. Dyslipidemia and its components including TG, LDL, HDL and total cholesterol were not significantly different in CC and non-CC subjects. However, future studies with more precise case selection might shed light on this area.

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**Conflict of Interest**

None of the authors declared any conflict of interest.

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