Liver Disorders in Type 2 Diabetes Mellitus

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ABSTRACT

Background: *Patients with type 2 diabetes mellitus (T2DM) are frequently diagnosed with some abnormal liver features. These liver abnormalities are suggested to be correlated with insulin resistance. The aim of this study was to evaluate liver abnormalities and fasting insulin levels in patients with T2DM.*

Method: *This study was conducted in Koja Hospital from February to July 2013. Study design was analytical study. Data for sex, age, complication, body mass index (BMI), liver function, liver enzyme, and fasting insulin level were collected. Univariate and bivariate statistical analyses were done using SPSS 20.*

Results: *Twenty eight patients were included in this study, 71.43% of them were female. The age group of 40-60 years was the highest among the patients (64.28%). Highest complication was neuropathy, BMI of most patients were obese. Liver abnormalities were documented in 35.8% patients, liver enzyme increased in 21.4% patients. Non alcoholic fatty liver disease (NAFLD) were noted in 46.6% patients, and one patient was positive for hepatitis B. Mean fasting insulin in T2DM with NAFLD were higher than in T2DM without NAFLD. However, it was not statistically significant (40.08 ± 36.8 μU/mL vs. 54.3 ± 37.1 μU/mL; p = 0.27).*

Conclusion: *Liver abnormalities found in T2DM patients were elevated liver enzyme, decreased albumin and increased of bilirubin. Through ultrasound, NAFLD and liver cirrhosis were found. Fasting insulin level was higher in T2DM with NAFLD but it was not statistically significant.*

Keywords: *type 2 diabetes mellitus, non alcoholic steato-hepatitis, fasting insulin*

ABSTRAK

Latar belakang: *Pada diabetes melitus tipe 2 (DMT2) sering ditemukan adanya gangguan hati. Gangguan hati ini diduga berhubungan dengan resistensi insulin. Tujuan penelitian ini adalah untuk mengevaluasi gangguan hati dan kadar insulin puasa pada DMT2.*

Metode: *Penelitian dilakukan di Rumah Sakit Koja dalam periode Februari – Juli 2013. Desain penelitian adalah studi analitik. Didata jenis kelamin, usia, komplikasi kronik, indeks massa tubuh (IMT), fungsi hati, enzim hati, dan kadar insulin puasa. Analisis data univariat dan bivariat dilakukan dengan menggunakan SPSS 20.*

Hasil: *Didapatkan 28 pasien sebagai subjek penelitian, terbanyak perempuan (71,43%), dan usia 40 - 60 tahun (64,28%). Sebagian besar pasien tergolong obesitas dan komplikasi kronik terbanyak adalah neuropatiperifer. Kelainan fungsi hati ditemukan pada 35,8% pasien, peninggian enzim hati pada 21,4% pasien. Gambaran hasil ultrasonografi (USG) penyakit perlemakan hati non alkoholik (PPHNA) didapatkan pada 46,4%, dan virus hepatitis B positif pada satu pasien. Rerata insulin puasa pada DMT2 dengan PPHNA lebih tinggi dari DMT2 tanpa PPHNA namun tidak bermakna secara statistik (40,08 ± 36,8 μU/mL vs. 54,3 ± 37,1 μU/mL; p = 0,27).*

Simpulan: *Gangguan hati pada DMT2 adalah peningkatan enzim hati, penurunan kadar albumin serta peningkatan bilirubin. Pada USG didapatkan PPHNA dan sirosis hati. Kadar insulin puasa lebih tinggi pada DMT2 dengan PPHNA, walaupun tidak bermakna secara statistik.*

Kata kunci: *diabetes melitus tipe 2, penyakit perlemakan hati non alkoholik, insulin puasa*

INTRODUCTION

American Diabetes Association (ADA) 2005 and World Health Organization (WHO) define diabetes mellitus (DM) as a group of metabolic diseases.[1,2,3,4] Several liver abnormalities are often observed in diabetic patients, e.g. liver enzymes elevation in alanin transaminase (ALT) and aspartate transaminase (AST), non-alcoholic fatty liver disease (NAFLD), liver cirrhosis, hepatitis B and hepatitis C.[5] This fact suggests the importance of liver enzymes evaluation before patients were prescribed with oral hypoglycemic agent.[6]

Approximately 50% patients with NAFLD were documented to have insulin resistance (IR). The strong correlation between metabolic syndromes with NAFLD is already highlighted.[7] In the study by Compean et al comparing hepatogenous diabetes (HD) and T2DM, the 2 hours postprandial glucose/fasting glucose ratio, fasting insulin level and homeostasis model assessment (HOMA) IR were higher in HD group. Population with hepatitis B or hepatitis C has higher prevalence for diabetes.[8] Another study performed in Greece revealed that 14% of patients with hepatitis B and 13% of patients with hepatitis C were diabetic. The co-existance between diabetes and chronic hepatitis are corellated with liver fibrosis severity.[9]

Insulin resistance is determined with various methods. The best method is the hyprinsulinemic-euglycemic clamp technique. However the technique is very complicated because it requires invasive procedure, time wasting and expensive. Another method is the indirect method by measuring fasting insulin level and HOMA IR.[10] Indirect fasting insulin level determination is widely used in clinical or epidemiological study. The aim of this study was to evaluate liver abnormalities and fasting insulin levels in patients with T2DM.

METHOD

All patients diagnosed with T2DM who visited Koja Hospital from February 1st – July 30th, 2013 were included in this study. Sampling method was consecutive sampling. Subjects were excluded if they were documented to use a hepatotoxic and/or hepatoprotector agent. Data for sex, age, chronic complication, body mass index (BMI); liver function (albumin, bilirubin and prothrombin time), liver enzyme (ALT and AST), hepatitis B and C virus, fasting insulin level, ultrasound of the liver were examined in order to capture fatty liver such as NAFLD or liver cirrhosis. Insulin resistance was determined by fasting insulin level. Initially all subjects with T2DM were collected for baseline characteristics.

Further we take the largest proportion among liver abnormalities, and performed sub-analysis in those subgroups. We compare those groups with control group. Control group consist of T2DM, same sample size, sex, and age, without liver abnormalities. Mean difference in both groups were determined using independent T-test. All statistical analysis was done using computer software SPSS 20.

RESULT

Total of 28 patients with T2DM were included. Most of the subjects were female, 40-60 years old age group, common chronic complication observed was peripheral neuropathy, length of DM < 5 years, and overweight/obese. Ten (35.8%) patients were noted to have abnormal liver function. Ten patients have a low plasma albumin and one patient also have elevated plasma bilirubin. Prothrombin time was within normal limit. Liver enzymes were elevated among 21.4% of patients. ALT was elevated in 6 patients, from which 3 of them also have elevated AST. Fatty liver or on-alcoholic steatohepatitis (NASH) was noted in 46.6% patients, and 1 patient HBsAg positive (Table 1).

We found liver abnormalities; 35.8% had abnormal liver function, 21.4% had elevated liver enzyme, 46.4% had fatty liver. Because fatty liver had the largest proportion among liver abnormalities (46.4%), we performed sub-analysis in this subgroup, by comparing fatty liver group with T2DM without fatty liver.

Sub analysis was done in 13 patients with T2DM and NAFLD. Among this group, mean age was 55.3 ± 9.8 years old, length of diabetes was 7.5 ± 5.2 years, BMI was 25.8 ± 3.9 kg/m^2, and mean fasting insulin level was 56.8 ± 37.5 μU/mL. Another sub analysis in 2 patients with liver cirrhosis revealed that the mean age was 55.5 ± 2.1 years old, length of DM 6.5 ± 2.1 years, BMI 24 ± 4.2 kg/m^2, and mean fasting insulin level 39.5 ± 23.2 μU/mL.

We did a sub analysis comparing 13 patients with NAFLD and 13 patients without NAFLD but the results were not statistically significant: mean age 55.3 ± 7.8 years vs. 55.3 ± 9.8 years; p = 1, length of DM 4.8 ± 4.5 years vs. 7.5 ± 5.2 years (p = 0.18), BMI 23.9 ± 4.5 kg/m^2 vs. 25.8 ± 3.9 kg/m^2; p = 0.28, and fasting insulin level 40.08 ± 36.8 μU/mL vs. 54.3 ± 37.1 μU/mL; p = 0.27 (Figure 1, 2, 3).

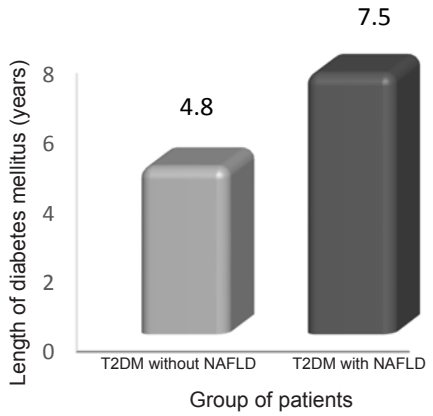

Figure 1. Length of diabetes mellitus in T2DM group with and without non-alcoholic fatty liver disease

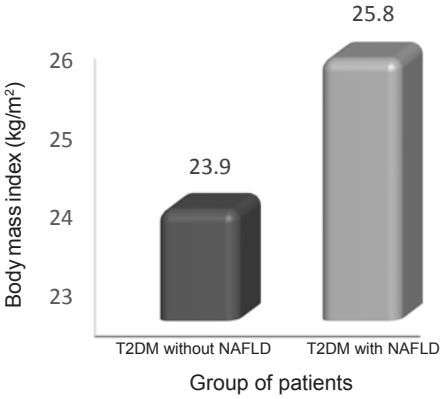

Figure 2. Body mass index in T2DM group with and without non-alcoholic fatty liver disease

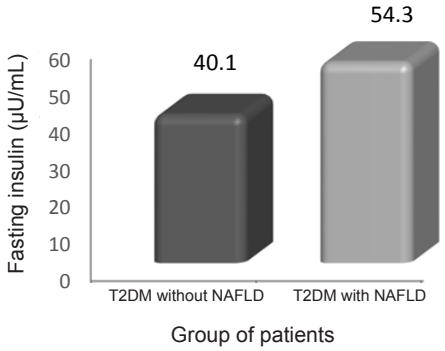

Figure 3. Fasting insulin in T2DM group with or without non-alcoholic fatty liver disease

DISCUSSION

Most of patients in this study were female (71.4%). This finding was in contrast with study by Wild et al, in which patients were distributed equally.[11] This happened because of the small sample size.

Most of patients were 40-60 years old (67.9%). This finding was consistent with study by Wild et al.[11] In his study most diabetic patients in developing country were around 45-64 years old, while in developed country most patients were ≥ 65 years old. Subgroup analysis were done in age subjects with NAFLD or without NAFLD, however the results were not statistically significant (55.3 ± 7.8 years old vs. 55.3 ± 9.8 years old; p = 1).

Diabetes mellitus are recognized as risk factor for NAFLD.[12] In our study, length of diabetes in T2DM with NAFLD was longer compared to T2DM without NAFLD, which are 4.8 ± 4.5 years vs. 7.5 ± 5.2 years. The difference was quite vary and confer the role of diabetes to develop NAFLD, however it was statistically significant (p = 0.18). BMI in 32.1% of patients were overweight, and 35.7% were obese. This number was lower compared to study by Kamath et al who found 48.9% subjects were obese.[13] BMI are usually correlated with insulin resistance and NAFLD.[12] In the subgroup analysis (T2DM with NAFLD and without NAFLD), mean BMI was higher in group with NAFLD. However, it was not statistically significant (23.9 ± 4.5 kg/m^2 vs. 25.8 ± 3.9 kg/m^2; p = 0.28). All finding above could be explained due to the small sample size.

Liver enzymes (ALT and/or AST) were elevated among 6 (21.4%) subjects. Among all patients 10 (35.8%) subjects have low serum albumin level (and elevated serum bilirubin). These findings were consistent with study by Tolman et al and Gonem et al.[5,14] They also documented the abnormal liver function and elevated liver enzyme in diabetic patients. They correlated the elevated liver enzymes and abnormal liver function with NAFLD. This phenomenon was associated with insulin resistance. Ultrasound results in our subjects recognized as NAFLD in 13 subjects (46.4%), and liver cirrhosis in 2 subjects. This findings consistent with previous study which approximately (37-74%) of diabetic patients have NAFLD.[5]

Fasting insulin off all patients were higher than normal; mean fasting insulin level 47.5 ± 36.3 µU/mL vs. 12-15 µU/mL in normal population.[15] In subgroup analysis, T2DM with NAFLD or T2DM without NAFLD, fasting insulin level were higher in the NAFLD group (40.08 ± 36.8 µU/mL vs. 54.3 ± 37.1 µU/mL; p = 0.27. These findings supports the evidence of insulin resistance in T2DM, especially in population with NAFLD, however it was not statistically significant. The underlying reason was due to unequal sample distribution. However, this issue could not be solved because of the small sample size.

CONCLUSION

Liver abnormalities found in T2DM were elevated liver enzyme, decreased albumin and increased of bilirubin, NAFLD and liver cirrhosis in ultrasound. Fasting insulin level was higher in T2DM with NAFLD but it was not statistically significant.

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