ORIGINAL ARTICLE

Deranged Liver Enzymes in Type 2 Diabetes Mellitus Subjects in a Tertiary Malaysian Hospital

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ABSTRACT

Introduction: The prevalence of diabetes mellitus (DM) in Malaysia is drastically increasing. Subjects with DM are more likely to have deranged liver function tests (LFT). This study aimed to determine the prevalence of abnormal liver enzymes [(alanine aminotransferase (ALT) and alkaline phosphatase (ALP)] and its associated factors among type 2 DM (T2DM) subjects visiting a referral diabetic clinic in a tertiary government hospital. **Methods:** This retrospective, cross-sectional study included electronic data of 300 T2DM subjects ≥18 years old in the outpatient specialist clinic from January 2011 to December 2014. Statistical analysis was performed using SPSS version 22. **Results:** The study population at large included Malays, of age >60 years with comparable gender percentage. Most subjects had long-standing DM, poor glycaemic control and were on treatment. The prevalence of abnormal ALT and ALP was 27.3% and 13%; with 90.2% and 97.4% having mild ALT and ALP elevations, respectively. Significant associations noted for age, body mass index (BMI) and duration of T2DM for ALT whereas for ALP, anti-diabetic medication was significant between groups of normal and abnormal levels. Deranged liver enzymes were associated significantly with dyslipidaemia. **Conclusion:** Our study on the crude prevalence of raised liver enzymes may help identify T2DM patients at increased risk of non-alcoholic fatty liver disease (NAFLD). Modification of metabolic risk factors, such as weight loss, control of dyslipidaemia rather than just tighter glycaemic control should be emphasised to reduce morbidity and mortality. Liver enzymes remain a simple and non- invasive marker of liver pathology in daily medical practice.

Keywords: Type 2 diabetes mellitus (T2DM), Alanine aminotransferase (ALT), Alkaline phosphatase (ALP), Dyslipidaemia, Non-alcoholic fatty liver disease (NAFLD)

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INTRODUCTION

In Malaysia, the overall prevalence of diabetes mellitus (DM) among adult population of more than 18 years old is 17.5% (1). By 2030, WHO has predicted the number of people with DM in Malaysia would be 2.48 million (2). Type 2 DM (T2DM) is often associated with liver function abnormalities covering the entire spectrum from asymptomatic raised liver enzymes to cirrhosis (3). Liver plays an essential part in glucose homeostasis (4). The link between T2DM and Non-Alcoholic Fatty Liver Disease (NAFLD) is insulin resistance, the underlying pathophysiology in both disease processes (5). NAFLD patients with T2DM are at increased risk of non-alcoholic steatohepatitis (NASH), fibrosis, and cirrhosis compared with patients without T2DM (6). In the insulin-resistant state, the excess in free fatty acids are directly toxic to liver cells. Alleged mechanisms include disruption of cell membrane, dysfunction of the mitochondria, toxins and disturbance in metabolic processes. Other potential explanations include reactive lipid peroxidation and peroxisomal beta-oxidation causing oxidative stress and increase in proinflammatory cytokines (4).

Liver function tests (LFTs) are used routinely for screening, support diagnosis, monitor progression, severity and treatment of liver disease as well as the side-effects of hepatotoxic medications (4). Derangement in LFT are found to be higher in subjects with T2DM than non-diabetics (3). In Malaysia, LFT profile in the government hospital setting comprises of the following parameters:

total protein (TP), albumin (ALB), total bilirubin (TBIL), alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Gamma glutamyl transferase (GGT) and aspartate aminotransferase (AST) are not routinely done unless requested by the clinician. Hence, liver enzymes assessed in this study were ALT and ALP only.

Although ALT is considered a suboptimal biomarker for liver pathology, its sensitivity in predicting steatosis, a surrogate marker for early NAFLD is 62.5%. This is significantly high compared with GGT and AST at 20% and 18%, respectively (6). Significant differences in ALT levels were found between subjects with mild NAFLD and those without NAFLD, and between those with severe and mild NAFLD, suggesting that serum ALT levels might offer the capacity to discriminate among different degrees of liver fat content (7).

ALP, predominantly in bone and liver, has been generally seen in patients with metabolic bone disorders and/or diseases with hyperfiltration of the kidney. Both these conditions are associated with T2DM (8). Kocabay et al. found that ALP was significantly increased in patients with liver fibrosis than patients without it, concluding that ALP may be a potential risk factor of liver fibrosis in T2DM patients with NASH (9).

An additional contribution to LFT abnormalities in these T2DM patients managed in a tertiary setting may be medications such as anti-diabetic medications and statins. Oral hypoglycaemic drugs (OHA) such as sulphonylureas, biguanide, meglitinides, pioglitazone and α-glucosidase inhibitors cause hepatotoxicity. Previous meta-analyses summarised the effects of statin therapy on liver injury from 13 RCTs involving 49,275 participants, indicating low-to-moderate doses of pravastatin, lovastatin, and simvastatin were not significantly associated with liver abnormalities (10). However, the meta-analysis by Liang X et al, based on 74,078 participants from 16 studies illustrated that the risk of liver injury was increased by 22% among patients on statin therapy. Subgroup analysis showed fluvastatin increased liver injury significantly rather than other types of statins (11). However, elevation of transaminases within three times the upper limit of normal is not a contraindication for starting OHA or statins (4, 12).

Previous studies in different geographical locations have suggested varying prevalence of deranged liver enzymes that are markers of asymptomatic NAFLD in T2DM (6, 13-22). There are limited assessments in the local setting. Thus, in the present pilot study, we aimed to examine the prevalence of elevated liver enzymes (ALT and ALP) and its associated factors in T2DM in a selected multiethnic Malaysian population visiting a referral diabetic clinic in Hospital Serdang, a tertiary government hospital.

MATERIALS AND METHODS

Study design

This retrospective, cross-sectional study included data of 300 T2DM subjects ≥ 18 years old who were seen in the outpatient diabetic clinic at Hospital Serdang from January 2011 to December 2014. Diagnosis of T2DM in the Ministry of Health hospitals was made based on the 4th edition of the Malaysian Clinical Practice Guidelines on Management of Type 2 Diabetes Mellitus (23). Sample size calculation for hypothesis testing purpose was done using the prevalence of increased ALT in obese (P1=0.192) and non-obese (P2=0.110) T2DM patients (24), giving a sample size of 298 patients.

Exclusion criteria included type 1 diabetes mellitus subjects, pregnant subjects, subjects with history of alcohol abuse, subjects on hepatotoxic drugs, subjects seropositive for HbsAg, HCV Ab, HIV infection and those who had autoimmune liver disease, cirrhosis and subjects with cor pulmonale or congestive cardiac failure and having proteinuria at least 1+ (qualitative) on urine dipstick method.

Data collection

Electronic records of the initial visit to the clinic were extracted. Retrospective laboratory data included initial fasting blood glucose (FBG), glycated haemogobin (HbA1c), fasting serum lipid [FSL: total cholesterol (TC), triglyceride (TG), low dense lipoprotein cholesterol (LDL) and high dense lipoprotein cholesterol (HDL)] and LFT (TP, ALB, TBIL, ALT and ALP) taken on the same day. Demographic factors [gender, age, ethnicity, body mass index (BMI)] and clinical findings [medications, duration of T2DM] were also recorded from electronic data.

Biochemical analysis

FBG, FSL and LFT were analysed on the automated Synchron LX20 Pro chemistry analyser (Beckman Coulter, Massachusetts, USA) whereas plasma HbA1c used ion-exchange high performance liquid chromatography (HPLC) method on the D10 BIORAD system (Biorad Laboratories, Hercules, California, USA). Abnormal ALT and ALP levels were defined as enzyme activity > 30 U/L and >150 U/L [upper limit of normal (ULN)], respectively as per the reference interval used by the hospital's laboratory on the Synchron LX20 Pro. The magnitude of liver enzyme alterations were categorised as mild (< 5x ULN), moderate (5x - 10x ULN) and marked (> 10x ULN) [25].

Statistical analysis

Statistical analysis was done using IBM SPSS Statistics version 22.0 (IBM, Armonk, NY, USA). Mann Whitney, Kruskal Wallis and Chi Square tests were used were

used to analyse non-Gaussian data. A p-value of ≤ 0.05 was taken to be statistically significant.

Ethics

The study was approved by both The Medical Research and Ethics Committee, Ministry of Health Malaysia (ID: NMRR-15-558-25499) and The Ethics Committee for Research involving Human Subjects of Universiti Putra Malaysia [Ref. no: FPSK (EXP15-MEDIC)U030].

RESULTS

The study population at large included Malays, of age more than 60 years with comparable gender percentage. Majority had long-standing DM and were on treatment with OHA. The rest were either on insulin or both OHA and insulin. Median BMI of study population was 26.5 kg/m^2 (Table I).

Table I: Demographics and clinical characteristics of study population (N=300)

Variable	n (%)
Gender	
Male	155 (51.7)
Female	145 (48.3)
Age (years)	
< 60	149 (49.7)
≥ 60	151 (50.3)
Ethnicity	
Malay	168 (56.0)
Chinese	72 (24.0)
Indian	60 (20.0)
BMI	
Obese (BMI > 27.5kg/m^2)	59 (19.7)
Non obese (BMI ≤27.5)	83 (27.7)
Missing data	158 (52.7)
Duration of T2DM	
< 5 years	53 (17.7)
≥ 5 years	122 (40.7)
Missing data	125 (41.6)
Anti-diabetic medication	
Oral hypoglycemic agent (OHA)	161 (53.7)
Insulin	74 (24.7)
OHA & insulin	65 (21.7)
Statin	
Yes	174 (58.0)
No	126 (42.0)

Table II shows the laboratory parameters of the study population. Median for all analytes were within the reference range except for FBG and HbA1c, which were raised and HDL, which was just below the lower limit of normal. The prevalence of abnormal ALT and ALP in this study was 27.3% and 13%; with 90.2% and 97.4% having mild ALT and ALP elevations, respectively (Table III).

Table IV compares associated factors of T2DM subjects with and without abnormal ALT. Significant associations were for age, BMI and duration of T2DM. Subjects with abnormal ALT had a significantly higher TG, TBIL, TP and ALP and a lower HDL level compared to the normal ALT group.

Table II: Laboratory parameters of study population

Parameter	n**	Median (IQR)	Min – Max	Reference range*
FBG (mmol/L)	232	**8.05 (6.85)**	1.4 – 19.95	3.89 – 5.8
HbA1c (%)	192	**8.00 (3.60)**	5.0 – 18.5	< 6.5
TC (mmol/L)	242	4.73 (1.85)	2.42 – 8.38	≤ 5.17
TG (mmol/L)	242	1.65 (1.04)	0.45 – 5.30	≤ 1.70
LDL-C (mmol/L)	242	2.81 (1.52)	0.56 – 5.72	≤ 3.37
HDL-C (mmol/L)	242	**1.02** (0.39)	0.13 – 2.10	≥ 1.04
Total protein (U/L)	300	73.0 (8.00)	39.00 – 89.0	64 – 83
ALB (g/L)	300	36.0 (8.00)	29.0 – 61.0	35 – 50
TBIL (µmol/L)	300	10.35 (7.75)	1.11 – 165.1	3.4 – 20.5
ALT (U/L)	300	19.0 (15.00)	6.0 – 374.0	3.0 – 30.0
ALP (U/L)	295	83.0 (45.50)	21.0 – 836.0	40.0 – 150.0

* based on Hospital Serdang LIS 2015.
** the number of subjects (n) differed for each analyte due to unrecorded data (missing data)

Table III: Classification of liver enzymes (ALT &ALP) based on magnitude of liver enzyme alteration

ALT (3 – 30) U/L	N = 82 n (%)	ALP (40 – 150) U/L	N = 39 n (%)
Mild (<5x ULN)	74 (90.2)	Mild (<5x ULN)	38 (97.4)
Moderate (5x-10x ULN)	4 (4.9)	Moderate (5x-10x ULN)	1 (2.6)
Severe (>10x ULN)	4 (4.9)	Severe (>10x ULN)	0 (0.0)

ULN: upper limit of normal

Tables V shows the comparison in associated factors between T2DM subjects with and without abnormal ALP. Only anti-diabetic medication was significant between the two groups. Subjects with abnormal ALP had a significantly higher ALT and a lower HDL and ALB level compared to the normal ALP group.

DISCUSSION

In this study, a much higher prevalence of increased ALT levels (27.3%) in T2DM was found compared to India (13, 14), Denmark (6), Myanmar (15), Italy (16), UK (17, 18), Jordan (24) and US (19) with prevalence of 19.8-24.5%, 20%, 18.5%, 16%, 12.1-15.7%, 10.4% and 7.8%, respectively. On the contrary, Bangladesh (20), Pakistan (21) and Nepal (22) reported higher prevalence of ALT with 31%, 34.6% and 57%, respectively compared to our study. The prevalence of increased ALP was 13% in our study, which was higher than UK; 10.4% (17) and Nepal; 7% (22) but much lower than India with prevalence between 33-41.2% (13, 14). The varied prevalence of deranged liver enzymes in T2DM among diverse populations may be due to the different study methodology and cut-off values used for liver enzymes. It may also depend on the prevalence of diabetes and its complications in the particular population suggesting other associated factors and pathophysiological mechanisms of T2DM may be contributory.

Table IV: Demographic factors, clinical findings and laboratory parameters between T2DM subjects with and without abnormal ALT

Variable	Normal ALT (ALT 3 – 30 U/L) n = 218		Abnormal ALT (ALT > 30 U/L) n = 82		χ^{2*}	p value***
	n (%)		n (%)			
Gender						
Male	113	(51.8)	42	(51.2)	0.009	0. 924
Female	105	(48.2)	40	(48.8)		
Age (years)						
< 60	95	(43.6)	54	(65.9)	11.827	**0.001**
≥ 60	123	(56.4)	28	(34.1)		
Ethnicity						
Malay	119	(54.6)	49	(59.8)	0.800	0.670
Chinese	53	(24.3)	19	(23.2)		
Indian	46	(21.1)	14	(17.0)		
BMI**					11.689	**0.001**
Obese	35	(34.3)	24	(60.0)		
Non obese	67	(65.7)	16	(40.0)		
Duration T2DM** (years)**						
<5	35	(26.9)	18	(40.0)	5.837	**0.016**
≥5	95	(73.1)	27	(60.0)		
Anti-diabetic medication						
OHA	114	(52.3)	47	(57.3)	2.525	0.283
Insulin	59	(27.1)	15	(18.3)		
OHA & insulin	45	(20.6)	20	(24.4)		
Statin						
Yes	120	(55.0)	54	(65.9)	2.856	0.091
No	98	(45.0)	28	(34.1)		
Laboratory parameters	**Median**	**(IQR)**	**Median**	**(IQR)**	**z****	**p value*****
FBG (mmol/L)	7.84	(6.82)	8.81	(7.37)	-1.264	0.206
HbA1c (%)	7.95	(3.65)	8.20	(3.45)	-0.396	0.692
TC (mmol/L)	4.76	(1.74)	4.6	(2.64)	-1.28	0.206
TG (mmol/L)	1.56	(0.92)	1.93	(0.86)	-3.368	**0.001**
LDL (mmol/L)	2.89	(1.46)	2.66	(2.06)	-1.413	0.158
HDL mmol/L)	1.06	(0.43)	0.93	(0.31)	-4.466	**< 0.001**
Total protein (U/L)	73.0	(7.75)	75.0	(9.00)	-2.078	**0.038**
ALB (g/L)	35.0	(8.00)	36.0	(8.00)	-1.943	0.052
TBIL (µmol/L)	9.80	(6.55)	12.75	(10.73)	-3.973	**< 0.001**
ALP (U/L)	80.5	(41.0)	96.5	(47.0)	-4.808	**< 0.001**

*Since n > 20 and there is no expected value less than 5, Pearson Chi-Square is used.
**Mann Whitney statistical test (z).
***Statistical significance at p < 0.05. The significant variables are shown in bold.
****For BMI (normal ALT n=102; abnormal ALT n=40) and duration of T2DM (normal ALT n=130; abnormal ALT n=45), missing data was excluded to calculate the respective percentages.

Table V: Demographic factors, clinical findings and laboratory parameters between T2DM subjects with and without abnormal ALP

Variable	Normal ALP (ALP 40 - 150 U/L) n = 256		Abnormal ALP (ALP > 150 U/L) n = 39		χ^{2*}	p value***
	n (%)		n (%)			
Gender						
Male	132	(51.6)	22	(56.4)	0.319	0.572
Female	124	(48.4)	17	(43.6)		
Age (years)						
< 60	121	(47.3)	25	(64.1)	3.838	0.050
≥ 60	135	(52.7)	14	(35.9)		
Ethnicity						
Malay	142	(55.5)	23	(59.0)	0.187	0.911
Chinese	62	(24.2)	9	(23.0)		
Indian	52	(20.3)	7	(18.0)		
BMI**						
Obese	50	(41.7)	8	(38.1)	3.685	0.055
Non Obese	70	(58.3)	13	(61.9)		
Duration T2DM** (years)**						
<5	44	(29.7)	8	(34.8)	0.013	0.910
≥5	104	(70.3)	15	(65.2)		
Anti-diabetic medication						
OHA	143	(55.9)	16	(41.0)	11.238	**0.004**
Insulin	55	(21.4)	18	(46.2)		
OHA & insulin	58	(22.7)	5	(12.8)		
Statin						
Yes	146	(57.0)	25	(64.1)	0.695	0.405
No	110	(43.0)	14	(35.9)		
Laboratory parameters	**Median**	**(IQR)**	**Median**	**(IQR)**	**z****	**p value*****
FBG (mmol/L)	7.99	(6.74)	9.75	(7.45)	-1.325	0.185
HbA1c (%)	8.00	(3.50)	8.00	(5.00)	-0.965	0.334
TC (mmol/L)	4.73	(1.82)	4.73	(2.79)	-1.116	0.265
TG (mmol/L)	1.64	(0.97)	1.88	(1.54)	-0.821	0.412
LDL (mmol/L)	2.80	(1.51)	2.86	(1.98)	-0.802	0.422
HDL mmol/L)	1.04	(0.39)	0.88	(0.51)	-2.752	**0.006**
Total protein (U/L)	73.0	(8.00)	74.0	(11.0)	-0.175	0.861
ALB (g/L)	36.0	(7.00)	29.0	(11.0)	-3.584	**< 0.001**
TBIL (µmol/L)	10.4	(7.20)	9.5	(12.4)	-0.421	0.674
ALT (U/L)	19.0	(15.0)	22.0	(25.0)	-2.493	**0.013**

*Since n > 20 and there is no expected value less than 5, Pearson Chi-Square is used.
**Mann Whitney statistical test (z).
***Statistical significance at p < 0.05. The significant variables are shown in bold.
****For BMI (normal ALP n=120; abnormal ALP n=21) and duration of T2DM (normal ALP n=148; abnormal ALP n=23), missing data was excluded to calculate the respective percentages.

Insulin resistance in T2DM is reflected by the chronic mild increase in transaminases. Similarly in this study, majority of patients had mild elevations of ALT and ALP. Considering that the ALT gene transcription is suppressed by insulin, the increase in ALT is hypothesised to be due to impaired insulin signaling rather than solely hepatocellular damage (4). High levels of liver ALP isoenzyme indicates cholestasis rather hepatocyte injury. Hepatosteatosis and insulin resistance in T2DM subjects may be responsible for ALP elevation (14).

Our results showed that there was significant difference between normal and abnormal ALT with respect to age, BMI and duration of T2DM in study subjects. The percentage of subjects with abnormal ALT was higher in the age group less than 60 years old. Similar to previous research (24, 26, 27), this finding suggests that hepatic steatosis indicated by increased ALT levels in response to hepatocyte damage, tends to occur earlier in the course of the disease. In older patients, ALT, a biomarker of hepatocyte integrity declines as steatosis progresses while there is an inverse rise in AST level. Kamimoto et al attributed the rise in AST to the fact that because AST is mainly cleared by liver sinusoidal cells, advancing fibrosis injures these cells leading to the high levels (28). In this study, however, AST was not included as it is not

a routine investigation in the local LFT profile.

Median BMI in our study population was 26.5 kg/m^2, which is in the overweight range. Our finding of obese subjects (BMI > 30 kg/m^2) having higher abnormal ALT compared to non-obese subjects is consistent with previous studies. Prevalence of raised ALT was higher among obese than non-obese diabetics with 10.6% and 6.6%, respectively in the US (19). Elevated ALT was significantly related to a BMI of > 25 kg/m^2 among T2DM subjects in India (29). These findings substantiate the link between NAFLD and metabolic syndrome.

Several constituents of metabolic syndrome such as insulin resistance, obesity, dyslipidaemia are also found in T2DM and are associated with NAFLD, suggesting that metabolic syndrome is a possible link between T2DM and NAFLD (6). Our study demonstrates statistically significant associations between the components of metabolic syndrome and raised ALT, which suggests that this can be used as a marker for NAFLD, albeit a non-specific one. Waist circumference to assess central obesity, which is a better parameter for metabolic syndrome was not measured (29). This can be considered as another limitation. However, we used BMI which is an accepted alternative to be a marker of metabolic syndrome (29).

Whether NAFLD is related to the pathogenesis of T2DM or NAFLD is a contributing factor for the progression of T2DM is unclear. Majority of subjects in this study had long-standing DM with poor glycaemic control. However there was no significant association between enzyme groups with HbA1c, for both ALT and ALP. Manifestations of the metabolic syndrome, which often precedes T2DM, such as obesity, hyperinsulinemia, peripheral insulin resistance, hypertriglyceridaemia, and hypertension, have been previously suggested as a cause of NAFLD (29). This study is in keeping with the current understanding of the pathogenesis of NAFLD as a hepatic manifestation of the metabolic syndrome itself, as elevated ALT was commonly elevated in people with diagnosis of T2DM, suggesting that development of NAFLD may precede the diagnosis of T2DM.

Our data, demonstrating higher TG and lower HDL in the abnormal liver enzyme groups, support the hypothesis that the principal pathophysiology in NAFLD, is insulin resistance. Insulin resistance leads accumulation of hepatic TG by increased lipolysis, TG synthesis, and increased hepatic uptake of free fatty acids. Plasma HDL is decreased in T2DM related to increased catabolism of HDL particles due to hypertriglyceridaemia. The transfer of TG to HDL through cholesteryl ester transfer protein (CETP) leads to TG-rich HDLs formation. Hepatic lipase catabolises these HDLs (30). It has been demonstrated that HDLs from T2DM subjects have reduced anti-oxidative and endothelium-dependent vasorelaxant properties (30), which may further contribute to liver damage.

Our study also found a significant association between normal and abnormal ALT groups with duration of T2DM. However, in the general study population as well as for both groups, higher percentage of subjects had T2DM for more than 5 years. This may be due to the fact that patients who are seen at the tertiary hospital are chronic diabetics and are only referred by the primary care physician when there is difficulty in glycaemic control and complications arise. Therapeutic lifestyle changes and early medical intervention are required to address the risk factors such as obesity, dyslipidaemia in younger diabetics to prevent progression of liver disease.

Although more than half the subjects were on treatment with OHA and/or statins, our results showed that the only significant association was for antidiabetic medication between T2DM patients with and without abnormal ALP. However, the type of OHA/statin was not documented, a limitation of this retrospective study. Metformin is a widely prescribed OHA and is the first-line treatment for T2DM (31). Several studies have documented the anabolic effects of metformin on bone metabolism and its effect on increasing ALP, a bone formation marker (32, 33). Sulfonylureas, GLP-1 receptor agonist and insulin also promote bone formation (32). No significant association was found between abnormal liver enzymes and statin use in this study, concurring with the observations by Patra TK et al (3).

Our study has several limitations. First, due to the retrospective nature of the study, some of the demographic factors, clinical findings and laboratory parameters were missing due to lack of recorded data. Most importantly, routine LFT was not done in all subjects. Only the results of the initial visit was extracted so the true details of the clinical condition may not be revealed. Hence, using only a single value of ALT and ALP as well as cut-off values, established from 2 standard deviations (SD) of respective enzyme estimations in apparently healthy subjects (laboratory reference range) to define derangement of liver enzymes may lead to underestimation of the burden of liver pathology in the population. Furthermore, being a cross-sectional study, temporal relationship could not be established as potential unmeasured confounders were not adjusted for. This leads to the question as to whether deranged liver enzymes preceded or followed some of the clinical and metabolic factors that were studied.

Further prospective studies should be carried out using a larger sample size involving other tertiary hospitals in Malaysia and including markers such as GGT, AST, adipokines, fasting insulin, HOMA-IR and ultrasound of the liver. These tests would help identify mechanisms behind abnormal liver enzymes in T2DM. Studies of interventions and therapeutic strategies for abnormal liver enzymes in T2DM subjects can also be done.

CONCLUSION

Our study on the crude prevalence of raised liver enzymes may help identify T2DM patients at increased risk of NAFLD. Modification of metabolic risk factors, such as weight loss, control of dyslipidaemia rather than just tighter glycaemic control should be emphasised in these patients to reduce morbidity and mortality. Liver enzymes remain a simple and non- invasive marker of liver pathology in daily medical practice.

ACKNOWLEDGEMENTS

The authors would like to thank the Director General of Health Malaysia for his permission to publish this article. The authors are grateful to the Director of Hospital Serdang for permitting this study as well as the clinicians of the Medical Department and staff of Pathology Department of Hospital Serdang for their assistance in this study. Sincere appreciation to Dr. Halimatus Sakdiah Minhat, Department of Community Health, Faculty of Medicine and Health Sciences, Universiti Putra Malaysia for assisting in the statistical analysis of this study.

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