Section: Miscellaneous

Original Research Article

ASSOCIATION BETWEEN DURATION OF TYPE 2 DIABETES MELLITUS AND HEPATIC STEATOSIS AND FIBROSIS ASSESSED BY TRANSIENT ELASTOGRAPHY

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ABSTRACT

Background: Type 2 Diabetes Mellitus (T2DM) is strongly linked to metabolic dysfunction diseases, such as metabolic dysfunction–associated steatotic liver disease (MASLD), liver steatosis and advanced liver fibrosis. Insulin resistance, metabolic inflammation, hyperglycemia and dyslipidemia can lead to liver damage in patients with diabetes. But the independent contribution of the duration of Type 2 Diabetes Mellitus (T2DM) to hepatic steatosis and fibrosis is unclear. **Objective:** To examine the independent link between Type 2 Diabetes Mellitus duration and hepatic steatosis and fibrosis as measured by transient elastography, by liver stiffness measurement and controlled attenuation parameter, respectively.

Materials and Methods: We conducted a cross-sectional observational study in patients with a diagnosis of T2DM who went for transient elastography. Diabetes duration was measured in years. Liver stiffness measurement was used to assess liver fibrosis, and controlled attenuation parameter to assess liver steatosis. Biochemical and metabolic parameters were also assessed. The variables did not have a normal distribution, so the correlation between diabetes duration and elastography-based variables was analysed using the Spearman correlation. A p-value <0.05 was taken as statistically significant.

Results: There was a weak positive correlation between duration of T2DM and liver stiffness, but this correlation was not statistically significant (rho = 0.08, p = 0.120). Likewise there was no significant association with controlled attenuation parameter measurements (rho = 0.01, p = 0.880). Fatty liver, grade of fatty liver, LDL and triglycerides were all significantly associated with liver stiffness and steatosis, and may be more important than duration.

Conclusion: No significant association was found between duration of Type 2 Diabetes Mellitus and the grade of liver fibrosis or steatosis in transient elastography. Our study highlights that the extent of metabolic disease, dyslipidemias, and diabetes control may have a greater impact on the liver in T2DM patients than simply diabetes duration.

Keywords: Type 2 Diabetes Mellitus; Hepatic Steatosis; Liver Fibrosis; Transient Elastography; Liver Stiffness Measurement; Controlled Attenuation Parameter; MASLD; NAFLD.

INTRODUCTION

2.1 Overview of Type 2 Diabetes Mellitus

Type 2 Diabetes Mellitus (T2DM) is a disease of chronic metabolic nature with insulin resistance, defective insulin secretion, chronic elevation of blood glucose levels and multiple vascular and metabolic complications.[1]

Metabolic Dysfunction–Associated Steatotic Liver Disease / NAFLD

Metabolic dysfunction-associated steatotic liver disease (MASLD) or non-alcoholic fatty liver disease (NAFLD) is the liver fat accumulation in the background of heart disease and metabolic health risk factors. It is now known to be a common liver disease worldwide and is increasingly associated with obesity, dyslipidemia, and T2DM.[2,3]

2.3 T2DM, Hepatic Steatosis and Fibrosis

T2DM is associated with a greater risk of hepatic steatosis, steatohepatitis, advanced fibrosis, cirrhosis, and liver complications. Insulin resistance induces hepatic steatosis, oxidative stress, inflammation and fibrogenesis pathways, thereby contributing to liver injury.[3,4]

2.4Impact of Diabetes Duration on Liver Disease

Theoretically, a longer duration of T2DM may lead to a greater exposure to hyperglycemia, insulin resistance and metabolic disease. But recent research indicates that the rate of progression of liver fibrosis may be more related to body weight, glucose control, dyslipidemia and total metabolic burden than duration of diabetes.[4,5]

2.5 Need for Transient Elastography

Transient elastography is a quick, safe and useful non-invasive technique to measure liver fibrosis (liver stiffness measurement) and steatosis (controlled attenuation parameter). There are currently recommendations for non-invasive liver testing in high-risk populations, such as those with T2DM.[2,6]

2.6 Aim and Objectives

Given the high prevalence of MASLD in diabetics, it is important to determine whether exposure time of T2DM (the duration of T2DM) is related to hepatic steatosis and fibrosis for risk stratification and early diagnosis benefits.

2.7 Aim and Objectives

Our aim is to evaluate the relationship of duration of T2DM with hepatic steatosis and fibrosis by transient elastography. The objectives are to check the association of the duration of diabetes with the liver stiffness measurement, controlled attenuation parameter, grade of fatty liver and other metabolic parameters.

MATERIALS AND METHODS

3.1 Study Design

The current study was a cross-sectional study aimed at examining the correlation between duration of Type 2 Diabetes Mellitus and liver steatosis and fibrosis by transient elastography.

3.2 Study Setting

This was a tertiary care hospital study which included patients referred to the medical/ gastroenterology out-patient clinic or inpatient services for evaluation of the metabolic and hepatic complications of diabetes.

3.3 Study Population

Adult patients with Type 2 Diabetes Mellitus who had transient elastography to detect liver stiffness and presence of fatty liver were included in the study.

3.4 Inclusion Criteria

The current study included patients between the age of 18 years and above who are diagnosed with Type 2 Diabetes Mellitus, known duration of diabetes and have results of transient elastography.

3.5 Exclusion Criteria

Patients with excessive alcohol-consumption, chronic viral hepatitis, autoimmune liver diseases, drug-related liver disease, known chronic liver disease of other causes, pregnancy or with those having incomplete clinical/biochemical data were excluded.

3.6 Data Collection Procedure

Data on demographic, clinical, biochemical and elastographic parameters were captured on a proforma. Data regarding age, gender, rural/urban, duration of diabetes, coexisting diseases, diabetes complications, Body Mass Index, Liver function tests, Hemoglobin A1C and Lipid profile were collected.

3.7 Variables Studied

Duration of Type 2 Diabetes Mellitus (DM) in years was the independent variable of primary interest. The dependent variables were liver stiffness and controlled attenuation parameter (CAP). BMI, HbA1c, lipid profile, liver function tests, and diabetes complications (nephropathy, retinopathy, neuropathy, and coronary artery disease) were explored as other factors.

3.8 Transient Elastography Assessment

A transient elastography was carried out to measure hepatic steatosis and fibrosis. Liver stiffness measurement values were measured in kilopascals and controlled attenuation parameter in decibels per meter.

3.9 Definitions of Hepatic Steatosis and Fibrosis

The controlled attenuation parameter was used to define hepatic steatosis, while hepatic fibrosis was defined using liver stiffness measurement and FibroScan grade.

3.10 Statistical Analysis

All data were analyzed appropriately. Data has been presented as mean and standard deviation or median and interquartile range. The Spearman correlation coefficient, Mann-Whitney U test and Kruskal-Wallis test test were applied. The p-value of less than 0.05 was considered as significant.

3.11 Ethical Considerations

Patient confidentiality was upheld throughout the study. The study was in accordance with institutional guidelines.

RESULTS

4.1 Baseline Demographic Characteristics

P2DM patients in the study who had been diagnosed with Type 2 Diabetes were subjected to transient elastography for evaluating hepatic fibrosis and steatosis. Age, sex, place of living, addictions and

BMI were analysed against the duration of diabetes. The duration of T2DM was not significantly associated with age, gender, urban or rural habitation, addictions, or BMI indicating that diabetes duration in this study was not significantly affected by the above-mentioned factors.[7,8]

4.2 Clinical Characteristics of Diabetic Patients

Nephropathy, retinopathy, neuropathy, coronary artery disease, hypertension, hypothyroidism, and chronic kidney disease were assessed for complications. No significant association was found between duration of diabetes and any of the above complications. This suggests that while duration may not completely account for the effects of diabetic complications.[9,10]

4.3 Frequency of Duration of Type 2 Diabetes Mellitus

Although mean duration of diabetes was not uniformly distributed among subgroups, it was similarly distributed among most clinical and demographic sub-groups. This suggests the importance of evaluating the metabolic risk factors together with duration of diabetes.[11,12]

4.4 Biocemical and Metabolic Parameters

There was no significant correlation between diabetes duration and bilirubin, AST, ALT, total protein, albumin, ALP, HbA1c or platelet count. We can speculate that the effect of duration of diabetes on liver damage cannot be directly reflected by biochemical abnormalities.[13]

4.5 Transient Elastography Findings

FibroScan grade, LSM and CAP were measured. LSM was positively correlated with total diabetes duration, but the correlation was weak. CAP did not have a significant correlation with diabetes duration.[8,11]

4.6-4.7 Association With Fibrosis and Steatosis

Duration of T2DM did not show significant association with hepatic fibrosis (LSM and FibroScan grade). On the other hand, fatty liver and fatty liver grade were significantly associated with duration of diabetes.[14,15]

4.8-4.10 Associations with Biochemical, Lipid and Overall

Lipid variables, LDL and triglycerides were positively associated with duration of diabetes. The association for HDL, TG/HDLratio, FIB-4 and APRI were non-significant. Fatty liver status and fatty liver grade, LDL and triglycerides were the significant factors associated with duration of T2DM.[15,16]

Table 1: Association Between Duration of T2DM and Demographic/Clinical Variables

Variable	Category / Statistic	Duration of DM2 Years	p-value	Interpretation
Age	Spearman rho	-0.04	0.424	Not significant
Age group	40–49 years	9.59 ± 3.71	0.254	Not significant
	50–59 years	9.81 ± 3.66		
	60–69 years	8.89 ± 3.38		
	70–79 years	9.00 ± 3.37		
	80–89 years	10.17 ± 2.14		
Gender	Male	9.24 ± 3.50	0.111	Not significant
	Female	9.99 ± 3.68		
Addictions	Nil	9.54 ± 3.61	0.428	Not significant
	Smoker	9.27 ± 3.47		
BMI	Spearman rho	0.02	0.730	Not significant
BMI group	23.0–24.9 kg/m²	8.66 ± 3.44	0.137	Not significant
	25.0–29.9 kg/m²	9.63 ± 3.61		
	30.0–34.9 kg/m²	9.97 ± 3.85		
	35.0–39.9 kg/m²	8.97 ± 2.88		

Explanation: Age, gender, addictions, and BMI did not show a statistically significant association with duration of Type 2 Diabetes Mellitus. Although females had slightly higher mean diabetes duration than males, and obese patients in the 30.0–34.9 kg/m² group had a higher mean duration, these differences were not statistically significant.

Table 2: Association Between Duration of T2DM and Diabetic Complications

Diabetic Complication	Category	Duration of DM2 Years	p-value	Interpretation
Any diabetic complication	Yes	9.52 ± 3.54	0.657	Not significant
	No	9.30 ± 3.60		
Nephropathy	Yes	9.36 ± 3.62	0.523	Not significant
	No	9.51 ± 3.52		
Retinopathy	Yes	9.55 ± 3.68	0.776	Not significant
	No	9.36 ± 3.48		
Neuropathy	Yes	9.83 ± 3.81	0.449	Not significant
	No	9.38 ± 3.52		
Coronary artery disease	Yes	10.06 ± 3.39	0.167	Not significant
	No	9.35 ± 3.58		

Explanation: Diabetic complications were not significantly associated with duration of diabetes. Patients with coronary artery disease and neuropathy had comparatively longer mean duration of diabetes, but the difference was not statistically significant.

Table 3: Association Between Duration of T2DM and Liver Function Parameters

Liver Function Parameter	Correlation with Duration of DM2	p-value	Interpretation
Bilirubin	rho = 0.02	0.696	Not significant
AST	rho = -0.05	0.329	Not significant
ALT	rho = -0.08	0.119	Not significant
Total protein	rho = -0.08	0.108	Not significant
Albumin	rho = -0.09	0.087	Not significant
ALP	rho = 0.03	0.589	Not significant

Explanation: Liver function parameters did not show a significant correlation with diabetes duration. Albumin, total protein, ALT, and AST showed weak negative correlations, while bilirubin and ALP showed weak positive correlations, but none reached statistical significance.

Table 4: Association Between Duration of T2DM and Transient Elastography Findings

Parameter	Category / Statistic	Duration of DM2 Years	p-value	Interpretation
FibroScan grade	F0–1	8.88 ± 3.11	0.096	Not significant
	F2	9.56 ± 3.48		
	F3	9.07 ± 3.37		
	F4	10.87 ± 4.69		
FibroScan grade category	F0–1/F2	9.29 ± 3.35	0.367	Not significant
	F3/F4	9.90 ± 4.11		
LSM	Spearman rho	0.08	0.120	Not significant
CAP	Spearman rho	0.01	0.880	Not significant

Explanation: Duration of T2DM showed a weak positive correlation with liver stiffness measurement, but this association was not statistically significant. CAP also showed almost no correlation with diabetes duration. Although patients with F4 fibrosis had higher mean diabetes duration, the overall association between FibroScan grade and diabetes duration was not statistically significant.

Table 5: Association Between Duration of T2DM and Fatty Liver Status

Variable	Category	Duration of DM2 Years	p-value	Interpretation
Fatty liver	Yes	9.28 ± 3.39	<0.001	Significant
	No	16.56 ± 3.54		
Grade of fatty liver	Bright echotexture / CLD	16.56 ± 3.54	<0.001	Significant
	Grade 1	9.68 ± 3.22		
	Grade 2	9.08 ± 3.36		
	Grade 3	9.76 ± 3.85		

Explanation: Fatty liver status and grade of fatty liver showed a statistically significant association with duration of diabetes. The highest mean duration of diabetes was observed in patients with bright echotexture/CLD. This suggests that liver parenchymal changes may be associated with longer diabetes duration, although simple fatty liver grades did not show a progressive increase across Grade 1, Grade 2, and Grade 3.

Table 6: Association Between Duration of T2DM and Non-Invasive Fibrosis Scores

Parameter	Category / Statistic	Duration of DM2 Years	p-value	Interpretation
FIB-4 score	Spearman rho	-0.03	0.501	Not significant
FIB-4 category	1.3–2.67	9.68 ± 3.56	0.676	Not significant
	>2.67	9.41 ± 3.56		
APRI	Spearman rho	-0.06	0.206	Not significant
APRI category	<0.5	10.17 ± 3.04	0.288	Not significant
	0.5–1	9.69 ± 3.75		
	>1–2	8.96 ± 3.29		
	>2	9.50 ± 3.19		

Explanation: FIB-4 score and APRI did not show significant association with duration of diabetes. These findings indicate that diabetes duration alone may not strongly reflect fibrosis risk when assessed through serum-based non-invasive fibrosis indices.

Table 7: Association Between Duration of T2DM and Lipid Parameters

Lipid Parameter	Category / Statistic	Duration of DM2 Years	p-value	Interpretation
HDL	Spearman rho	0.03	0.501	Not significant
HDL category	<40 mg/dL	9.31 ± 4.05	0.431	Not significant
	≥40 mg/dL	9.46 ± 3.49		
LDL	Spearman rho	0.12	0.016	Significant

LDL category	<100 mg/dL	9.67 ± 4.25	0.984	Not significant
	≥100 mg/dL	9.43 ± 3.53		
Triglycerides	Spearman rho	0.12	0.013	Significant
TG/HDL ratio	Spearman rho	0.07	0.188	Not significant
TG/HDL ratio category	2–3	8.00 ± 0.00	0.602	Not significant
	3–3.5	10.31 ± 2.66		
	3.5–4	9.14 ± 3.16		
	>4	9.45 ± 3.64		

Explanation: LDL and triglyceride levels showed statistically significant positive correlations with duration of diabetes. This indicates that longer duration of T2DM may be associated with worsening lipid abnormalities. HDL and TG/HDL ratio did not show statistically significant associations.

Overall Result Summary

Finding	Result
Duration of T2DM vs LSM	Weak positive but not significant
Duration of T2DM vs CAP	No meaningful association
Duration of T2DM vs FibroScan grade	Not significant
Duration of T2DM vs Fatty liver status	Significant
Duration of T2DM vs Grade of fatty liver	Significant
Duration of T2DM vs LDL	Significant
Duration of T2DM vs Triglycerides	Significant
Major non-significant variables	Age, gender, BMI, HbA1c, liver enzymes, diabetic complications, FIB-4, APRI

Overall Explanation: The analysis shows that duration of Type 2 Diabetes Mellitus was not significantly associated with liver stiffness, CAP score, FibroScan fibrosis category, HbA1c, BMI, liver enzymes, or diabetic complications. However, significant associations were observed with fatty liver status, grade of fatty liver, LDL, and triglyceride levels. Therefore, the results suggest that metabolic and lipid-related factors may have a stronger relationship with hepatic involvement than diabetes duration alone.

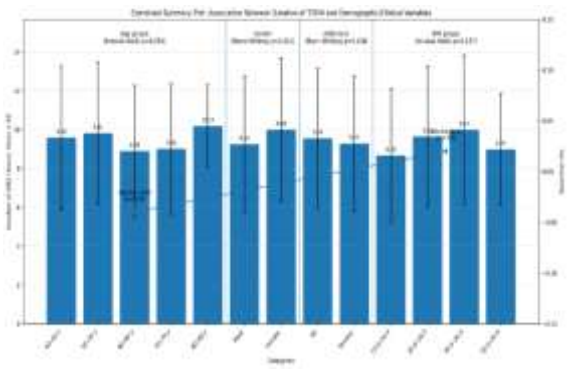
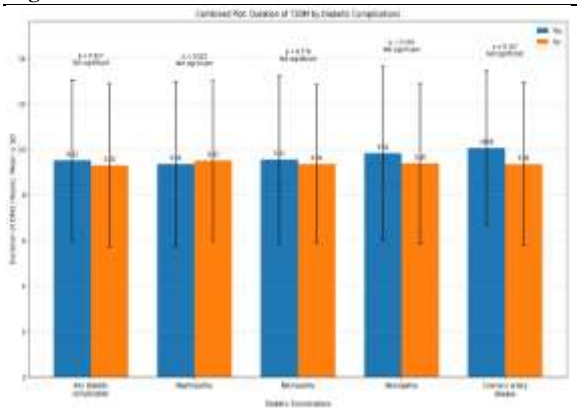


Figure 1



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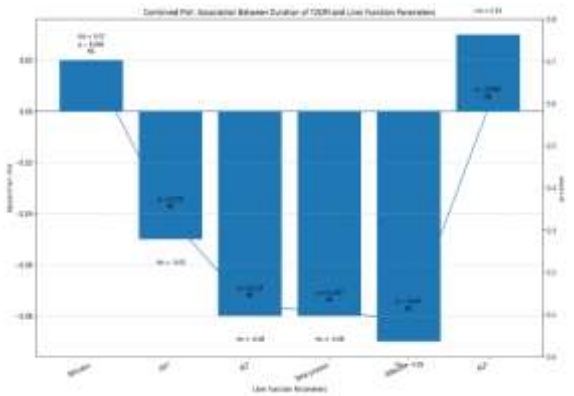

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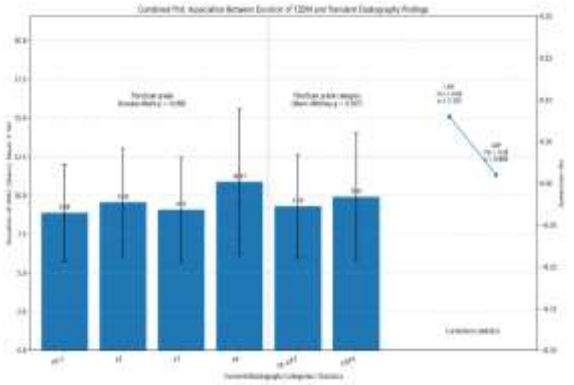

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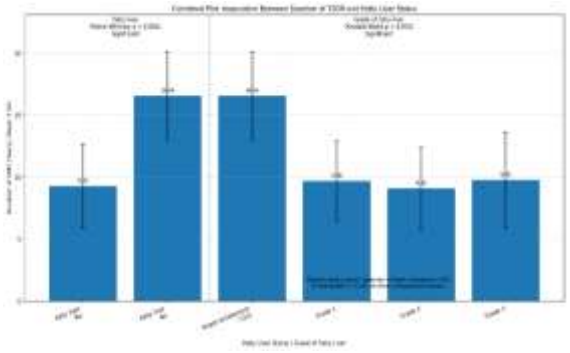

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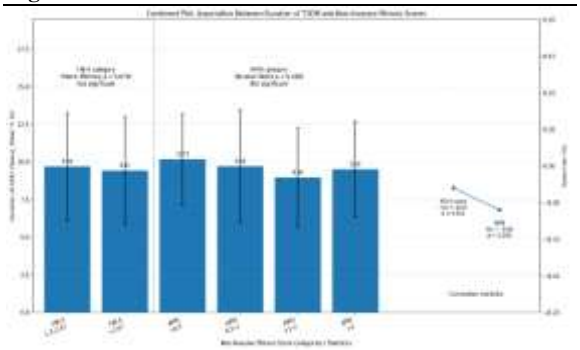

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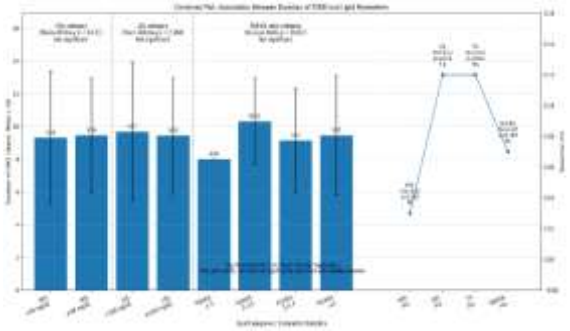

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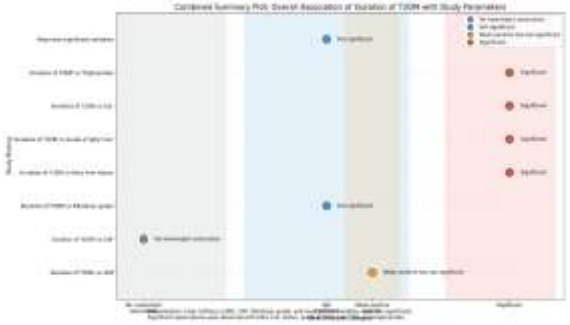

Figure 8

DISCUSSION

6.1 Summary of Major Findings

In the current study, the duration of T2DM was not significantly associated with liver stiffness measurement (LSM) and controlled attenuation parameter (CAP). LSM was only weakly and positively correlated, but insignificantly, with duration of diabetes, whereas CAP was not at all significantly correlated. But the status of fatty liver, grade of fatty liver, LDL and triglycerides were significantly correlated with duration of T2DM.

6.2 Duration of T2DM and Liver Fibrosis

Fibrosis is often present in higher frequencies in patients with T2DM, although our findings suggest that duration of T2DM may not be a good predictor of fibrosis burden. Although advanced fibrosis has been reported to be common in T2DM, factors such as obesity, insulin therapy, metabolic syndrome, and other cardiovascular risk factors are known to influence fibrosis risk.[17-19]

6.3 T2DM Duration and Hepatic Steatosis

CAP was not significantly associated with the duration of diabetes, but rather that hepatic steatosis might be more associated with ongoing metabolic activities. This suggests that risk factors for MASLD include obesity, dyslipidemia, glucose control, and other metabolic disorders, as noted in the guidelines.[20-22]

6.4 Comparison With Previous Studies

The results are partially in line with prior studies that report increased risk of steatosis, progressive fibrosis, hepatic decompensation, and hepatocellular carcinoma in T2DM patients but add that including metabolic factors in addition to diabetes status will improve risk prediction.[19,23,24]

6.5 Possible Pathophysiological Explanation

Disordered insulin signalling, adipocyte dysfunction, lipid derangement, oxidative stress and persistent inflammation may result in steatosis and fibrogenesis in the liver. Thus, metabolic burden may be more relevant than duration.[24]

6.6 Contribution of Metabolic Burden

The association with LDL and triglycerides in our study is consistent with metabolic factors playing a more critical role in the development of hepatic complications.

6.7 Clinical Implications

Early risk stratification for liver disease should be done in patients with T2DM even with short diabetes duration, particularly when they have dyslipidemia, obesity or fatty liver.[20-22]

6.8 Study Strengths

We used non-invasive transient elastography to objectively assess fibrosis and steatosis.

6.9 Limitations of the Study

The cross-sectional approach precluded causal inferences, and did not include longitudinal progression.

6.10 Future Research

Longitudinal and glycemic control measures, insulin resistance, medication and metabolic risk factors should be incorporated.

CONCLUSION

Overall Conclusion

The current research has shown that the duration of Type 2 Diabetes Mellitus was not significantly linked to severity of hepatic fibrosis, as well as severity of hepatic steatosis, measured with transient

elastography. While there was a weak positive association with liver stiffness measurement and controlled attenuation parameter, this was found to be insignificant.

Key Finding on Diabetes Duration

The main limitation was that steatosis and liver stiffness measurement were not directly associated with duration of diabetes. CAP had negligible association and LSM had a weak but positive correlation with duration of T2DM. So, duration of diabetes shouldn't be used as the sole predictor of liver disease in T2DM patients.

Importance of Metabolic Risk Assessment

The results suggest that metabolic load may be more significant than disease duration. Dyslipidemia, total triglyceride (TG) levels, low-density protein (LDL), obesity, blood glucose control and fatty liver disease should be taken into account when assessing the liver in diabetics. LDL and triglyceride level were significantly associated with duration of diabetes, confirming metabolic derangement is involved in the disease process.

Early Liver Screening in T2DM

Screening for early liver disease should be offered to T2DM patients, particularly those with metabolic abnormalities and/or dyslipidaemia. Transient elastography is important as it gives non-invasive information on liver fibrosis and steatosis. It may help early detection to prevent severe liver disease.

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