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A Study of Association between Lipid Profile and Liver Function Tests in Type 2 Diabetes Mellitus Patients

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Abstract
Objective: *To study the association between lipid profile and liver function test in type 2 diabetics.*
Methods: *The study population consisted of 100 type 2 diabetic patients attending Diabetics clinic,at a tertiary care hospital in Chennai.*
FBS,PPBS,LFT ,FLP and USG abdomen for detecting fatty liver were done for all participants. ALT /AST >30 and TC>200,TGL>150 were taken as elevated and their association with fatty liver was studied.
Results: *The 100 participants in the study included 49 females and 51 males.Mean age was 52.6 +/- 10.426.).7 out of the 100 were alcoholics. 73 of the total had raised ALT/AST.47 participants had raised TC and TGL.Both LFT and FLP were raised in 46 individuals. Out of the 71 participants with elevated LFT (alcoholics excluded) 62 had fatty liver. 43 of the 44 participants with elevated FLP had fatty liver.43 participants had all the 3 findings-elevated FLP,LFT and fatty liver in USG.Statistical analysis showed there is significant association between FLP and LFT and FLP,LFT and fatty liver(p <0.01).*
Conclusion: *there is significant association between FLP and LFT and FLP in type 2 diabetics.*
Keywords: *Diabetes,Fasting lipid profile,Liver function test,Non alcoholic fatty liver disease,Ultrasonography*
Abbreviations: *DM -Diabetes Mellitus,FLP -Fasting Lipid Profile,LFT-Liver Function Test,TC-Total Cholesterol, TGL –Triglycerides,AST-Aspartate Amino TransferaseALT-Alanine Amino Transferase,NAFLD-Non Alcoholic Fatty Liver Disease*

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I. Introduction

Diabetes mellitus (DM) is currently defined as "a group of common metabolic disorders that share the phenotype of hyperglycemia". The prevalence of both type 1 and type 2 DM is increasing worldwide.This is attributed to increasing obesity, reduced activity levels , and the aging of the

population.DM is expected to be a leading cause of morbidity in the future due to itsincreasing incidence.Multiple organ systems are affected due to the metabolic dysregulation associatedwith DM .Lipolysis and free fatty acid flux from adipocytes are increased, leading toincreased lipid synthesis in hepatocytes due to insulin resistance in adipocytes. Thisaccounts for the dyslipidemia found in type 2 DM . There is an association betweendiabetes and liver injury. Accumulation of glycogen in liver leads to hepatomegaly andliver enzyme abnormalities in poorly controlled diabetes patients.Nonalcoholic fatty liver disease (NAFLD) is frequently encountered in type 2diabetic patients.NAFLD represents a spectrum of histological findings from hepaticsteatosis or fat accumulation in hepatocytes to hepatic steatosis with a necroinflammatory component that may or may not have fibrosis, or NASH.The lipid profile,liver function and histopathological changes in type 2 diabeticindividuals are areas of active research.This study is aimed at studying the association of lipid profile and liver function in type 2 diabetic individuals –through FLP,LFT and USG for fatty liver,in individuals attending an Institute of Non-Communicable diseases at a tertiary care teaching hospital in Tamil Nadu,India.Information from this study could beof utility for protocol formation in the management and prevention of diabetes and itscomplications.

II. Aim Of The Study

To study the association between lipid profile and liver function tests in type 2 diabetic patients.Early diagnosis of NAFLD and reversal/ prevention of progression to NASH,Cirrhosis and liver malignancy.

III. Materials And Method

Study design:-Descriptive cross sectional study.
Study period-6 months
Study area- Tertiary health care centre.
Study population:- Type 2 diabetic patients attending diabetologyOP,tertiary healthcare centre.
Conflict of interest: Nil
Sample Size:- Calculated using formula 4pq/d2
p=prevalence(56%) q=(1-P) d=precision(20% of P)
=100

Ethical clearance: Ethical committee clearance was obtained.
Consent: Informed consent obtained from all subjects.Patient confidentiality maintained.
Inclusion criteria: Type 2 diabetic patients with age >32yrs attending diabetology op in a tertiary care centre.
Exclusion criteria: Patients with alcoholic liver disease were excluded from this study.

Data analysis: Data was collected using predesigned proforma.The study population consisted of 100 non-hospitalized diabetic patients, both males and females of age >35 years, who attended diabetology OP.FBS,PPBS,LFT and FLP were done. USG abdomen fordetecting fatty liver was also done for all patients.ALT and AST value of more than 30 and TC>200 ,TGL>150 as elevated and their association with fatty liver was studied.Alcoholics with fatty liver were not included.

IV. Statistics

The collected data were analyzed with IBM.SPSS statistics software 23.0 Version.Todescribe about the data descriptive statistics frequency analysis, percentage analysis wereused for categorical variables and the mean & S.D were used for continuous variables.Tofind the association in the categorical data Fisher's exact test was used. In the above statistical tools the probability value .05 is considered as significant level.

V. Results

There were 100 participants in the study.Mean age was52.6 +/- 10.426(table 7).There were 49 females and 51 males (table 1).7 out of the 100 were alcoholics. Table 4 shows 73 of the total had raised ALT/AST.47 participants had raised TC and TGL-depicted in table 5.Both LFT and FLP were raised in46 individuals as shown in table 6.Figure 2 shows the association between LFT and FLP.Out of the 71 participants with elevated LFT (alcoholics excluded) 62 had

fatty liver.Table 8 depicts this.Figure 3 shows this association.43 of the 44 participants with elevated FLP had fatty liver. This is demonstrated in table 9.Figure 4 shows the pictoricalrepresentation.Table 10 shows the data on association between FLP,LFT and Fatty liver inUSG.43 participants had all the 3 findings.Fishers exact test shows significantassociation-table 11.Figure 5 gives the pictorical representation.

Table.1 SEX

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Female	49	49.0	49.0	49.0
	Male	51	51.0	51.0	100.0
	Total	100	100.0	100.0	

Table.2 ALCOHOLISM

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Absent	93	93.0	93.0	93.0
	Present	7	7.0	7.0	100.0
	Total	100	100.0	100.0	

Table.3 USG-FATTY LIVER

		Frequency	Percent	Valid Percent	Cumulative Percent
	Absent	30	30.0	32.3	32.3
	Present	63	63.0	67.7	100.0
	Total	93	93.0	100.0	
Missing	0	7	7.0		
Total		100	100.0		

Table.4 LFT

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Negative	27	27.0	27.0	27.0
	Positive	73	73.0	73.0	100.0
	Total	100	100.0	100.0	

Figure.1

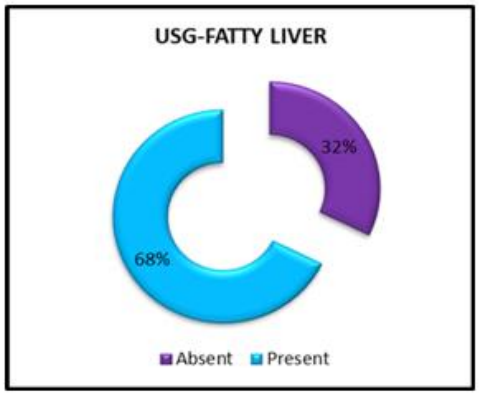


Table.5 FLP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Negative	53	53.0	53.0	53.0
	Positive	47	47.0	47.0	100.0
	Total	100	100.0	100.0	

Table.6 LFT & FLP

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	Negative	54	54.0	54.0	54.0
	Positive	46	46.0	46.0	100.0
	Total	100	100.0	100.0	

Table.7

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
AGE	100	33	82	52.16	10.426
FBS	100	74	234	116.23	26.339
PPBS	100	100	298	169.52	32.535
TC	100	152	344	210.47	31.921
TGL	100	88	198	139.66	29.398
TP	100	5.0	8.0	6.390	.7263
ALB	100	3.0	5.0	3.865	.4604
GLB	100	2.0	3.5	2.530	.4781
BIL	100	.5	66.0	2.573	8.9631
ALT	100	18	88	42.30	13.475
AST	100	18	96	44.11	14.728
Valid N (listwise)	100				

Table.8

Crosstab

			USG-FL		Total
			Absent	Present	
LFT	Normal LFT	Count	21	1	22
		% within USG-FL	70.0%	1.6%	23.7%
	Elevated LFT	Count	9	62	71
		% within USG-FL	30.0%	98.4%	76.3%
Total		Count	30	63	93
		% within USG-FL	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	52.667[a]	1	.000		
Continuity Correction[b]	48.947	1	.000		
Likelihood Ratio	54.835	1	.000		
Fisher's Exact Test				.0005	.000
N of Valid Cases	93				

a. 0 cells (0.0%) have expected count less than 5. The minimum

b. Computed only for a 2x2 table

Figure 2

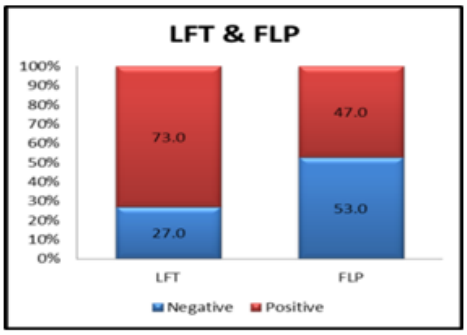


TABLE 9

Crosstab

			USG-FL		
			Absent	Present	Total
FLP	Normal FLP	Count	29	20	49
		% within USG-FL	96.7%	31.7%	52.7%
	Elevated FLP	Count	1	43	44
		% within USG-FL	3.3%	68.3%	47.3%
Total		Count	30	63	93
		% within USG-FL	100.0%	100.0%	100.0%

TABLE 10

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	34.361[a]	1	.000		
Continuity Correction[b]	31.806	1	.000		
Likelihood Ratio	41.145	1	.000		
Fisher's Exact Test				.0005	.000
N of Valid Cases	93				

a. 0 cells (0.0%) have expected count less than 5. The minimum

b. Computed only for a 2x2 table

Crosstab

			USG-FL		
			Absent	Present	Total
LFT & FLP +VE	Normal	Count	29	20	49
		% within USG-FL	96.7%	31.7%	52.7%
	Elevated LFT & FLP	Count	1	43	44
		% within USG-FL	3.3%	68.3%	47.3%
Total		Count	30	63	93
		% within USG-FL	100.0%	100.0%	100.0%

Chi-Square Tests

	Value	df	Asymp. Sig. (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	34.361[a]	1	.000		
Continuity Correction[b]	31.806	1	.000		
Likelihood Ratio	41.145	1	.000		
Fisher's Exact Test				.0005	.000
N of Valid Cases	93				

a. 0 cells (0.0%) have expected count less than 5. The minimum

b. Computed only for a 2x2 table

Figure 4

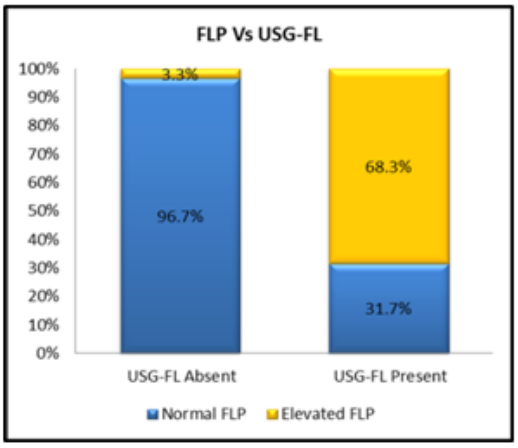
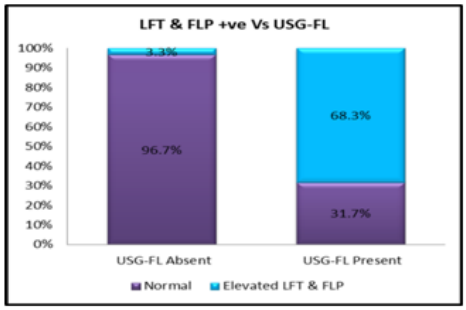


Figure 5



VI. Discussion

The main findings of the study are as follows:-

1.Type 2 diabetic patients are prone to elevations in lipid profile.

2.Individuals with Type 2 diabetes have a higher incidence of LFT abnormalities than non diabetic individuals.

3.There is higher incidence of fatty liver in type 2 diabetics.

4.Derangement of FLP and LFT has statistically significant correlation with fatty liver. Diabetes mellitus (DM) may be defined as "a group of common metabolicdisorders that share the phenotype of hyperglycemia". The prevalence of both type 1 andtype 2 DM is increasing worldwide, the prevalence of type 2 DM is rising more rapidly,due to increasing obesity, reduced activity levels , and the aging of the population. DM ispredicted to be a leading cause of morbidity in the future due to its increasing incidence. Multiple organ systems are affected due to the metabolic dysregulation associatedwith DM causing secondary pathophysiologic changes.Lipolysis and free fatty acid fluxfrom adipocytes are increased, leading to increased lipid synthesis in hepatocytes due toinsulin resistance in adipocytes. This accounts for the dyslipidemia found in type 2 DM(elevated triglycerides, reduced high-density lipoprotein [HDL], and increased low-density lipoprotein. There is an association between diabetes and liver injury (30).Liver helps in the regulation of carbohydrate homeostasis. Accumulation of glycogenin liver leads to hepatomegaly and liver enzyme abnormalities in poorly controlled diabetes patients. It has been observed that the biochemical disturbances andhepatomegaly are reversible with good glycemic control.Nonalcoholic fatty liver disease (NAFLD) is frequently encountered in type 2 diabetic patients.NAFLD represents a spectrum of histological findings from hepatic steatosis or fat accumulation in hepatocytes without inflammation, to hepatic steatosiswith a necroinflammatory component that may or may not have fibrosis, or NASH.NAFLD management focuses on treatment to improve the risk factors for NASH-obesity, insulin resistance, metabolic syndrome and dyslipidemia.In our study,100 type 2 DM patients of age more than 32 years were included.The meanage of the study population was 52.96.Out of 100 total patients,51 were females and 49 were males.7 out of the total 100 patients were alcoholics.In our study,47 participants out of 100 (47%) were found to have raised FLP.A studyconducted by Swaminathan S et al (31) had similar results.Many other multicenterstudies have also proved the increased occurrence of dyslipidemia in type 2 diabetes. Individuals found to have an elevated LFT (ALT/AST) in the current study were 73 outof 100 (73%).The study by Samela et al (32) showed 57% diabetics without any chronicliver disease had elevated LFT. An Iranian cross sectional study demonstrated a rise of ALT and AST in 10.4% and 3.3% of type 2 diabetes patients respectively(33). In a UK cohort study of 959 diabetic patients over four year period, 15.7% had raised ALT, 10.4% had elevated alkaline phosphatase whereas only 3.9% had hyperbilirubinaemia(34).The present study showed that 63 out of 100 (63%) had fatty liver in USG.This wasafter excluding the alcoholics with fatty liver. A large cohort study done in India reported the presence of fatty infiltration of liver in ultrasonography in 62.25% (127 out of 204 diabetes patients)[(35). Another study done in Myanmar revealed presence of fatty liver in 16 % of diabetes patients on ultrasound scan(36).The association between FLP and LFT,FLP and fatty liver,LFT and fatty liver andFLP,LFT and fatty liver was determined in our study.Out of the 47 patients with elevatedFLP,46 had raised LFT also.Of the 44 participants with elevated FLP(alcoholics excluded) 43 had fatty liver.The p value was found to be significant.Out of the 71 patients with elevated LFT (alcoholics excluded),62 had fatty liver in USG.Also the p value for the association between FLP,LFT and fatty liver was found to be significant.The merit of this study is that it is an eye opener in to the association in type 2 DM between FLP and LFT.Inaddition,it also shows the association between fatty liver,FLPand LFT. Based on the above observations,it could be recommended that routine monitoring of LFT ,FLP and USG for fatty liver in patients with type 2 diabetes shouldoccur at the start of drug therapy to screen the possibility of underlying fatty liver, which might need further evaluation and early intervention to prevent from progression intocirrhosis and chronic liver disease and periodic screening thereafter based on clinical judgment. There are some limitations for our study.Ourstudy,being a cross sectional one,could notaddress the effect of glycemic control over FLP,LFT and fatty liver.Although,alcoholicswith fatty liver were excluded,other risk factors like viralhepatitis,hemochromatosis,drugs etc.were not taken intoaccount.However,we believethis is a valuable addition because of the scope for early intervention to prevent from progression of fatty liver into cirrhosis and chronic liver disease through monitoring of FLP,LFT and fatty liver.

VII. Conclusion

1.Type 2 diabetic patients are prone to elevations in lipid profile.

2.Individuals with Type 2 diabetes have a higher incidence of LFT abnormalities than non diabetic individuals.

3.There is higher incidence of fatty liver in type 2 diabetics.

4.Derangement of FLP and LFT has statistically significant correlation with fatty liver. The prevalence of both type 1 and type 2 DM is increasing worldwide, the prevalenceof type 2 DM is rising more rapidly. Dyslipidemia,liver enzyme abnormalities and Nonalcoholic fatty liver disease (NAFLD) is frequently encountered in type 2 diabetic patients. With good glycemic control and regular monitoring of FLP,LFT and

fatty liver,there is scope for prevention from progression of fatty liver into cirrhosis and chronic liver disease. Hence routine monitoring of LFT and USG for faty liver along with flp inpatients with type 2 diabetes should occur at the start of drug therapy.

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