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Research Article

A Case Control Study to Determine Early Hepatic Disease in Type 2 Diabetic Patients Secondary to Insulin Resistance Using SGPT -Serum Glutamic Pyruvic Transaminase as a Biomarker

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Abstract

Introduction: Liver disease can be secondary to insulin resistance in type 2 DM patients. There are number of biomarkers available to predict the association between the two. However, we aim to evaluate role of SGPT for the same in this study.

Aim of the Study: This case control study aims at evaluating early liver disease secondary to insulin resistance in patients with type 2 DM. For the prediction of this association SGPT has been used as a Biomarker.

Methods and Results: A Case control study in which 102 patients were enrolled. Out of these, Cases (n = 26) were selected with early liver disease who were of age group 40 - 80 years. The mean SGPT levels in cases were found to be 62.10. The standard deviation for the SGPT in cases was calculated to be 33.58053.Total number of controls which were matched with all the aspects similar with the cases except the liver disease was n = 76. The mean SGPT levels in controls were found to be 20.917. The standard deviation for the SGPT in cases was calculated to be 6.99611.

Conclusion: It is quite evident from the results that insulin resistance in type 2 DM can lead to the early hepatic disease as predicted by increased levels of the SGPT as a biomarker. However, the study needs to be conducted on a larger scale in which biomarkers like IGFBP-1 and GGT and SGPT should be compared for their prediction of liver disease in the diabetic patients.

Keywords: *Diabetes Mellitus; Hepatic Disease; SGPT; Hepatic Disease Biomarkers; Type 2 Diabete*

Abbreviations

Anti CCP: Anti-Cyclic Citrullinated Peptide; DM: Diabetes Mellitus; DPP-4: Dipeptidyl Peptidase-4; GIP: Glucose-Dependent Insulinotropic Polypeptide; GLP-1: Glucagon-Like Peptide-1; GGT: Gamma-Glutamyl Transferases; HbA1C: Glycosylated Hemoglobin; IDDM: Insulin Dependent Diabetes Mellitus; NASH: Non-Alcoholic Steotic Hepatitis; NIDDM: Non-Insulin Dependent Diabetes Mellitus; RA: Rheumatoid Arthritis; SGPT: Serum Glutamic Pyruvic Transaminase; SGOT: Serum Glutamic Oxaloacetic Transaminase

Introduction

Diabetes Mellitus is a clinical syndrome in which there is deranged glucose metabolism secondary to decreased insulin levels or deformity in the insulin structure [1]. Other metabolisms like fat, proteins and electrolytes are also impacted in this disease. According to the epidemiological studies, global diabetic patients will turn upto 300 million by the end of year 2025 [2]. It is estimated that by the end of year 2025 the number of diabetic patients in India will increase upto 57 million [2]. Modernization and stress are few important causes of increased incidence of the diabetes type 2. Food habits in children and youngsters with decreased physical activities and increased stress are important contributing factors.

The association of the hepatic insulin resistance followed by the insulin resistance in the periphery has been studied for long period. One of popular concept says that liver fat accumulation leads to its insulin resistance. A study conducted on rats provides evidence that hepatic insulin resistance develops secondary to the fat accumulation in the liver [3]. Another studied showed that mitochondrial dysfunction can lead to insulin resistance and type 2 diabetes mellitus [4]. One of the important untouched aspects of the development of insulin resistance seems to be inflammation [5]. Weight reduction has also been found associated with improved glucose levels in the body [6]. In a 16 week study conducted on humans (n = 20) it comparing rosiglitazone and metformin treatments, it was found that out of the two groups there is decrease in the hepatic fat accumulation by the rosiglitazone and the drug is responsible for the reduction in the liver insulin resistance [7]. In another study in humans it was found that out of 152 patients of Hepatitis-C infection approximately 75 patients had developed impaired glucose function and finally type 2 diabetes mellitus [8].

Literature review suggests that there is an association of Hepatic disease and Type 2 Diabetes Mellitus. Our current study focusses on the key question i.e. how to predict the association between the hepatic disease and type 2 DM and coming to a conclusion that the type 2 DM is secondary to hepatic disease and vice versa. In the current study we focus using the already existing biomarker SGPT-Serum Glutamic Pyruvic Transaminase to predict this association.

Materials and Methods

Current study is an Observational, Analytical, Retrospective, Case Control study and aims to find the casual relationship between the insulin resistance and the liver disease. Study has been conducted on 102 patients in a hospital setting after seeking the appropriate Ethics approval and patient consent. For the determination of the association of insulin resistance and liver disease, SGPT has been used as biomarker.

The normal lab range of SGPT is 0 - 37 IU/L. In this study patients with SGPT levels greater than 37 IU/L are considered as having early hepatic injury (with or without clinical presentation)are taken into the inclusion criteria.

Inclusion and exclusion criteria

Inclusion Criteria	Exclusion Criteria
Must be of age group between 40 - 80 years.	Patients of age less than 40 years were excluded.
Early Liver disease of unknown cause and the former was defined as increase in SGPT levels of the patients greater than 37 U/L.	Patients with a history of “Chronic Liver Disease” were excluded.
Patients of Type 2 Diabetes as defined by “American Diabetic Association Criteria” [9].	Patients admitted with the “Acute liver disease” of known etiology were excluded.
	Patients with a history of Hepatic Disease of any etiology prior to six months of hospitalization were excluded.
	Patients with a history of “Chronic Renal Disease” were excluded.
	Patients with Type 1 DM were excluded.
	Patients with alcohol and drug abuse were excluded.

Table 1: *Inclusion and exclusion criteria.*

Cases were defined as the patients who had developed early liver disease of unknown etiology based on increased levels of SGPT of the patients greater than 37 U/L. These cases were then looked for the exposure to Type 2 DM [9] in the past.

Controls were defined as patients who had no evidence of liver disease as defined as increase in SGPT levels of the patients ranging from 5 - 37 U/L with a history of Diabetes Mellitus for at least 5 years. Total number of the patients who were selected as per the inclusion/exclusion criteria counted to 102 (n = 102). Out of these number of Cases counted to n = 26 and the number of Controls counted to n = 76.

Study endpoints: Estimation of the liver injury as evident from the increased levels of SGPT greater than normal range. Further, to draw a conclusion between the causal association of insulin resistance in type 2 diabetics leading to early liver disease.

For the statistical analysis Mean SGPT levels in cases and controls and comparing both of them to evaluate the clinical significance of the data generated. Standard deviations of the SGPT levels in cases and controls have also been calculated. Frequencies of SGPT levels in cases and controls and their respective pie and bar graphs have been done. All the statistical analysis was done using trial version of the SPSS-17.0 software.

Results

The maximum value of SGPT in cases (n = 26) was recorded to be 171U/L. The standard deviation for the SGPT was calculated to be 33.58053. Total number of controls (n = 76) which were matched with all the aspects similar with the cases except the liver disease. The mean SGPT levels in controls were found to be 20.917. It is clear that this value is not significant clinically as it is within the in the normal range (5 - 37 U/L). The minimum value of the SGPT in cases was recorded as 09 U/L. The maximum value of SGPT in cases was recorded to be 34 U/L. Both of these values lie well within the normal limits. The standard deviation for the SGPT was calculated to be 6.99611.

Patient Code	SGPT (U/L)
101 SHNRS	60
102 SHNRS	44
103 SHNRS	47
104 SHNRS	60
105 SHNRS	63.6
106 SHNRS	126
107 SHNRS	171
108 SHNRS	37
109 SHNRS	115
110 SHNRS	107
111 SHNRS	44
112 SHNRS	51
113 SHNRS	40
114 SHNRS	65
115 SHNRS	39
116 SHNRS	55
117 SHNRS	38
118 SHNRS	38
119 SHNRS	54
120 SHNRS	40
121 SHNRS	41
122 SHNRS	44
123 SHNRS	45
124 SHNRS	43
125 SHNRS	48
126 SHNRS	99

Table 2: *Cases with hepatic derangement as predicted by SGPT levels.*

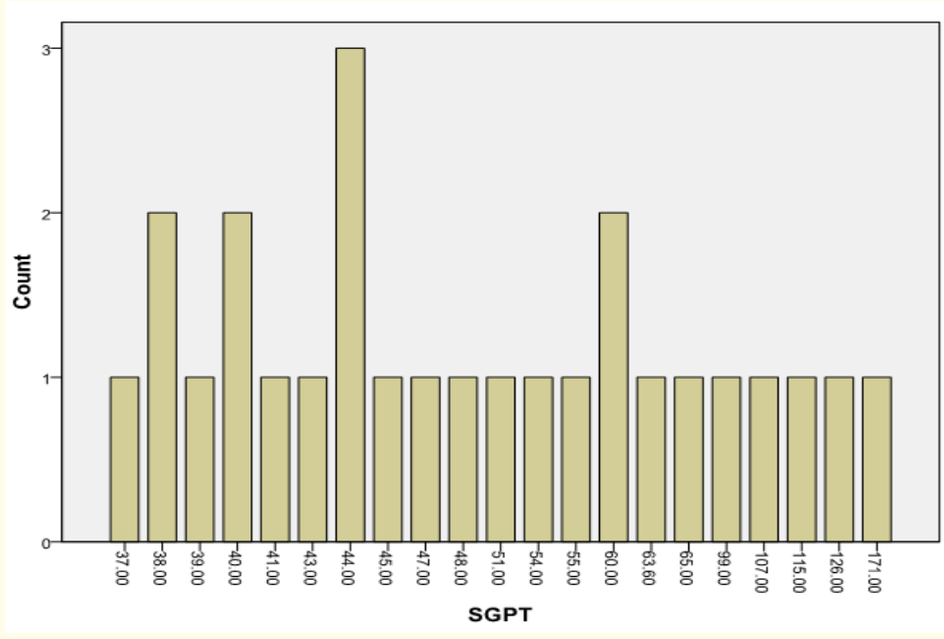

Figure 1: *Frequency bar for cases.*

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	37.00	1	3.8	3.8	3.8
	38.00	2	7.7	7.7	11.5
	39.00	1	3.8	3.8	15.4
	40.00	2	7.7	7.7	23.1
	41.00	1	3.8	3.8	26.9
	43.00	1	3.8	3.8	30.8
	44.00	3	11.5	11.5	42.3
	45.00	1	3.8	3.8	46.2
	47.00	1	3.8	3.8	50.0
	48.00	1	3.8	3.8	53.8
	51.00	1	3.8	3.8	57.7
	54.00	1	3.8	3.8	61.5
	55.00	1	3.8	3.8	65.4
	60.00	2	7.7	7.7	73.1
	63.60	1	3.8	3.8	76.9
	65.00	1	3.8	3.8	80.8
	99.00	1	3.8	3.8	84.6
	107.00	1	3.8	3.8	88.5
	115.00	1	3.8	3.8	92.3
	126.00	1	3.8	3.8	96.2
	171.00	1	3.8	3.8	100.0
	Total	26	100.0	100.0	

Table 3: *Frequency of SGPT in cases.*

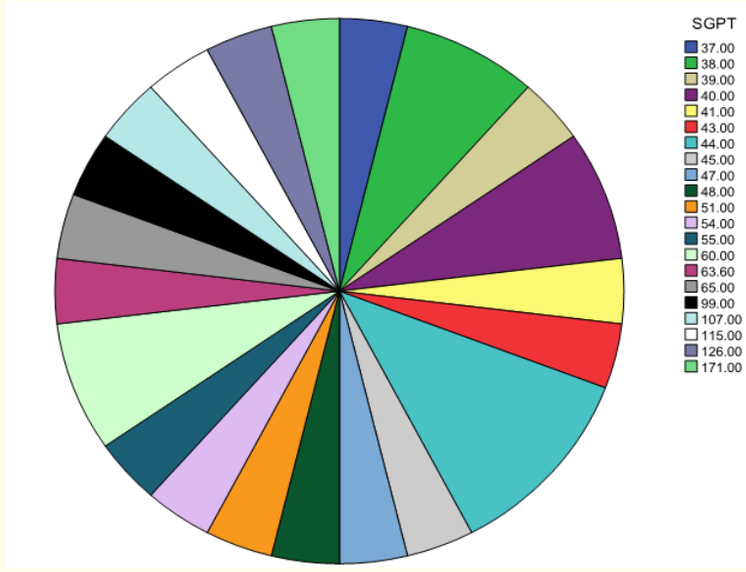

Figure 2: *Frequency pie chart for cases*

	N	Minimum	Maximum	Mean	Std. Deviation
SGPT	26	37.00	171.00	62.1000	33.58053
Valid N (list wise)	26				

Table 4: *Descriptive statistics in cases.*

The mean SGPT levels in cases were found to be 62.100. It is clear that this value is clinically significant as it is way above the normal range (5 - 37 U/L). The minimum value of the SGPT in cases was recorded as 37 U/L. The maximum value of SGPT in cases was recorded to be 17 1U/L.

The standard deviation for the SGPT was calculated to be 33.58053.

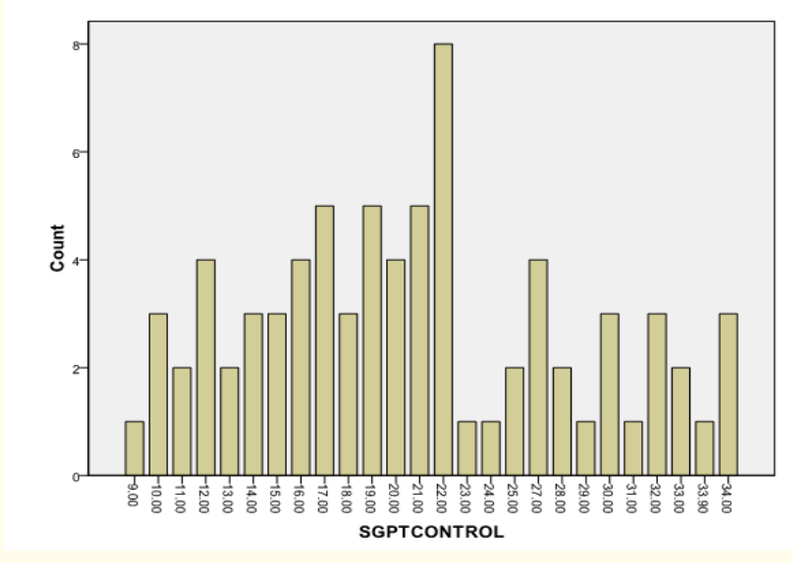

Figure 3: *Frequency graph SGPT in controls.*

Patient code	SGPT (U/L)
127 SHNRS	16
128 SHNRS	25
129 SHNRS	16
130SHNRS	16
131 SHNRS	10
132 SHNRS	28
133 SHNRS	13
134 SHNRS	15
135 SHNRS	22
136 SHNRS	33
137 SHNRS	34
138 SHNRS	22
139 SHNRS	20
140 SHNRS	31
141 SHNRS	27
142 SHNRS	22
143 SHNRS	34
144 SHNRS	14
145 SHNRS	21
146 SHNRS	13
147 SHNRS	17
148 SHNRS	33
149 SHNRS	14
150 SHNRS	34
151 SHNRS	12
152 SHNRS	21
153 SHNRS	19
154 SHNRS	20
155 SHNRS	22
156 SHNRS	22
157 SHNRS	29
158 SHNRS	19
159 SHNRS	21
160 SHNRS	27
161 SHNRS	30
162 SHNRS	10
163 SHNRS	19
164 SHNRS	18
165 SHNRS	19
166 SHNRS	20
167 SHNRS	22
168 SHNRS	14
169 SHNRS	17

170 SHNRS	32
171 SHNRS	21
172 SHNRS	17
173 SHNRS	18
174 SHNRS	32
175 SHNRS	27
176 SHNRS	19
17 7 SHNRS	32
178 SHNRS	22
179 SHNRS	11
180 SHNRS	34
181 SHNRS	30
182 SHNRS	11
183 SHNRS	9
184 SHNRS	21
185 SHNRS	12
186 SHNRS	27
187 SHNRS	30
188 SHNRS	16
189 SHNRS	17
190 SHNRS	12
191 SHNRS	15
192 SHNRS	25
193 SHNRS	28
194 SHNRS	18
195 SHNRS	22
196 SHNRS	15
197 SHNRS	10
198 SHNRS	17
199 SHNRS	24
200 SHNRS	23
201 SHNRS	20
202 SHNRS	12

Table 5: *Controls with no hepatic disease but with type -2 DM.*

Total number of controls which were matched with all the aspects similar with the cases except the liver disease was n = 76. The mean SGPT levels in controls were found to be 20.917. It is clear that this value is not significant clinically as it is within the in the normal range (5 - 37 U/L). The minimum value of the SGPT in cases was recorded as 09 U/L. The maximum value of SGPT in cases was recorded to be 34 U/L. Both of these values lie well within the normal limits.

The standard deviation for the SGPT was calculated to be 6.99611

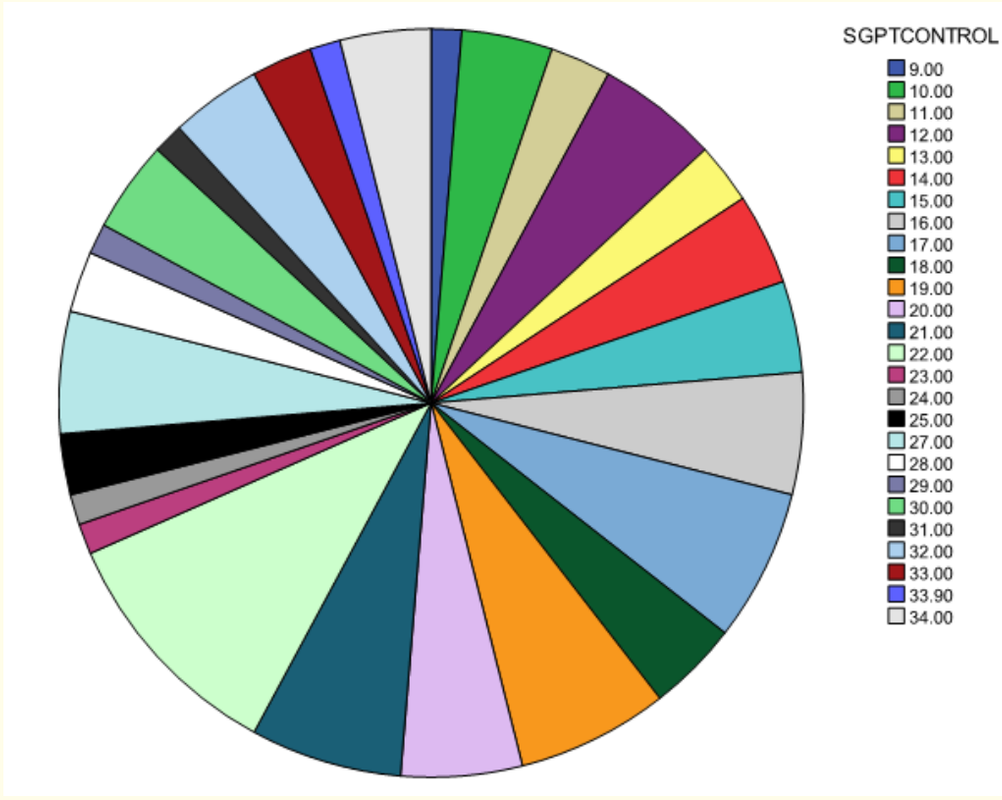

Figure 2: *SGPT frequency pie chart for controls*

Discussion

Liver enzymes SGPT derangement is a very good indicator of the early liver cell injury [1]. In a non-diseased state these are present with in the liver cells. In a pathological state or any disease these enzymes get into the circulation and hence the serum levels are increased [1]. The increased levels of SGPT are present in number of diseases like-Acute and Viral Hepatitis and various other liver related diseases.

In the current study we evaluated hepatic disease based on the levels of SGPT as it is one of the important indicator of the early liver injury. Another important aspect for the selection of the SGPT as a biomarker is the feasibility of conduction of the investigation. It is comparatively low cost as compared to GGT and investigations.

In the current study, we evaluated SGPT levels of 102 patients to find out the whether diabetes mellitus type 2 can lead to early hepatic disease or not. The maximum value of SGPT in cases (n = 26) was recorded to be 171 U/L. The standard deviation for the SGPT was calculated to be 33.58053. Total number of controls (n = 76) which were matched with all the aspects similar with the cases except the liver disease. The mean SGPT levels in controls were found to be 20.917. It is clear that this value is not significant clinically as it is within the in the normal range (5 - 37 U/L). The minimum value of the SGPT in cases was recorded as 09 U/L. The maximum value of SGPT in cases was recorded to be 34 U/L. Both of these values lie well within the normal limits. The standard deviation for the SGPT was calculated to be 6.99611.

This study clears the picture regarding the insulin resistance in type 2 DM as a cause of liver disease. In this study we have used SGPT as a predictor if this association. We have got significant results which show that the mean increase in the SGPT levels in cases was way above the clinically significant value. Hence it is quite clear that liver disease can be secondary to the insulin resistance in type 2 DM.

Although the current study provides a strong relationship between the hepatic disease leading to Diabetes mellitus type 2 using SGPT as a biomarker, however there are certain limitations of the study which need to be further evaluated in future.

SGPT as a biomarker can have certain negative aspects as well. Certain studies suggest that SGPT may not be increased in hepatic diseases also [10]. Hence there are other options like GGT and liver biopsy which can be used to find this sort of association. However owing to various factors like cost factors and popularity among the physicians still SGPT is one of the most common investigation tool to determine hepatic sufficiency.

As it a case control study the number of the patients enrolled were less. To get a better picture of the scenario the study should have conducted on a larger scale so that more appropriate statistical results are achieved. Further there is a possibility of the selection as well by the investigating team and recall bias by the patients.

Future Considerations

As far the future considerations are concerned on of the most important aspects is the conduction of the similar studies on a larger number of population over a longer period of time. This will lead to the results which are clinically as well as statistically more significant.

Along with this studies comparing efficacy of the biomarkers like SGPT, SGOT, GGT predicting liver disease in type 2DM can be done on a larger scale and for a longer period of time. Various other markers like radio diagnosis and the liver biopsies techniques should be adopted along with the basic investigations so that a much clear picture of the situation can be obtained.

One of the latest concept in the prediction of hepatic insulin resistance and the diabetes mellitus is the "Role of IGFBP-1" [11]. IGFBP-1 is synthesized in liver itself. There have studies conducted which indicate the association of the liver insulin resistance and the fat accumulation in liver type 2 DM [11]. It is evident now that Fasting Serum IGFBP-1 is related to the liver fat in an inverse proportion i.e. increase in the liver fat will reduce the levels of circulating IGFBP -1 [11]. More over this enzyme is also not related with the obesity related biomarker which is much more specific to liver [11]. This marker can be used in the prediction of liver injury in both diabetic as well as non - diabetic patients equally well [11].

Hence it is quite clear that there are number of options in the pipeline for predicting liver disease in type 2 DM patients, however role of SGPT will always remain important as a baseline marker for the prediction of such an association.

Conclusion

It is quite evident from the results that insulin resistance in type 2 DM can lead to the early hepatic disease as predicted by increased levels of the SGPT as a biomarker. However, the study needs to be conducted on a larger scale in which biomarkers like IGFBP-1 and GGT and SGPT should be compared for their prediction of liver disease in the diabetic patients.

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