ORIGINAL ARTICLE

Evaluation of Alanine Aminotransferase (ALT) and Gamma-glutamyl Transferase (GGT) in Patients with Type 2 Diabetes Mellitus at the Diabetic Clinic, Guyana

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ABSTRACT

Objective: *To determine the prevalence of alanine aminotransferase (ALT) and gamma-glutamyl transferase (GGT) abnormalities and contributing factors in adult patients with type 2 diabetes mellitus at the diabetic clinic of public hospital, Guyana.*

Methods: *A prospective study was carried out on 60 randomly selected diabetic patients from the public hospitals' diabetic clinics. Patients were included in the study once they had to get tested for ALT and GGT on their request form from the physician and their informed consent. Analysis was done using SPSS 20.*

Results: *Analysis of ALT and GGT showed mean ALT ± SD as 61.9 ± 28.9 (95% CI: 54.5, 69.4) and mean GGT ± SD as 19.6 ± 9.7 (95% CI: 17.1, 83.3). Family history (RR 2.3 95% CI: 0.6, 8.6) showed a greater risk factor of high ALT followed by current illness (RR 1.3 95% CI: 0.4, 4.7). Correlation analysis between ALT and GGT shows a significant positive correlation.*

Conclusion: *The research showed a prevalence of elevated levels of ALT and GGT in type 2 diabetic patients and a strong association to metformin and ethnicity in particular those of Indian decent. Therefore, further research within a controlled environment should be done in order to evaluate the efficacy of the action of metformin as compared to other diabetic drugs in concert with other contributing factors.*

Keywords: Alanine aminotransferase, alanine aminotransferase, type 2 diabetes mellitus.

INTRODUCTION

Diabetes is a chronic disease that occurs either when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. Insulin is a hormone that regulates blood sugar (1). In 2012, an estimated 1.5 million deaths were directly caused by diabetes and more than 80% of diabetes deaths occur in low- and middle-income countries (2). WHO projects that diabetes will be the 7th leading cause of death in 2030 (3).

Liver plays a major role in maintenance of normal glucose levels during fasting as well as in the post-prandial period. It is also documented that alanine aminotransferase (ALT), aspartate aminotransferase (AST), and gamma-glutamyl transferase (GGT) are the common liver enzymes and together make the liver function tests (4). Alanine aminotransferase and AST represent the health status of liver cells and GGT represents the health of biliary tract (5, 6).

Elevated GGT levels among diabetic patients and association between elevated GGT and poor glycaemic state have been studied since years (7, 8). The liver enzymes, AST, ALT, and GGT are very often used in the evaluation of liver function (9). Literature on prospective studies shows associations between concentrations of AST, ALT, GGT and the incidence of type 2 diabetes (10–15).

The purpose of this study is to estimate the associations of serum liver enzyme (ALT and GGT) in patients with type 2 diabetes at the public hospital, Guyana.

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SUBJECT AND METHODS

Description of subjects

This research was carried out at the Georgetown Public Hospital Cooperation (GPHC) Diabetic Clinic in association with the GPHC Medical Laboratory in which type 2 diabetic patients were randomly selected to participate in the study after giving informed consent.

Study design

A prospective, criterion-based study was carried out and the variables were collected simultaneously.

Variables

Independent: Type 2 diabetes mellitus.
Dependent: Levels of ALT and GGT.

Method of measuring variables

Testing was done at the GPHC Medical Laboratory in a Chem-Well Chemistry Analyzer. A proper control procedure was carried out to ensure the validity and reliability of the results. The results were then tabulated and analysed. Participants were asked to answer a questionnaire on related issues and relevant information such as family history and personal activities.

Data analysis

The data obtained were analysed using SPSS version 20 and Microsoft Excel.

Ethical considerations

Approval for the study was granted from the Chief Executive Officer of the Georgetown Public Hospital Cooperation through the Director of Medical and Professional Services and the Director of the Georgetown Public Hospital Cooperation Medical Laboratory. Patient forms were coded to protect the identity of each patient. Patients were also informed that participation was voluntary and they reserve the right to stop participation at any time during the study period.

RESULTS

The present study had 60 participants confirmed with type 2 diabetes. Demographic and clinical characteristics of study participants are shown in Table 1. The majority of the patients were female (71.7%) and most patients were between 51 and 60 age group (31.7%) ($p \leq 0.005$). Mean age among the participants was 62. Indo-Guyanese accounted for 58.3% of the total sample population and as such recorded the highest prevalence. 41.6% of patients were on metformin while 57.0% were on other drugs other than metformin, statin, fibrate and thiazolidinediones. Blood pressure was recorded high in 35% population and 31.7% reported no other medical conditions.

Table 1: Demographic and clinical characteristics of study participants

	n (%)	*p*-value
Gender		
Male	17 (28.3)	
Female	43 (71.7)	< 0.05
Age group		
40–50	17 (28.3)	
51–60	19 (31.7)	
61–70	16 (26.7)	
71–80	8 (13.3)	> 0.05
Ethinicity		
Afro Guyanese	18 (30.0)	
Indo Guyanese	35 (58.3)	
Mixed	7 (11.7)	< 0.05
Drugs		
Metformin	25 (41.6)	
Metformin + other	11 (18.3)	
Other	23 (38.3)	
Statin	1 (1.7)	< 0.05
Medical conditions		
BP	21 (35.0)	
BP + HD	1 (1.7)	
HD	7 (11.7)	
High cholestrol	5 (8.3)	
High cholestrol + BP	4 (6.7)	
High cholestrol + BP + HD	1 (1.7)	
None	19 (31.7)	
Others	1 (1.7)	< 0.05

Analysis of ALT and GGT showed mean ALT ± SD as 61.9 ± 28.9 (95% CI: 54.5, 69.4) and mean GGT ± SD as 19.6 ± 9.7 (95% CI: 17.1, 83.3). Increased ALT level was recorded among 78.3% (95% CI: 73.3, 83.3); however, GGT did not show any significant increase (Table 2).

Table 2: Mean value of ALT and GGT values

	Mean ± SD	95% CI
ALT	61.9 ± 28.9	54.5–69.4
Min	12	
Max	118	
GGT	19.6 ± 9.7	17.1–22.1
Min	3	
Max	35	
	n (%)	
> ALT	47 (78.3)	73.3–83.3
< ALT	13 (21.7)	16.7–26.7

Family history (RR 2.3 95% CI: 0.6, 8.6) showed a greater risk factor of high ALT followed by current illness (RR 1.3 95% CI: 0.4, 4.7), gender (RR 1.1 95% CI: 0.8, 1.4), physical exercise (RR 0.96 95% CI: 0.7, 1.3) and smoking (RR 0.7 95% CI: 0.6, 0.8) (Table 3). Correlation analysis between ALT and GGT shows a significant positive correlation (Figure).

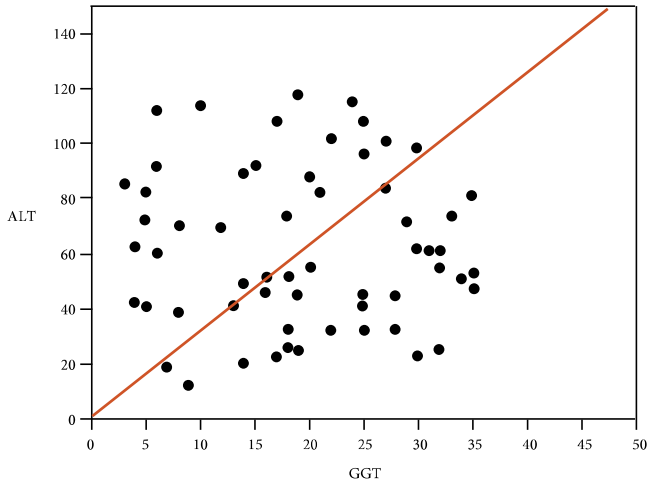

Figure: Bivariate analysis of GGT and ALT among diabetes 2 patients (ALT = 0.5 + 3.1*GGT).

DISCUSSION

Abnormal liver function tests (LFT) is one of the most common findings among type 2 diabetes patients and elevated ALT being the most common abnormality (16). In a case-controlled study in Nigeria showed that ALT and GGT values were significantly higher (52.9 IU/L and 24.3 U/L respectively) in diabetic group compared to the non-diabetic groups (34.4 IU/L and 9.2 IU/L respectively). This study also revealed the most predominant LFT abnormality in diabetic group with elevated GGT (17).

This study also showed metformin as most common drug used among the diabetes population. This could be because of the act that metformin is more readily available and at a lesser cost than most of the other recommended drugs. In addition, in some regards this can be stated as the reason as for a positive correlation with elevated ALT and GGT in patients on that drug. One study has reported that drugs such as statins were a possibility for the increase in ALT and GGT liver function enzyme levels (18). However, in this study it is shown that metformin had a strong association to the elevation of ALT and GGT. The reason for this is unknown and needs to be explored.

Other studies have indicated a link between family history and diabetes; however, this study showed most respondents with no family history of diabetes which firmly places an association to lifestyle and diet. Ethnicity played an important role in the majority of the patients with elevated ALT and GGT being Indo-Guyanese. However, on the account the more than half the sample population was Indo-Guyanese, this can be the causal factor for that outcome. A positive correlation between elevated ALT and GGT was also noted to among patients with duration of 5–10 years type 2 diabetes.

Many studies have proposed different mechanisms to explain this phenomenon, that ALT and GGT liver function enzymes are elevated in people with type 2 diabetes and this leads to a higher incidence of liver enzymes test abnormalities. Aithal *et al* supported the claim that ALT is a specific marker of liver pathology, as it is found primarily in the liver, and is considered to be the marker most closely correlated to liver fat. Although GGT is a less specific marker of liver, higher GGT levels have also been linked with obesity, physical inactivity, hypertension, dyslipidaemia, and hyperinsulinemia, implying

Table 3: Risk factors associated with type 2 diabetes patient at the public hospital, Guyana

		ALT		RR	OR
		Yes	No		
Gender	Female	33 (76.7)	10 (23.3)	1.1 (0.8–1.4)	0.7 (0.2–2.9)
	Male	14 (82.4)	3 (17.6)		
Smoking	Yes	10 (100)	0	0.7 (0.6–0.8)	0
	No	37 (74.4)	13 (26.0)		
Family history	Yes	37 (82.2)	8 (17.8)	2.3 (0.6–8.6)	0.8 (0.6–1.2)
	No	10 (68.7)	5 (33.3)		
Physical exercise	Yes	31 (79.5)	8 (20.5)	0.96 (0.7–1.3)	1.2 (0.3–4.3)
	No	16 (76.2)	5 (23.8)		
Current illness	Yes	32 (80.0)	8 (20.0)	1.3 (0.4–4.7)	0.9 (0.7–1.2)
	No	15 (75.0)	5 (25.0)		

that elevated GGT belongs in the cluster of the metabolic syndrome (19, 20).

In addition, a study by Anderwalt *et al* the elevated ALT and GGT values were significantly higher in men than in women, which is contrary to this study where women showed higher levels of liver function test (21). This study had some major limitations such as Body Mass Index, waist circumference, plasma fasting insulin levels and heavy alcohol consumptions which were not examined as parameters to influence the results, and future studies should take them into consideration. In terms of the severity of elevations recorded in this study, the majority were mild elevations. Since most studies have not reported on the severity of elevated liver enzymes, the exact implications of this finding are not known.

CONCLUSION

In conclusion, the research showed a prevalence of elevated levels of ALT and GGT in type 2 diabetic patients within the Guyanese diabetic population and strong association to metformin and ethnicity in particular those of Indian decent. Therefore, further research within a controlled environment should be done in order to evaluate the efficacy of the action of metformin as compared to other diabetic drugs in concert with other contributing factors.

REFERENCES

1. Definition, diagnosis and classification of diabetes mellitus and its complications. Part 1: Diagnosis and classification of diabetes mellitus. Geneva, World Health Organization, 1999 (WHO/NCD/NCS/99.2).
2. World Health Organization. Global health estimates: deaths by cause, age, sex and country, 2000–2012. Geneva, WHO, 2014.
3. Mathers CD, Loncar D. Projections of global mortality and burden of disease from 2002 to 2030. PLoS Med 2006; **3:** e442.
4. Hanley AJ, Williams K, Festa A, Wagenknecht LE, Kempf J, Zinman B, Haffner SM. Elevations in marker of liver injury and risk of type 2 diabetes—the insulin resistance atherosclerosis study. Diabetes 2004; **53:** 2623–32.
5. Lee DH, Silventonein K, Jacobs DR, Jousilhati P, Tuomileto J. Gamma glutamyltransferase, obesity and the risk of type 2 diabetes observational cohort study among 20,158 middle aged men and women. J Clin Endocrinol Metab 2014; **89:** 5410–14.
6. Lee DH, Ha MH, Kim JH, Christiani DC, Gross MD, Steffes M, Blomhoff R, Jacobs DR. Gamma glutamyltransferase and diabetes—a four year follow up study. Diabetologia 2003; **46:** 359–64.
7. Whitfield JB. Gamma glutamyl transferase. Crit Rev Clin Lab Sci 2001; **38:** 263–355.
8. Trell E, Kristenson H, Peterson B, Fex G, Henningsen NC, Berntorp K et al. Two-hour glucose and insulin responses after a standardized oral glucose load in relation to serum gamma-glutamyl transferase and alcohol consumption. Acta Diabetol Lat 1981; **18:** 311–7.
9. Ahn HR, Shin MH, Nam HS, Park KS, Lee YH, Jeong SK, Choi JS and Kweon SS. The association between liver enzymes and risk of type 2 diabetes: the Namwon study. Diabetol Metab Syndr 2014; **6:** 14.
10. Hanley AJ, Williams K, Festa A, Wagenknecht LE, D'Agostino RB Jr, Kempf J, Zinman B, Haffner SM: Elevations in markers of liver injury and risk of type 2 diabetes—the insulin resistance atherosclerosis study. Diabetes 2004; **53:** 2623–32.
11. Goessling W, Massaro JM, Vasan RS, D'Agostino RB Sr, Ellison RC, Fox CS: Aminotransferase levels and 20-year risk of metabolic syndrome, diabetes, and cardiovascular disease. Gastroenterology 2008; **135:** 1935–44.
12. Monami M, Bardini G, Lamanna C, Pala L, Cresci B, Francesconi P, Buiatti E, Rotella CM, Mannucci E: Liver enzymes and risk of diabetes and cardiovascular disease: Results of the Firenze Bagno a Ripoli (FIBAR) study. Metabolism 2008; **57:** 387–92.
13. Jiamjarasrangsi W, Sangwatanaroj S, Lohsoonthorn V, Lertmaharit S: Increased alanine aminotransferase level and future risk of type 2 diabetes and impaired fasting glucose among the employees in a university hospital in Thailand. Diabetes Metab 2008; **34:** 283–9.
14. Sato KK, Hayashi T, Nadamura Y: Liver enzymes compared with alcohol consumption in predicting the risk of type 2 diabetes. Diabetes Care 2008; **31:** 1230–36.
15. Andre P, Balkau B, Born C, Charles MA, Eschwege E: Three-year increase of gamma-glutamyltransferase level and development of type 2 diabetes in middle-aged men and women: the D.E.S.I.R. cohort. Diabetologia 2006; **49:** 2599–603.
16. Harris E H. Elevated liver function tests in type 2 diabetes. Clin Diabetes 2005; **23:** 115–9.
17. Balogun WO, Adeleye JO, Akinlade KS, Adedapo KS, Kuti M. Frequent occurrence of high gamma-glutamyl transferase and alanine amino transferase among Nigerian patients with type 2 diabetes. Afr J Med Sci 2008; **37:** 177–83.
18. Harris HE: Elevated Liver Function Tests in Type 2 Diabetes, Clin Diabetes 2005; 23: 115–119. https://doi.org/10.2337/diaclin.23.3.115.
19. Aithal GP, Bennet A, Brousil J, Gazis A, Jackson L, Mansell P, West J. Elevated serum alanine trasaminase in patients with type 1 or type 2 diabetes mellitus. Q J Med 2006; **99:** 871–6.
20. Baldi S, Ferrannini E, Gonzales C, Haffner S, Nannipieri M, Posadas R, Stern M, and Williams K. Liver Enzymes, The metabolic syndrome and incident diabetes, The Mexico city diabetes study. Diabetes Care 2005; **28:** 1757–62.
21. Anderwald H C, Balkau B, Bonnet, Ducluzeau P H, Gastaldelli A, Laville M, Konrad T, Mari Andrea. Liver enzymes are associated with hepatic insulin resistance, insulin secretion, and glucagon concentration in healthy men and women. Diabetes 2011; **60:** 1660–7.