

**Evaluation of Alanine Aminotransferase (ALT) and Gamma-glutamyl Transferase (GGT)
in Patients with Type 2 Diabetes Mellitus (T2DM) at the Diabetic Clinic, Guyana**

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Running head: ALT and GGT among Diabetes Type 2 Patients

Synopsis: High prevalence of elevated ALT and GGT in type 2 diabetic patients showed a strong association to metformin and ethnicity in particular those of Indian decent. Family history showed a greater risk factor of high ALT followed by current illness.

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 sixty (60) randomly selected diabetic patients from the public hospitals diabetic clinic. 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 \pm SD as 61.9 ± 28.9 (95% CI 54.5-69.4) and mean GGT \pm 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 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: ALT, GGT, 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 ALT, AST and GGT are the common liver enzymes and together makes the liver function tests (4). ALT and AST represent the health status of liver cells were as GGT represents health of biliary tract (5-6).

Elevated GGT levels among diabetic patients and association between elevated GGT and poor glycemic state is studied since years (7-8). The liver enzymes, aspartate aminotransferase (AST), ALT, and GGT are very often used in 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.

METHODOLOGY

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 validity and reliability of the results. The results were then tabulated and analyzed. 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 was analyzed 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. Majority of the patients were female (71.7%) and most patients were between 51-60 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 thiazolidiliones. Blood pressure was recorded high in 35 % population and 31.7% reported no other medical conditions.

Analysis of ALT and GGT showed mean ALT \pm SD as 61.9 ± 28.9 (95% CI 54.5-69.4) and mean GGT \pm 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 showed any significant increase Table 2.

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) respectively Table 3. Correlation analysis between ALT and GGT shows a significant positive correlation Fig 1.

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 diabetes population. This could be because of the fact 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 need 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 that 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,

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

In addition, a study by Anderwalt et al correlated the elevated ALT and GGT values were significantly higher in men than in women which is in contrary to this study were women showed higher levels of liver function test (21). This study had some major limitation such as Body Mass Index (BMI), 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 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.

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