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Assessment of HbA1C and Fructosamine in Alcoholic Liver Disease: A Case Control Study

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ABSTRACT

This study aims to evaluate the effectiveness of serum fructosamine and glycated hemoglobin (HbA1C) as markers for assessing glycemic control and determining the severity and prognosis of chronic alcoholic liver disease. Specifically, it aims to identify the superior marker between HbA1C and fructosamine in this context. A total of 90 individuals, both male and female, aged between 20 and 70 years, diagnosed with chronic alcoholic liver disease, were included in the study. Additionally, 45 healthy individuals, matched for age and sex, served as controls. The patient group was further divided into non-complicated and complicated subgroups. HbA1C levels were measured using the immunoturbidimetry method, while serum fructosamine levels were determined using colorimetry with nitro blue tetrazolium. The estimation of SGOT was performed according to the IFCC method and serum total protein levels were assessed using the biuret method. In both groups of chronic alcoholic liver disease patients, the mean concentrations of HbA1c and serum total protein were decreased, while the mean concentrations of serum fructosamine and SGOT were increased. There was no significant difference in serum total protein between non-complicated cases and controls. The mean value of HbA1c did not differ significantly between non-complicated and complicated cases. SGOT exhibited a significant negative correlation with serum total protein, a significant positive correlation with serum fructosamine and no correlation with HbA1c. A significant negative correlation was found between serum total protein and serum fructosamine. The findings of this study indicate that serum fructosamine is a more effective marker for monitoring chronic glucose control and assessing the severity of chronic alcoholic liver disease in comparison to HbA1c.

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Key Words

Fructosamine, glycated hemoglobin, liver diseases, blood glucose, alcohol

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INTRODUCTION

Chronic alcoholic liver disease is characterized by the gradual deterioration and regeneration of liver tissue, resulting in fibrosis and cirrhosis. This condition is defined by the persistence of clinical or biochemical indications of liver disease for a period exceeding six months[1]. The liver plays a crucial role in regulating glucose metabolism and ensuring stable plasma glucose levels. Inadequate control of plasma glucose in individuals with chronic liver disease is often associated with a negative prognosis and the potential development of complications[2,3].

The complications arising from chronic alcoholic liver disease stem from the impaired functioning of hepatocytes. These complications encompass variceal hemorrhage, hepatic encephalopathy, coagulopathy, ascites, spontaneous bacterial peritonitis and portal hypertension. While cirrhosis typically has a gradual onset, it can progress rapidly following severe chronic alcoholic liver disease. The majority of deaths associated with chronic alcoholic liver disease are caused by cirrhosis-related complications, including ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, encephalopathy and variceal hemorrhage[2,4,5].

According to recent data, the mortality rate attributed to alcoholic liver disease in France stands at 14.3 per 100,000 individuals[6]. In district general hospitals within the UK, alcohol is responsible for 80% of cases of liver cirrhosis[6]. Alcoholic cirrhosis is also becoming more prevalent in countries such as Japan and India, where the disease historically had a low prevalence[4].

The measurement of HbA1C concentration offers a valuable means of evaluating long-term glycemic control and is closely associated with the development of complications related to diabetes mellitus. It is important to note that impaired liver function can affect the results of HbA1C tests[2].

Serum fructosamine, a glycated protein, is employed as an indicator of glycemic status over a span of 2-4 weeks. Since fructosamine is formed through the glycation of serum proteins, the fructosamine measurement is influenced by this process. It is important to consider that impaired liver function, which can lead to reduced hepatic protein synthesis, may potentially alter fructosamine results[2].

This study aimed to examine the levels of HbA1C and serum fructosamine in individuals diagnosed with chronic alcoholic liver disease, both in those without complications and those with complications, as well as in a group of healthy controls.

MATERIALS AND METHODS

A case-control study was conducted to investigate the levels of HbA1c, SGOT, serum total protein and serum fructosamine in individuals with chronic alcoholic liver disease. Prior to participation, all subjects provided informed consent and the research study was conducted as per the standard ethical guidelines[7]. Following the application of inclusion and exclusion criteria, a total of 135 subjects were included in the study. Among them, 45 were individuals with chronic alcoholic liver disease but without complications, 45 had chronic alcoholic liver disease with complications and the remaining 45 were healthy controls.

The target population consisted of individuals diagnosed with chronic alcoholic liver disease, comprising a total of 90 cases. The diagnosis was based on clinical history, liver function tests and/or ultrasonography. The age range of the participants encompassed 20-70 years and both sexes were included. To further analyze the cases, they were divided into two distinct groups. Group A comprised 45 cases of chronic alcoholic liver disease without any complications. Group B, on the other hand, consisted of 45 cases of chronic alcoholic liver disease accompanied by complications such as ascites, splenomegaly, hepatic encephalopathy and portal hypertension.

To establish a comparison, a control group of 45 healthy individuals was selected. The control group was carefully matched with the cases in terms of age and sex. These controls were free from any known liver diseases or alcohol-related disorders. By employing this design, the study aimed to assess and contrast the clinical characteristics and outcomes between the chronic alcoholic liver disease cases and the healthy controls.

Patients with liver diseases other than chronic alcoholic liver disease, Diabetes Mellitus, Renal Disease, history of significant blood loss or transfusion, anemia, reticulocytosis, undergoing erythropoietin treatment, history of myocardial infarction, Ischemic Heart Disease and hypertension were not included in the study. These criteria were put in place to ensure a homogeneous population of participants with chronic alcoholic liver disease, devoid of additional liver disorders or significant comorbidities that could impact the study outcomes. Following a thorough assessment of the inclusion and exclusion criteria, age-matched cases and controls were selected for participation and informed consent was obtained from each individual. A standardized proforma was utilized to record pertinent information, including patient data and investigation reports, ensuring consistent and comprehensive data collection for subsequent analysis.

Aseptic precautions were strictly followed during the blood collection process, where approximately 5 mL of blood was drawn from a large peripheral vein using a sterile disposable syringe. The blood was collected in two separate tubes: A sterile

plain bulb and a sterile EDTA bulb. The blood in the plain bulb was allowed to clot, after which the serum was separated by centrifugation. The serum samples were then stored at a temperature of 4°C until further analysis. Similarly, the EDTA blood samples were also kept at 4°C until analysis and were utilized for the preparation of hemolysate for HbA1c measurement.

The concentrations of SGOT (Serum Glutamic Oxaloacetic Transaminase) and serum total protein were determined using analytical kits. The concentration of HbA1c and fructosamine was estimated using a commercial available diagnostic kit. All these parameters were measured using a semi-autoanalyzer enabling efficient and automated analysis of the samples.

The statistical analysis was conducted using SPSS software, specifically version 20.0. Descriptive statistics were employed to present the data, with the Mean±standard deviation and range values being reported. To compare the means of two groups, the Student's "t" test was utilized. Additionally, the relationship between two parameters was assessed using Pearson's correlation coefficient. A probability value (p-value) of less than 0.05 was deemed statistically significant, indicating a strong level of confidence in the obtained results.

RESULTS

Table 1 demonstrates that there was no statistically significant difference observed in terms of age between the cases and control group. Table 2 provides the values of serum total protein, SGOT, serum fructosamine and HbA1c for the control group, cases in Group A and cases in Group B. Furthermore, the statistical analysis, conducted using an unpaired Student's "t" test, indicated that there was no significant difference in the serum total protein levels between the control group and cases in Group A. Additionally, the analysis revealed no significant difference in the levels of HbA1c between cases in Group B and cases in Group A.

Table 3 presents the observed associations between various variables. It demonstrates a negative correlation between serum glutamic oxaloacetic transaminase (SGOT) and glycated hemoglobin (HbA1c) However, this correlation did not reach statistical significance. Conversely, a positive and statistically significant correlation was found between SGOT and serum fructosamine levels. Furthermore, a statistically significant negative correlation was observed between SGOT and serum total protein. A significant negative correlation was identified between serum total protein and serum fructosamine levels.

DISCUSSIONS

In this study, it was observed that serum total protein levels were significantly decreased in complicated cases of chronic alcoholic liver disease compared to controls and between the two groups of cases. Excessive alcohol consumption was found to contribute to reduced hepatic protein synthesis. However, despite the decrease in synthesis, the concentration of serum total protein remained within the reference range due to decreased degradation. Hypoproteinemia was more common in chronic liver disease with complications, indicating the severity of the liver disease. These findings align with previous research of Sherwood and Bomford[8] and Chawla[9] emphasizing the association between hypoproteinemia, complications in chronic liver disease and disease severity.

Additionally, the study revealed that the mean values of SGOT and fructosamine were significantly higher in both Group A and Group B cases compared to the control group. Moreover, there was a notable difference observed in the levels of SGOT and fructosamine between the two case groups. The increase in SGOT levels in Group 2 cases can be attributed to mitochondrial damage in hepatocytes, as suggested by previous research[10]. This finding suggests a potential link between elevated SGOT levels and hepatocyte mitochondrial damage in cases with more severe complications.

Table 1: Age and gender distribution of study population

Variables	Cases (n = 90)	Controls (n = 45)	p-value
Age (years)	43.31±10.41	44.51±11.35	0.54
Gender			
Male	45	45	No difference
Female	0	0	

Table 2: Comparison of serum total protein, SGOT, serum fructosamine and HbA1c

Variables	Case group A (n = 45)	Case group B (n = 45)	Controls (n = 45)	p-value
Serum total protein (g dL^{-1})	6.85±0.42	5.69±0.44	7.19±0.85	0.27
SGOT (U L^{-1})	32.04±10.19	88.30±27.21	18.86±8.1	<0.05
Fructosamine (µmol L^{-1})	293.60±26.9	362.10±48.8	253.50±43.1	<0.05
HbA1c (%)	4.41±1.15	4.34±1.00	6.35±0.93	<0.05

Table 3: Correlations between different variables in study population

Variables	Correlation coefficient	p-value
SGOT and HbA1c	-0.08	0.73
SGOT and serum fructosamine	0.84	<0.05
SGOT and serum total protein	-0.90	<0.05
Serum total protein and serum fructosamine	-0.85	<0.05

The reason behind the increase in serum fructosamine concentration in Group B cases was attributed to a decrease in protein synthesis. This decrease in protein synthesis led to an extended half-life of proteins, resulting in increased glycation of the proteins. As a consequence, higher levels of serum fructosamine were observed in cases with more severe complications (group 2), as supported by previous research[11]. This finding suggests that impaired protein synthesis and subsequent glycation processes contribute to the elevated levels of serum fructosamine in individuals with complicated chronic alcoholic liver disease.

The negative correlation between SGOT and serum total proteins suggests that as SGOT levels increase, serum total protein levels decrease. SGOT reflects hepatocytic function and damage, while serum total proteins indicate hepatic synthetic function. The negative correlation between serum fructosamine and serum total proteins indicates that as serum total protein levels decrease, serum fructosamine levels increase. In chronic alcoholic liver disease, decreased serum protein levels lead to increased protein half-life and glycation, resulting in elevated fructosamine levels. The positive correlation between serum fructosamine and SGOT suggests that as SGOT levels rise, serum fructosamine levels also increase. This may be attributed to worsening disease severity, decreased protein synthesis, increased protein half-life and heightened protein glycation. HbA1c levels were significantly decreased in both case groups compared to controls but no significant difference was observed between the case groups. There was no correlation between SGOT levels and HbA1c, indicating no association between hepatic dysfunction and HbA1c levels, as well as no correlation between HbA1c and disease severity. These findings are consistent with numerous previous studies in the field[1,2,10-14].

A limitation of the study is the lack of consideration for the expenses and feasibility associated with measuring serum fructosamine levels in routine patient care. This omission raises concerns about the practical implementation and cost-effectiveness of using serum fructosamine as a marker for long-term glucose control in clinical practice. Another limitation is the absence of serum albumin concentration analysis, which is an important indicator of liver function and disease severity in chronic liver disease. The exclusion of this parameter hinders a comprehensive understanding of the relationship between liver function, glycemic control and disease progression. Future studies should address these limitations by assessing the practicality and cost-effectiveness of measuring serum fructosamine levels and incorporating the analysis of serum albumin concentrations, thereby enhancing the clinical relevance and robustness of the findings.

CONCLUSION

HbA1c, a widely recognized marker for assessing glycemic control over a span of 3-4 months, is influenced by both glucose concentration and the lifespan of red blood cells (RBCs). In cases where complications arise, there is a significant elevation in SGOT levels. Surprisingly, no difference is observed in the HbA1c levels between complicated and non-complicated cases. This indicates that the reduction in RBC lifespan serves as the underlying cause for the decrease in HbA1c concentration. Consequently, HbA1c may not be a reliable indicator for evaluating glycemic control and prognosis in individuals with chronic alcoholic liver disease. Alternatively, the findings of this study suggest that serum fructosamine is a more effective marker for assessing long-term glucose control and the severity of chronic alcoholic liver disease when compared to HbA1c. Serum fructosamine may provide more valuable insights into the overall management and prognosis of the disease.

REFERENCES

1. Bomford, A. and R.A. Sherwood, 2014. Acute and Chronic Liver Disease. In: Clinical Biochemistry: Metabolic and Clinical Aspects., Marshall, W.J., M. Lapsleyand R.M. Ayling, (Ed.)., Elsevier, ISBN-17: 978-0-7020-5140-1, pp: 250-272.
2. Lahousen, T., K. Hegenbarth, R. Ille, R.W. Lipp, R. Krause, R.R. Little and W.J. Schnedl, 2004. Determination of glycated hemoglobin in patients with advanced liver disease. World J. Gastroenterol., 10: 2284-2286.
3. Koga, M., S. Kasayama, H. Kanehara and Y. Bando, 2008. CLD (chronic liver diseases)-Hba1C as a suitable indicator for estimation of mean plasma glucose in patients with chronic liver diseases. Diabetes Res. Clin. Pract., 81: 258-262.
4. Walsh, K. and G. Alexander, 2000. Alcoholic liver disease. Postgraduate Med. J., 76: 280-286.
5. Seitz, H.K., R. Bataller, H. Cortez-Pinto, B. Gao and A. Gual *et al*., 2018. Alcoholic liver disease. Nat. Rev. Dis. Primers, Vol. 4. 10.1038/s41572-018-0014-7.
6. Gramenzi, A., F. Caputo, M. Biselli, F. Kuria, E. Loggi, P. Andreone and M. Bernardi, 2006. Review article: Alcoholic liver disease pathophysiological aspects and risk factors. Aliment. Pharmacol. Ther., 24: 1151-1161.

7. World Medical Association, 2013. World medical association declaration of Helsinki: Ethical principles for medical research involving human subjects. JAMA, 310: 2191-2194.
8. Sherwood, R.A. and A. Bomford, 2014. Assessment of hepatic function and investigation of jaundice. In: Clinical Biochemistry: Metabolic and Clinical Aspects., Marshall, W.J., M. Lapsley and R.M. Ayling, (Eds.)., Elsevier, ISBN-17: 978-0-7020-5140-1, pp: 231-249.
9. Chawla, R., 2003. Serum Total Proteins and Albumin-Globulin Ratio. In: Practical Clinical Biochemistry Methods and Interpretations., Chawla, R., (Ed.)., Jaypee Brothers Medical Publishers (P) Ltd., ISBN-13: 9788180611087, pp: 136-141.
10. Nyblom, H., U. Berggren, J. Balldin, R. Olsson, 2004. High ast/alt ratio may indicate advanced alcoholic liver disease rather than heavy drinking. Alcohol Alcoholism, 39: 336-339.
11. Trenti, T., A. Cristani, G. Cioni, R. Pentore, C. Mussini and E. Ventura, 1990. Fructosamine and glycated hemoglobin as indices of glycemic control in patients with liver cirrhosis. Res. Clin. Lab., 20: 261-267.
12. Mula-Abed, W.A. and B.E. Hanna, 2001. Measurement of serum fructosamine as an index of glycated protein in patients with nephritic syndrome and with chronic liver disease. Bahrain Med. Bull., 23: 169-174.
13. Das, S.K. and D.M. Vasudevan, 2005. Biochemical diagnosis of alcoholism. Indian J. Clin. Biochem., 20: 35-42.
14. Cacciatore, L., G. Cozzolino, M.G. Giardina, F. de Marco and L Sacca *et al*., 1988. Abnormalities of glucose metabolism induced by liver cirrhosis and glycosylated hemoglobin levels in chronic liver disease. Diabetes Res., 7: 185-188.