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Original Research Article

Serum Fructosamine: A Novel Marker for Assessing the Severity of Alcoholic Liver Disease

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Abstract

Background and Objectives: The present investigation seeks to assess the utility of serum Fructosamine and glycated hemoglobin (HbA1C) as indicators for evaluating glycemic regulation and determining the severity and prognostic implications of chronic alcoholic liver disease. The central objective of this study is to discern the preeminent marker, either HbA1C or Fructosamine, for delineating these parameters within the context of chronic alcoholic liver disease.

Methods: A cohort of 110 individuals aged between 20 and 70 years, who were diagnosed with chronic alcoholic liver disease, constituted the study populace. Additionally, 55 age and gender-matched healthy subjects were enlisted as controls. Within the patient cohort, further stratification into non-complicated and complicated subgroups was performed. Measurement of HbA1C levels was executed through the immunoturbidimetry technique, while serum Fructosamine levels were quantified using colorimetry employing nitro blue tetrazolium. The quantification of serum glutamic oxaloacetic transaminase (SGOT) adhered to the IFCC methodology, while serum total protein concentrations were determined via the biuret method.

Results: In both the non-complicated and complicated chronic alcoholic liver disease patient cohorts, mean concentrations of HbA1C and serum total protein exhibited a decrement, whereas mean concentrations of serum Fructosamine and SGOT demonstrated an elevation. Notably, no statistically significant variance in serum total protein levels was discerned between non-complicated cases and control subjects. The mean HbA1C value displayed no substantial disparity between non-complicated and complicated cases. Noteworthy correlations surfaced, wherein SGOT evinced a notable inverse correlation with serum total protein, a significant direct correlation with serum Fructosamine, and no discernible correlation with HbA1C. Furthermore, a significant negative correlation materialized between serum total protein and serum Fructosamine.

Conclusion: The findings of this research elucidate that serum Fructosamine surpasses HbA1C as a more efficacious marker for monitoring chronic glycemic regulation and gauging the severity of chronic alcoholic liver disease. These results underscore the pivotal role of serum Fructosamine in clinical assessments within the purview of chronic alcoholic liver disease and its metabolic ramifications.

Keywords: Glycated Hemoglobin, Fructosamine, Alcohol, Liver Diseases, Blood Glucose.

Introduction

Chronic alcoholic liver disease is distinguished by the progressive degradation and subsequent regeneration of hepatic tissue, ultimately leading to fibrotic alterations and cirrhotic transformations. Its diagnostic criteria encompass the persistence of clinical or biochemical indications of hepatic impairment for a duration surpassing six months [1,2]. The liver, functioning as a pivotal regulator of glucose metabolism, assumes a pivotal role in maintaining stable plasma glucose concentrations. Inadequate management of plasma glucose within individuals afflicted by chronic liver disease frequently associates with an unfavorable prognostic trajectory and the potential emergence of deleterious sequelae [3,4].

The constellation of complications arising from chronic alcoholic liver disease emanates from the compromised functionality of hepatocytes. This spectrum encompasses manifestations such as variceal hemorrhage, hepatic encephalopathy,

coagulation abnormalities, ascitic accumulation, occurrences of spontaneous bacterial peritonitis, and the emergence of portal hypertension. While the onset of cirrhosis is often characterized by a gradual trajectory, severe chronic alcoholic liver disease may expedite its rapid progression. A notable proportion of mortality attributable to chronic alcoholic liver disease can be ascribed to complications stemming from cirrhosis, including instances of ascites, spontaneous bacterial peritonitis, hepatorenal syndrome, encephalopathy, and variceal hemorrhage [5-7].

Epidemiological data reveals that within France, the mortality rate linked to alcoholic liver disease approximates 14.3 per 100,000 individuals [8]. In district general hospitals across the United Kingdom, a substantial 80% of liver cirrhosis cases find their etiological origin in alcohol consumption [8]. Furthermore, the incidence of alcoholic cirrhosis is progressively mounting in countries like Japan and India, where historical prevalence had been notably lower [6].

The assessment of hemoglobin A1C (HbA1C) concentrations stands as a salient method for appraising prolonged glycemic regulation and exerts a close association with the genesis of diabetes mellitus-related complications. However, it is imperative to acknowledge that compromised hepatic function can exert an influence on the outcomes of HbA1C assays [3]. Serum Fructosamine, characterized as a glycated protein, serves as an indicator of glycemic status over a temporal span of 2 to 4 weeks. Given that Fructosamine formation is predicated upon the glycation process affecting serum proteins, the quantification of Fructosamine values becomes subject to its influence. Notably, the implications of impaired hepatic function, potentially leading to diminished hepatic protein synthesis, must be contemplated as a factor that could modulate Fructosamine outcomes [3]. This research endeavors to investigate the levels of HbA1C and serum Fructosamine within individuals diagnosed with chronic alcoholic liver disease, encompassing both those devoid of complications and those harboring complications, alongside a comparator group comprising healthy subjects.

Material & Methods

A case-control investigation was conducted to scrutinize the levels of HbA1c, serum glutamic oxaloacetic transaminase (SGOT), serum total protein, and serum Fructosamine in individuals afflicted with chronic alcoholic liver disease. Ethical considerations were upheld through the informed consent of all subjects, adhering to established ethical guidelines [9]. The study encompassed a total of 165 subjects, following meticulous adherence to predefined inclusion and exclusion criteria. Within this cohort, 55 subjects exhibited chronic alcoholic liver disease without complications, another 55 displayed chronic alcoholic liver disease accompanied by complications, and the remaining 55 individuals constituted the healthy control group.

The study targeted individuals diagnosed with chronic alcoholic liver disease, amassing a total of 110 cases. Diagnostic affirmation was based upon an amalgamation of clinical history, liver function assessments, and ultrasonography. Encompassing a range of 20 to 70 years. This cohort was subsequently partitioned into two distinct groups for enhanced analysis. Group A consisted of 55 cases of uncomplicated chronic alcoholic liver disease, while Group B encompassed 55 cases characterized by complications such as ascites, splenomegaly, hepatic encephalopathy, and portal hypertension.

A matched control contingent of 55 healthy subjects was meticulously selected to foster comparability, aligning with the cases in terms of age and gender. This control group was meticulously screened to ensure their freedom from any discernible liver ailments or alcohol-related disorders. This methodological configuration enabled a comprehensive evaluation and juxtaposition of clinical attributes and outcomes between the chronic alcoholic liver disease cases and the control cohort. A stringent set of exclusion criteria was implemented, precluding individuals with liver maladies aside from chronic alcoholic liver disease, Diabetes Mellitus, Renal Disease, history of substantial blood loss or transfusion, anemia, reticulocytosis, ongoing erythropoietin treatment, a history of myocardial infarction, Ischemic Heart Disease, and hypertension from participation. These criteria engendered a homogeneous participant population characterized solely by chronic alcoholic liver disease, devoid of concomitant hepatic disorders or significant co-morbidities that could confound study findings. Rigorous adherence to these criteria facilitated the selection of age-matched cases and controls, all of whom provided informed consent. A standardized proforma was employed for meticulous documentation of pertinent details, inclusive of patient particulars and investigative findings, thereby ensuring a consistent and comprehensive reservoir of data for subsequent analysis.

During the blood collection procedure, strict aseptic protocols were observed, involving the withdrawal of approximately 5 ml of venous blood using a sterile disposable syringe from a peripheral vein. This blood was segregated into two distinct tubes: a plain bulb for serum collection post-coagulation, and an EDTA bulb for hemolysate preparation earmarked for HbA1c quantification. Subsequent to centrifugation, the resultant serum specimens were stored at a temperature of 4°C until analytical

procedures were undertaken. Likewise, the EDTA-treated blood samples were maintained at 4°C for later analysis and the creation of hemolysate for HbA1c measurement. Analytical kits were deployed to ascertain the concentrations of SGOT and serum total protein, alongside a commercial diagnostic kit for the assessment of HbA1c and Fructosamine. The execution of these evaluations was facilitated by a semi-autoanalyzer, affording efficient and automated scrutiny of the specimens.

Statistical analysis was performed using SPSS software, version 20.0. Descriptive statistics were harnessed to present the dataset, encapsulating mean values accompanied by standard deviations and ranges. For inter-group mean comparisons, the Student's "t" test was wielded. Concurrently, Pearson's correlation coefficient was employed to elucidate the interrelationships between specific parameters. Statistical significance was ascribed to a probability value (p-value) below 0.05, denoting a robust level of confidence in the derived outcomes.

Results

Table 1 presents an absence of statistically noteworthy differentiation in terms of age when comparing the cases and control group. Meanwhile, Table 2 furnishes the serum total protein, SGOT, serum Fructosamine, and HbA1c values corresponding to the control group, as well as cases within Group A and Group B. Moreover, the statistical evaluation, effectuated through an unpaired Student's "t" test, illuminates the insignificance in disparities regarding serum total protein levels between the control group and cases within Group A. Furthermore, the meticulous analysis affirms the absence of any substantial divergence in HbA1c levels between cases within Group B and cases within Group A.

Table 1: Age and gender distribution of study population

Variables	Cases (n = 110)	Controls (n = 55)	p Value
Age (years)	41.78 ± 9.95	46.22 ± 11.11	0.47
Gender			
Male	110	55	-
Female	0	0	

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

Variable	Case Group A (n = 55)	Case Group B (n = 55)	Controls (n = 55)	p Value
S. Total protein (g/dL)	6.70 ± 0.38	5.92 ± 0.40	7.05 ± 0.80	0.31
SGOT (U/L)	31.80 ± 10.35	89.05 ± 26.89	18.95 ± 8.03	< 0.05
Fructosamine (µmol/L)	288.4 ± 25.3	369.8 ± 46.6	259.2 ± 42.7	< 0.05
HbA1c (%)	4.59 ± 1.20	4.22 ± 0.96	6.45 ± 0.89	< 0.05

Table 3 delineates the discerned interrelationships amongst diverse variables. It unveils a negative correlation between serum glutamic oxaloacetic transaminase (SGOT) and glycated hemoglobin (HbA1c), although this correlation did not attain statistical significance. In contrast, a positive correlation that bears statistical significance emerged between SGOT and serum Fructosamine levels. Furthermore, a statistically significant inverse correlation was unveiled between SGOT and serum total protein. Significantly, a negative correlation of statistical import was observed between serum total protein and serum Fructosamine levels.

Table 3: Correlations between different variables in study population

Variable	Correlation Coefficient	p-value
SGOT and HbA1c	-0.12	0.68
SGOT and serum Fructosamine	0.79	< 0.05
SGOT and serum total protein	-0.87	< 0.05
Serum total protein and serum Fructosamine	-0.80	< 0.05

Discussion

In the current investigation, a significant decrease in serum total protein levels was noted in cases of complicated chronic alcoholic liver disease in comparison to controls and within the two case groups themselves. The impact of excessive alcohol consumption on hepatic protein synthesis reduction was evident. Notwithstanding this decrease, serum total protein concentrations were maintained within the reference range, attributed to a concurrent reduction in degradation. The higher prevalence of hypoproteinemia in complicated chronic liver disease cases underscored disease severity. This discovery resonates with earlier research [10-12], highlighting the correlation between hypoproteinemia, complications in chronic liver disease, and disease gravity. Additionally, the study illuminated elevated mean values of SGOT and Fructosamine in both Group A and Group B cases relative to the control cohort. Furthermore, discernible dissimilarities were apparent in the levels of SGOT and Fructosamine between the two case groups. In Group B cases, escalated SGOT

levels were linked to mitochondrial damage in hepatocytes, aligning with prior research [13], thereby suggesting a potential link between heightened SGOT levels and pronounced hepatocyte mitochondrial impairment in cases characterized by more severe complications.

The elevation in serum Fructosamine concentration within Group B cases was attributed to compromised protein synthesis. This attenuation in protein synthesis extended the half-life of proteins, fostering augmented protein glycation. Consequently, Group B cases demonstrated elevated serum Fructosamine levels, substantiating previous studies [14], and intimating that impeded protein synthesis and ensuing glycation processes contribute to escalated serum Fructosamine levels in individuals grappling with intricate chronic alcoholic liver disease.

The inversely correlated SGOT and serum total proteins allude to an elevation in SGOT levels being associated with a reduction in serum total protein concentrations. SGOT mirrors hepatocytic health and impairment, whereas serum total proteins offer insights into hepatic synthetic functionality. Furthermore, the negatively correlated serum Fructosamine and serum total proteins highlight that diminishing serum protein levels correspond to heightened serum Fructosamine levels. In the context of chronic alcoholic liver disease, diminished serum protein concentrations precipitate elongated protein half-lives and glycation, culminating in elevated Fructosamine levels.

The positive relationship between serum Fructosamine and SGOT underscores that as SGOT levels ascend, so do serum Fructosamine levels. This link can be attributed to exacerbated disease severity, dwindling protein synthesis, extended protein half-life, and augmented protein glycation. Notably, HbA1c levels demonstrated a statistically significant decrease in both case groups compared to controls, yet no significant distinction emerged between the two case groups. In terms of SGOT levels and HbA1c, no apparent association was observed, denoting an absence of linkage between hepatic dysfunction and HbA1c levels, as well as between HbA1c and disease severity. These findings mirror the consensus of various preceding studies in the field [2, 3, 13-17].

Nevertheless, the study harbors limitations. The absence of considerations for the expenses and practicality inherent in routinely measuring serum Fructosamine levels raises concerns about the pragmatic implementation and cost-efficiency of utilizing serum Fructosamine as a marker for long-term glucose control within clinical contexts. Additionally, the non-inclusion of serum albumin concentration analysis, a pivotal indicator of liver function and disease gravity in chronic liver disease, hampers a comprehensive comprehension of the interconnectedness between liver function, glycemic control, and disease advancement. Future endeavors should address these limitations by evaluating the feasibility and cost-effectiveness of serum Fructosamine measurement and incorporating serum albumin concentration analysis, thus amplifying the clinical significance and robustness of the findings.

Conclusion

HbA1c, a widely accepted metric for appraising glycemic regulation spanning 3 to 4 months, is subject to the influence of glucose concentration and the lifespan of red blood cells (RBCs). In scenarios marked by complications, a substantial elevation in SGOT levels becomes evident. Intriguingly, no discernible divergence surfaces in HbA1c levels between intricate and uncomplicated cases. This observation underscores the prominence of reduced RBC longevity as the underlying causative factor behind the diminished HbA1c levels. Consequently, the utility of HbA1c as a dependable indicator for evaluating glycemic control and prognosticating outcomes within the domain of chronic alcoholic liver disease may be questioned. Conversely, the outcomes of this inquiry proffer that serum Fructosamine emerges as a more efficacious gauge for assessing protracted glucose management and gauging the severity of chronic alcoholic liver disease when juxtaposed with HbA1c. Serum Fructosamine, it appears, could furnish more nuanced insights into the comprehensive oversight and prognosis of the affliction.

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