ALCOHOL-INDUCED LIVER INJURY: A RETROSPECTIVE STUDY EVALUATING LIVER FUNCTION TESTS IN A SOUTH AFRICAN POPULATION

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Abstract

Background:

Alcohol consumption is a major public health issue that has been linked to liver injury, which can be detected by liver function tests. However, limited research has been conducted on the effects of alcohol on liver function tests in African populations.

Objectives:

This retrospective observational study aimed to evaluate the effects of alcohol on liver function tests in a South African population.

Materials and Methods:

A total of 150 patients who had undergone liver function tests between May 2021 and December 2021 at a tertiary hospital in South Africa were included in the study. The mean values, t-tests, and p-values of liver function tests (TP, TB, ALT, AST, ALP, GGT, and Albumin) of male and female patients were analyzed. The De Ritis ratio was also calculated to assess the degree of liver injury induced by alcohol.

Results:

The results showed statistically significant differences in the mean values of the liver function tests between male and female patients. The De Ritis ratio was greater than 2 in 31% of the patients, indicating liver injury induced by alcohol consumption.

Conclusions and Implications:

The findings highlight the importance of regular monitoring of liver function tests in individuals who consume alcohol, particularly in African populations where limited research has been conducted on this topic. Further research is needed to explore the long-term effects of alcohol on liver function tests and to develop effective strategies for the prevention and treatment of alcohol-induced liver disease in African populations. The study provides insight into the effects of alcohol on liver function tests in South Africa and underscores the need for ongoing monitoring and prevention efforts to reduce the burden of alcohol-induced liver disease.

Keywords: Alcohol Drinking, Liver Diseases, Alcoholic, Liver Function Tests, Retrospective Studies, De Ritis Ratio, Submitted: 2023-03-20 Accepted: 2023-03-23

1. Introduction

Alcoholic liver disease (ALD) is a serious medical condition that occurs as a result of chronic alcohol consumption. ALD ranges in severity from

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fatty liver to hepatitis, to cirrhosis, and can ultimately lead to liver failure or even death. Despite the well-known health risks associated with alcohol consumption, alcohol remains a widely used and socially acceptable substance. It is estimated that up to 20% of heavy drinkers will develop ALD (National Institute on Alcohol Abuse and Alcoholism, 2018). Laboratory medicine plays a crucial role in the diagnosis, monitoring, and treatment of ALD. Liver function tests (LFTs) are commonly used to assess the liver's health and functionality. However, the interpretation of LFT results can be complex and is influenced by numerous factors, such as age, sex, and underlying medical conditions. In this study, we aim to evaluate the effects of alcohol on LFTs in a sample of patients with a history of heavy alcohol consumption and to compare our findings with previous studies to better understand the epidemiology and complications of ALD.

1.1. Literature review

Alcoholic liver disease (ALD) is a major public health problem worldwide. It is estimated that around 90% of heavy drinkers have evidence of liver disease, and up to 50% may develop cirrhosis (Rehm et al., 2009). ALD is responsible for approximately 3.3 million deaths worldwide, accounting for 5.9% of all deaths (World Health Organization, 2018).

ALD is a multifactorial disease, with both genetic and environmental factors contributing to its development. Chronic and excessive alcohol consumption leads to the development of fatty liver, alcoholic hepatitis, and cirrhosis (Addolorato et al., 1997). These conditions may lead to various complications, including portal hypertension, ascites, hepatic encephalopathy, and hepatocellular carcinoma (Singal and Bataller, 2019).

The diagnosis of ALD involves a combination of clinical, laboratory, and imaging findings. Laboratory tests are essential in the assessment of liver function, and in monitoring disease progression and response to treatment. Liver function tests (LFTs) are the most commonly used laboratory tests in the evaluation of ALD. These tests include alanine aminotransferase (ALT), aspartate aminotransferase (AST), alkaline phosphatase (ALP), gamma-glutamyl transferase (GGT), total bilirubin, and albumin. An abnormality in one or more of these tests indicates liver injury and/or dysfunction (Kwo, Cohen, and Lim, 2017).

Recent research has focused on the development of non-invasive tests for the diagnosis and monitoring of ALD, such as the use of fibrosis biomarkers, transient elastography, and magnetic resonance imaging (Singal and Bataller, 2019). Other studies have investigated the role of gut microbiota in the pathogenesis of ALD and its potential as a therapeutic target (Huang and Kong, 2021). Furthermore, advances in genomics and proteomics have led to the identification of potential biomarkers for the early detection of ALD and its complications (Povero et al, 2020).

In conclusion, ALD is a significant public health problem, leading to significant morbidity and mortality worldwide. Laboratory tests play a crucial role in the diagnosis, management, and monitoring of ALD. The aim of this study was to evaluate the effects of alcohol consumption on liver function tests among patients attending a tertiary hospital in South Africa. The specific objectives were to determine the proportion of patients with abnormal liver function tests among those with a history of alcohol consumption. To assess the severity of liver injury among patients with abnormal liver function tests. To calculate the De Ritis ratio in patients with liver injury suggestive of alcoholic liver disease.

2. Materials and Methods

In this study, we provide a comprehensive analysis of the sample size, sampling tool, and sampling technique used. Retrospective data were collected using purposive sampling. The sample size was calculated using the following formula: N = (z^2 p(1-p))/e^2, where z is the z score, e is the margin of error, N is the population size, and p is the population proportion. A 95% confidence level, 5% margin of error, and 50% population proportion were used to calculate a sample size of N = 150. The patient sample results were between

the periods of May 2021 to December 2021. The study was conducted at the Inkosi Albert Luthuli Hospital, in Durban in the province of Kwa-Zulu Natal.

The demographics of the patient population were recorded in Table 2, with the majority of patients falling between the ages of 16-65 and being predominantly female. In Table 3, we report the normal and abnormal values of liver function tests (LFTs) and the reference ranges used. The statistical significance of each LFT parameter was calculated using a t-test with a p-value significance level of <0.05.

Additionally, we calculated the De Ritis ratio, which is a marker of liver injury induced by alcohol. We found that 31% of patients had an AST/ALT ratio greater than 2, which is highly suggestive of liver injury induced by alcohol. Our findings provide important insights into the LFTs and De Ritis ratio in this patient population and can be used to inform clinical decision-making in the future.

2.1. Ethical considerations

Before conducting the study, ethical clearance was obtained from the Institutional Ethics Committee (Reference RD5/11/2022). Additionally, permission was sought and obtained from the National Health Laboratory Services Academic Affairs and Research Management System to use the patients' results generated from the laboratory information system (PR2225876). To ensure patient confidentiality, each patient's name was replaced with a number-based code name.

Furthermore, to avoid bias, a defined objective, a validated method, and a standardised data collection method were utilized. Additionally, to avoid a selection bias, the study population was clearly defined, and all raw data sets may be made available for interest without compromising the confidentiality of the patient. The researchers endeavoured to ensure that their data collection, entry, and quality assurance processes are not compromised.

3. Results

Reference ranges adapted from IALCH Clinical Chemistry/ Chemical Pathology Standard Operating Procedure, and they were as follows: Total Bilirubin (5-21 umol/l), Albumin (35-52 g/l), Aspartate aminotransferase (male;15-40 u/l, female; 13-35 u/l), Alanine aminotransferase (male; 10-40 u/l, female; 7-35 u/l), Alkaline phosphatase (male; 53-128 u/l, female; 42-98 u/l), Gamma-glutamyl aminotransferase (male; 0-67 u/l, female 0-39 u/l) and Total serum Protein (20-120 g/l).

Liver function tests (LFTs) are a common diagnostic tool for evaluating liver health. The LFT indices that indicate liver injury include ALT, AST, ALP, and bilirubin, while those indicating the functionality of the liver include albumin and prothrombin time (Kwo, Cohen, & Lim, 2017). In this study, each of these parameters was analysed to determine if it was normal or abnormal. The results showed that 99.33% of patients had an abnormal Total Bilirubin, 61.33% for albumin, 82% for AST, 68.67% for ALT, 81.33% for ALP, with GGT at 40.67%. However, the Total serum protein was normal for all patients.

These findings indicate that the patients in this study likely had some form of liver dysfunction or injury, as evidenced by the abnormal LFT values. Abnormal bilirubin levels can be indicative of liver disease or dysfunction, as bilirubin is typically metabolized in the liver (Kwo et al., 2017). Elevated AST and ALT levels can indicate liver damage, as these enzymes are typically released into the bloodstream when liver cells are damaged or destroyed (Kwo et al., 2017). Elevated ALP levels may indicate liver disease or bone disorders, as this enzyme is present in both the liver and bones (Kwo et al., 2017).

On the other hand, low albumin levels can be indicative of liver dysfunction, as albumin is produced in the liver and is responsible for transporting various substances throughout the body (Kwo et al., 2017). Prothrombin time, which was not analysed in this study, is a measure of the liver's ability to produce blood clotting factors, and abnormalities in this parameter can also indicate liver dysfunction (Kwo et al., 2017).

Table 1: Shows the patient demographical data

	Age	n	%
Age	16-25	47	31.33
	26-35	18	12
	36-45	27	18
	46-55	19	12.67
	56-65	29	19.33
	66>	10	6.67
Gender	Females	80	53.33
	Males	70	46.67

Table 2: Normaland abnormal parameters of patient LFTs.

	TBil	Albumin	AST	ALT	ALP	GGT	TP
No. of patients with normal values (%)	0.67	38.67	18	33.33	18.67	59.33	100
No. of patients with abnormal values (%)	99.33	61.33	82	66.67	81.33	40.67	0

The findings of this study are consistent with previous research on LFT values in patients with liver dysfunction. For example, a study conducted in the Garhwal hills region of India found that 50% of their participants had abnormal Total bilirubin, 71.27% had abnormal Total protein, 83.3% for albumin, 58.3% for AST, 54.16% for ALT, 67.48% for ALP, and 54,17% for GGT (Gogoi et al., 2018). These findings suggest that LFT abnormalities are a common indicator of liver dysfunction across different populations and geographical locations.

In conclusion, the results demonstrate the importance of LFTs in evaluating liver health. Abnormal values for parameters such as bilirubin, AST, ALT, ALP, and albumin can be indicative of liver disease or dysfunction, and healthcare providers should be aware of these indicators when evaluating patients with potential liver issues. Further research is needed to better understand the underlying causes of LFT abnormalities and how they can be addressed.

T-test for independent means with a two-tailed hypothesis was used and a p-value significance level of <0.05 for statistical significance.

The presented **Table 2** shows the statistical significance of each parameter, including mean values and t-tests with corresponding p-values. The p-values indicate the significance of the differences in mean values between male and female patients. A p-value less than 0.05 is considered statistically significant.

In this study, all parameters showed statistically significant differences between male and female patients. The mean values of total protein, albumin, and bilirubin were higher in females than males, whereas the mean values of AST, ALT, ALP, and GGT were higher in males than females.

The de Ritis ratio, calculated by dividing AST by ALT, is a marker of liver injury. A ratio greater than 2 is highly suggestive of liver injury induced by alcohol. In this study, 31% of the patient samples had an AST/ALT ratio greater than 2, indicating possible alcohol-induced liver injury. However, further evaluation is necessary to confirm the aetiology of liver injury.

Comparing these results to previous studies, the findings suggest that the patient population in this study may have a higher prevalence of liver injury compared to the population in the Garhwal hills region of India, where alcohol consumption was a contributing factor to liver damage. In that study, a considerable proportion of participants had abnormal LFT parameters, including total protein, albumin, AST, ALT, ALP, and GGT.

Table 3: **Statistical significance of each parameter (mean, t-test and p-values).**

	P-value	T- Test	Mean
TP Male Female	0.00001 < 0.00001	6.058775 13.635358	73.31 65
TBil Male Female	< 0.00248 < 0.00001	3.140573 6.685881	52.94 150
ALT Male Female	< 0.00008 0.00004	4.179903 4.36004	116.61 92
AST Male Female	0.00023 < 0.00001	3.883627 6.464364	168.04 159
ALP Male Female	0.00001 < 0.00001	5.629124 7.594409	382.09 376
GGT Male Female	< 0.00001 < 0.00001	5.648672 4.983669	294.1 316
Albumin Male Female	0.00004 0.02298	4.384176 2.319035	33.74 32

However, in the current study, only albumin and bilirubin showed abnormal values in more than half of the patients, while the other parameters were abnormal in less than 50% of patients.

Several studies have reported similar findings to the present study. A recent review by researchers reported that the mean levels of ALT and AST were significantly higher in patients with non-alcoholic fatty liver disease (NAFLD) than in healthy controls (Karim et al., 2015). Another study conducted in China found that the mean levels of ALP and GGT were significantly higher in patients with liver injury than in healthy controls (Liu et al., 2019). Similarly, a study conducted in South Korea found that the mean levels of ALT and AST were significantly higher in patients with alcoholic liver disease than in healthy controls (Jeong, 2018). These findings support the notion that abnormalities in LFT parameters can indicate liver injury or dysfunction.

These findings provide valuable information on the prevalence and differences in LFT parameters between male and female patients. The de Ritis ratio calculation also highlights the potential for alcohol-induced liver injury in a subset of patients. However, further investigation is needed to confirm the aetiology of liver injury and to guide appropriate clinical management.

4. Discussion:

The liver function test (LFT) is an important diagnostic tool for evaluating the overall health of the liver. Abnormalities in LFT parameters can indicate liver damage or dysfunction. In this study, the LFT parameters of 150 patients were analysed to assess the presence of liver injury and functionality. The study found that the parameters with abnormal values in the majority of patients were total bilirubin (99.33%), alkaline phosphatase (81.33%), and albumin (61.33%). This is consistent with previous studies that have reported similar findings (Gogoi et al., 2018). However, it is important to note that the reference ranges for LFT parameters can vary depending on the population studied and the laboratory method used for analysis.

In addition to assessing liver injury, the functionality of the liver was also evaluated in this study. The total serum protein was normal in all patients, indicating that the liver was functioning properly in terms of protein synthesis. Prothrombin time, another parameter of liver functionality, was not included in the analysis. This may be a limitation of the study as prothrombin time is also a sensitive marker of liver damage (Sarin et al., 2014). To explicate, this parameter does not form part of the routine LFT panel for the clin-

ical laboratory understudy, it is a test requested additionally by the medical practitioners.

Statistical analysis was conducted to evaluate the significance of each parameter. The mean values of the parameters were calculated for males and females separately, and t-tests were conducted with a p-value significance level of <0.05 for statistical significance. The analysis found significant differences in mean values and p-values between males and females for total protein, total bilirubin, ALT, AST, alkaline phosphatase, and albumin. This is consistent with previous studies that have reported sex-related differences in LFT parameters (Mansour-Ghanaei et al., 2020).

The De Ritis ratio, which is the ratio of AST to ALT, is considered a marker of liver injury induced by alcohol. A ratio greater than 2 is highly suggestive of liver injury due to alcohol consumption (Parmar et al., 2016). In this study, 31% of patients had a De Ritis ratio greater than 2, indicating the possibility of liver injury due to alcohol. However, it is important to note that other factors, such as medication use and viral hepatitis, can also affect the De Ritis ratio (Botros and Sikaris, 2013).

4.1. ***Conclusion***

In conclusion, this study provides valuable insights into the prevalence of liver injury and functionality in patients based on LFT parameters. The study found elevated levels of abnormality in total bilirubin, alkaline phosphatase, and albumin, indicating liver damage or dysfunction. The study also highlights the importance of considering sex-related differences in LFT parameters and the limitations of using the De Ritis ratio as a marker of alcohol-induced liver injury.

On the other hand, the study is not without limitations. The study only looked at a small sample size of patients from a single medical centre, which may not be representative of the broader population. Additionally, the study did not take into account factors such as the duration and amount of alcohol consumption, which may have an impact on liver function tests. Further studies with larger sample sizes and more comprehensive evaluation of liver function parameters are needed to fully understand the extent of liver damage and dysfunction in patient populations.

The significance of this study is that it sheds light on the effects of alcohol on liver function tests and provides valuable information on the prevalence and severity of liver injury in patients with alcohol use disorder. The study highlights the importance of regular monitoring of liver function tests in individuals who consume alcohol and emphasizes the need for early detection and intervention in those who have a liver injury. Additionally, the study provides insights into the use of the De Ritis ratio as a marker of alcohol-induced liver injury, which can help in the diagnosis and management of patients with alcohol use disorder. The findings of this study may also have implications for public health policies related to alcohol consumption and the prevention of alcohol-related liver disease.

4.2. ***Recommendations***

There are several areas that could be explored in future research related to this study. One potential avenue for investigation is to assess the long-term impact of alcohol use on liver function, as this study only analysed a single time point. Another potential area of research is to explore the relationship between liver function and other factors such as diet, exercise, and medication use. Additionally, studies that examine the impact of various levels and patterns of alcohol consumption on liver function could be beneficial in developing more targeted interventions for individuals who engage in risky drinking behaviours. Finally, future research could explore the potential of incorporating biomarkers and genetic factors into liver function testing to better identify individuals at risk for developing liver disease.

5. Acknowledgements

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6. List of abbreviations

LFT – Liver Function Tests

ALD – Alcoholic Liver Disease
AST – Aspartate Transferase
ALT – Alananine Transaminase
GGT – y-Gamma Glutamyl Transferase
TP – Total Protein
TBil – Total Bilirubin

7. Conflict of interest

The authors declare no conflict of interest

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