Original Article

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Assessment of Glutathione Level in Non-Alcoholic Fatty Liver Disease Patients

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Abstract

Background: Non-alcoholic fatty liver disease (NAFLD) is a range of hepatic disorders associated with fatty deposits in liver, which occur in the absence of alcohol consumption or alcohol abuse. NAFLD. The present study assessed glutathione level in non-alcoholic fatty liver disease patients. **Subjects and Methods:** The present study was conducted in Department of Internal Medicine, Narayana Medical College & Hospital, Chintareddy Palem, Nellore, Andhra Pradesh. Duration of the study was from February 2018 to January 2019. 40 patients of NAFLD and 20 cases of fatty liver disease were recruited. Serum levels of 8-OHdG were measured using the highly sensitive 8-OHdG Check enzyme-linked immunosorbent assay (ELISA). Serum levels of GGT were measured using the Qualigent® GGT kit. Serum levels of glutathione (GSH) were measured using the GSH kit. **Results:** The mean total bilirubin in group I was 1.2 mg/dL and in group II was 0.7 mg/dL, aspartate transaminase was 58.2 U/l in group I and 62.6 U/l in group II, alanine transaminase in group I was 142.4 U/l in group I and 128.2 U/l in group II, alkaline phosphatase was 284.2 U/l in group I and 302.4 U/l in group II and γ-glutamyltranspeptidase in group I was 98.2 U/l and 118.4 U/l in group II. The difference was non- significant (P> 0.05). The mean glutathione level in group I was 0.6 and in group II was 0.4 and which increased to 1.4 in group I and 1.2 in group II after 3 months. The difference within the group found to be significant (P< 0.05). **Conclusion:** Authors found that there was reduction in alanine transaminase, glutathione and gamma-glutamyltranspeptidase level. Antioxidant therapy with glutathione may reduce the pathological oxidative stress in the liver in NASH, preventing the progression from NAFLD to NASH cases.

Keywords: Alanine Transaminase, Fatty Liver, Glutathione

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Introduction

The presence of a significant (>5% of hepatocytes) fat accumulation in the liver, in the absence of an "unsafe" quantity of alcohol consumption and any other cause of liver diseases, is a potentially pathological condition that is defined as nonalcoholic fatty liver disease (NAFLD).

Non-alcoholic fatty liver disease (NAFLD) is a range of hepatic disorders associated with fatty deposits in liver, which occur in the absence of alcohol consumption or alcohol abuse. NAFLD begins with an initial stage of fatty liver also known as hepatic steatosis.[1] The progression from steatosis into cirrhosis of the liver due to inflammation and fibrosis results in irreversible damage to the liver. This condition is called non-alcoholic steatohepatitis (NASH)—a term first introduced by Ludwig et al. in clinical subjects with no history of alcohol consumption or abuse.[2]

In oxidative stress, the serum level of oxidized glutathione increases and hepatic GGT is induced; this then dismantles the oxidized glutathione and converts it to reduced glutathione.[3]Gammaglutamyltranspeptidase, therefore, has an important role in antioxidant defense systems at the cellular level and is a valuable marker of oxidative stress in NAFLD.[4] It has been reported that levels of GGT in FL patients may compensate for mild oxidative stress by repressing 8-OHdG levels and preventing progression to NASH; oxidative stress leads to increased levels of 8-OHdG and the development of NASH. It may also contribute to clinical progression from simple FL to NASH.[5] The present study assessed glutathione level in non-alcoholic fatty liver disease patients.

Subjects and Methods

The present study was conducted in Department of Internal Medicine, Narayana Medical College & Hospital, ChintareddyPalem, Nellore, Andhra Pradesh. Duration of the study was from February 2018 to January 2019. 40 patients of NAFLD and 20 cases of fatty liver disease. All patients were informed regarding the study and written consent was obtained. Ethical approval was obtained from institute prior to the study.

Patient data such as name, age, gender etc. was recorded. A through clinical examination was performed. Serum levels of 8-OHdG were measured using the highly sensitive 8-OHdG Check enzyme-linked immunosorbent assay (ELISA) kit according to the manufacturer's instructions. Serum levels of GGT were measured using the Qualigent® GGT kit. Serum levels of glutathione (GSH) were measured using the GSH kit. Results thus obtained were subjected to statistical analysis. P value less than 0.05 was considered significant.

Results

Table 1: Distribution of patients

Total- 60		
Groups	**Group I (FLD)**	**Group II (NAFLD)**
Number	40	20

Table 1 shows that patients were divided into 2 groups. It consisted of 20 cases of fatty liver disease in group I and 40 patients of NAFLD in group II.

Table 2: Clinical parameters

Groups	Group I (FLD)	Group II (NAFLD)	P value
Total bilirubin (mg/dL)	1.2	0.7	0.82
Aspartate transaminase (U/l)	58.2	62.6	0.13
Alanine transaminase (U/l)	142.4	128.2	0.17
Alkaline phosphatase (U/l)	284.2	302.4	0.21
γ-Glutamyltransp (U/l)	98.2	118.4	0.71

Table 3: Serum glutathione levels in both groups

Glutathione levels	Group I (FLD)	Group II NAFLD)	P value
Before	0.6	0.4	0.52
After 3 months	1.4	1.2	0.71
P value	0.01	0.01	NA

*NA (Not Applicable)

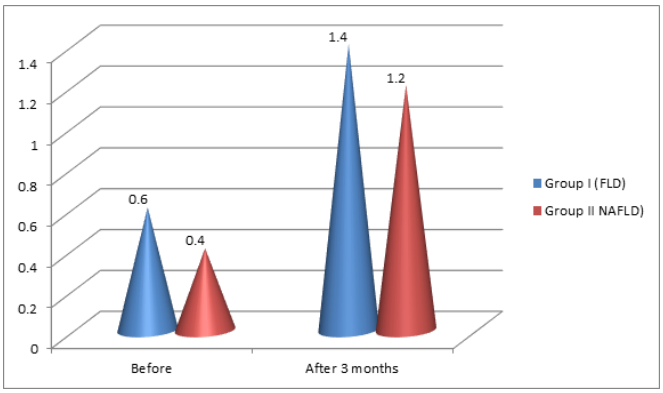

Figure 1: Serum glutathione levels in both groups

Table 4: Comparison of parameters in both groups

Groups	Period	Group I	Group II	P value
Alanine	Before	142.4	128.2	0.17
	3 months	130.2	120.6	0.12
8-	Before	102.8	104.6	0.14
	3 months	98.4	94.2	0.11
γ-	Before	98.2	118.4	0.71
	3 months	86.4	102.4	0.01

Table 2 shows that mean total bilirubin in group I was 1.2 mg/dL and in group II was 0.7 mg/dL, aspartate transaminase was 58.2 U/l in group I and 62.6 U/l in group II, alanine transaminase in group I was 142.4 U/l in group I and 128.2 U/l in group II, alkaline phosphatase was 284.2 U/l in group I and 302.4 U/l in group II and γ-glutamyltranspeptidase in group I was 98.2 U/l and 118.4 U// in group II. The difference was non- significant (P> 0.05).

Table 3 & Figure 1 shows that mean glutathione level in group I was 0.6 and in group II was 0.4 and which increased to 1.4 in group I and 1.2 in group II after 3 months. The difference within the group found to be significant (P< 0.05).

Table 4 & Figure 2 shows that there was reduction in value of alanine transaminase, 8-hydroxy-2-deoxyguanosine and γ-glutamyltranspeptidase in both groups after 3 months.

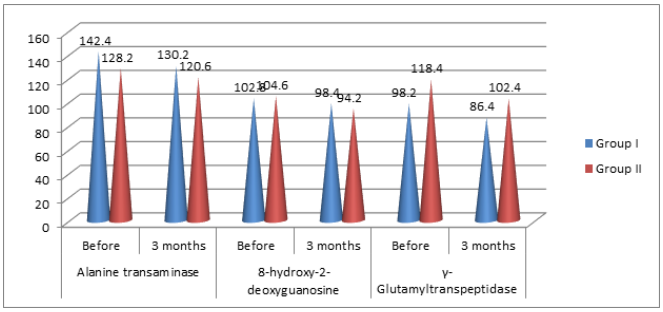

Figure 2: Comparison of parameters in both groups

Discussion

The prevalence of NAFLD is estimated to be as high as 17–33% in the general population, while it reaches 75% in obese individuals and even more in patients with type 2 diabetes mellitus (T2DM).[6] The concomitant presence of T2DM increases the risk of progression of liver damage and constitutes a significant risk for cardiovascular diseases. Although obesity, particularly central (abdominal) obesity, is a well-recognized risk factor for it, NAFLD has been also reported in lean individuals (body mass index < 30 kg/ m^2).[7] Furthermore, the prevalence of NAFLD differs depending on the gender, ethnicity, and race as a proof of probable involvement of genetic and epigenetic factors in the pathogenesis of the disease. Insulin resistance (IR) is the major pathophysiological factor implicated in NAFLD, as well as metabolic syndrome (MS), a cluster of cardiovascular risk factors comprising visceral obesity, blood hypertension, glucose intolerance, and dyslipidemia. In this way, NAFLD has been considered as the liver expression of MS, not only burdened with high cardiovascular risk but also responsible of a progressive metabolic, cardiovascular, and/or kidney disease, even without an overt MS.[8] The present study assessed glutathione level in non-alcoholic fatty liver disease patients.

In present study, patients were divided into 2 groups. It consisted of 20 cases of fatty liver disease in group I and 40 patients of NAFLD in group II. Irie et al,[9] evaluated whether an antioxidant agent, glutathione, prevents the development of NASH from FL. Five patients with FL and 10 with NASH were enrolled in the study. Three hundred milligrams per day of glutathione was given orally to patients with nonalcoholic fatty liver disease (NAFLD) every day, and an oxidative stress marker and biochemical tests were analyzed before treatment and 1 and 3 months after starting the treatment. They measured serum levels of 8-hydroxy2-deoxyguanosine (8-OHdG) and gamma-glutamyltranspeptidase (GGT). Immunohistochemistry for glutathione was performed on formalin fixed liver specimens obtained from liver biopsies. Before treatment, the NASH group had higher serum 8-OHdG and lower serum glutathione levels than the FL group. Immunohistochemistry revealed that a strong expression of glutathione was observed in zone 3 in both NASH and FL before treatment. Serum levels of alanine transaminase and 8-OHdG were significantly decreased after treatment in the NASH group. Gamma-glutamyltranspeptidase was decreased after treatment, although the decrease was statistically not significant.

We found that mean total bilirubin in group I was 1.2 mg/dL and in group II was 0.7 mg/dL, aspartate transaminase was 58.2 U/l in group I and 62.6 U/l in group II, alanine transaminase in group I was 142.4 U/l in group I and 128.2 U/l in group II, alkaline phosphatase was 284.2 U/l in group I and 302.4 U/l in group II and γ-glutamyltranspeptidase in group I was 98.2 U/l and 118.4 U// in group II. The mean glutathione level in group I was 0.6 and in group II was 0.4 and which increased to 1.4 in group I and 1.2 in group II after 3 months.

The pathophysiology of NASH was originally explained by the "two-hit" hypothesis. In this hypothesis, the first hit is responsible for producing steatosis (fat accumulation in liver), and the second hit is from oxidative stress causing lipid peroxidation.[10] The pathogenesis and progression of NAFLD is complex, and was not completely explained by the "two hit" hypothesis. Currently, NASH is described by the "multiple hit" hypothesis. In this hypothesis, metabolic syndrome plays a major role due to insulin resistance and the inflammatory process mediated by interaction of different proteins and immune system. The components of the multiple "hits" are yet to be fully defined and they may vary in different patients.[11] However, from available information, the "first hit" is caused by metabolic syndrome and insulin resistance, increased fat loading in hepatocytes leading to steatosis and liver injury. The accumulation of fat in the liver occur as a result of imbalance between the rate of influx and removal of triglycerides a mechanism thought to protect hepatocytes from the lipotoxicity that may result from excessive influx of free fatty acids (FFAs).[12]

Conclusion

Authors found that there was reduction in alanine transaminase, glutathione and gamma-glutamyltranspeptidase level. Antioxidant therapy with glutathione may reduce the pathological oxidative stress in the liver in NASH, preventing the progression from NAFLD to NASH cases.

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