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Serum Malondialdehyde Levels in Patients with Non Alcoholic Fatty Liver Disease

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Abstract: ***Background: Non alcoholic fatty liver disease (NAFLD) is one of the most common liver diseases in the western world and its prevalence is increasing in countries like India. It manifests as a spectrum of disorders starting from simple fatty liver to non alcoholic steatohepatitis (NASH) and cirrhosis. Exact etiology of NAFLD is still under investigation. Malondialdehyde (MDA) is a lipid peroxidation product which can be used as a biomarker for oxidative stress. This study attempts to examine the role of oxidative stress in development of NAFLD. Methods: A case - control study was conducted at a tertiary care hospital in Assam for one year. The study consisted of 70 ultrasound diagnosed patients of NAFLD under the age of 70 years. The control group consisted of 70 healthy volunteers under the age of 70 years. Serum samples were evaluated for MDA in the Department of Biochemistry, GMCH by Enzyme - Linked Immunosorbent Assay (ELIZA). Results: A total of 70 cases and 70 controls were taken up for the study with a mean age of 41.26 and 40.06 years in case and control groups, respectively. The results were analyzed using Graphpad Prism version. The mean value of serum MDA in NAFLD patients is 55.76± 2.92 ng/ml and in control group is 39.66± 2.86ng/ml with p value of <0.0001. Conclusion: MDA levels were significantly higher in NAFLD patients suggesting a state of higher oxidative stress. MDA can be used as biomarker for detection as well as prevention of NAFLD.***

Keywords: Non alcoholic fatty liver disease (NAFLD), Malondialdehyde (MDA)

1. Introduction

Non alcoholic fatty liver Disease is the most common chronic liver disease and its prevalence is on the rise. [(1)] NAFLD is the most common liver disorder in western countries which affects 17 - 46% of adults with variability according to the diagnostic methods, age sex and race. In general NAFLD is present in 40 - 50% in general population [(2)]. NAFLD is defined as accumulation of fat (>5%) in the liver cells in absence of excessive alcohol consumption or other causes of disease including autoimmune disease, drug induced, or viral hepatitis. The spectrum of NAFLD ranges from simple steatosis (Non Alcoholic Fatty Liver or NAFL) to Nonalcoholic Steatohepatosis (NASH). NASH is characterised by inflammation, swelling of the hepatocytes and varying degrees of fibrosis and is capable of progressing to cirrhosis and hepatocellular carcinoma (HCC). Even though the exact cause of NAFLD in not yet defined well, recent studies have shown that oxidative stress (OS) due to insulin resistance and hepatic steatosis may be major cause of NAFLD and may play vital role in progression to NAFLD. Oxidative stress is the state of imbalance between reactive oxygen species (ROS) and the ability of a biological system to detoxify the reactive intermediates. [(3)] Lipid peroxides which are derived from PUFA are highly unstable. They spontaneously metabolise to form a series of compounds, which include malondialdehyde (MDA). MDA is product of arachidonic acid metabolism. It is a reliable marker for oxidative stress. [(4)] MDA is toxic biomolecule and is marker for oxidative stress.

Aims and Objectives:

1) To estimate the levels of serum MDA in patients with Non alcoholic fatty liver disease (cases) and in control group.
2) To determine if there is significant difference in MDA levels in cases and controls.

2. Materials and Methods

It is hospital based case control study conducted in Gauhati Medical College and Hospital during the period of 1st June 2021 to 31st May 2022. Informed consent was taken from every study participant and patient proforma was prepared. Detailed histories, clinical findings, laboratory results of routine investigations were obtained.

Selection of patients (case group): 70 patients with Non Alcoholic Fatty Liver Disease (USG diagnosed) in the OPD and IPD of Department of Gastroenterology, GMCH were taken as case group. Selection of healthy controls: 70 subjects for the control group were selected from the attendants of the participants in the department of Gastroenterology who were apparently healthy.

Inclusion criteria: Patients under the age of 70 years with NAFLD (USG diagnosed) were included in the study.

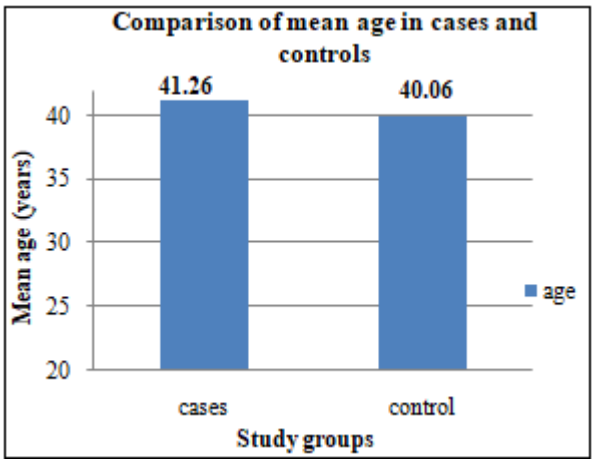
Exclusion criteria: Patients above the age of 70 years, without a definite clinical diagnosis were excluded from the study. Patients with history of alcohol use, smoking, connective tissue disorders, inflammatory disorders, known liver disorders, bariatric surgery, and drug intake causing steatohepatitis, starvation or parenteral nutrition were refrained from taking part in the study.

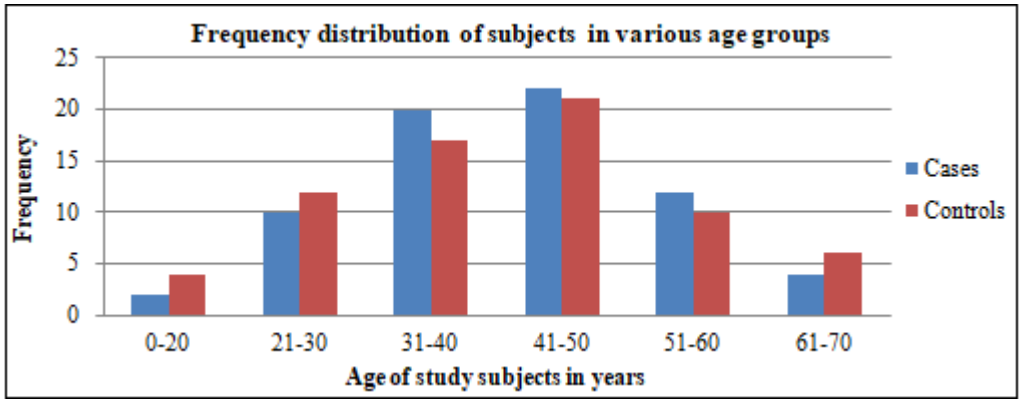
Blood samples for MDA estimation were collected in clot vials and stored at - 20^{O}C. Estimation of MDA was done using ELIZA standard kits within the same week.

Statistical Analysis: Mean and standard deviations were calculated. Students unpaired t test was done to compare the data of both the groups. P value of <0.05 was considered significant. Graph Pad and Microsoft excel were used for data analysis and graph preparation.

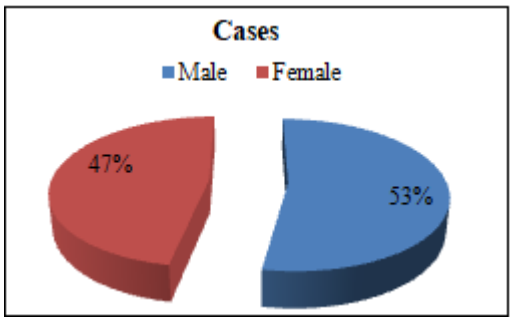
3. Results and Observation

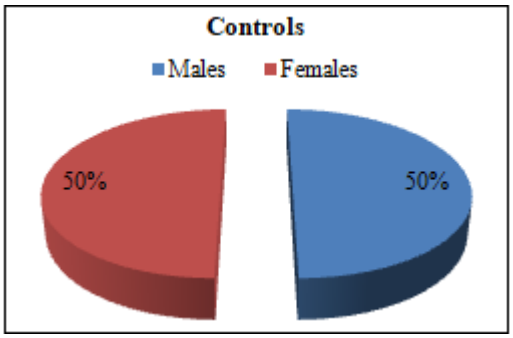
In our study, mean age of the case group was 41.26±11.08 years and in the control group was 40.06±12.80. (p=0.27)



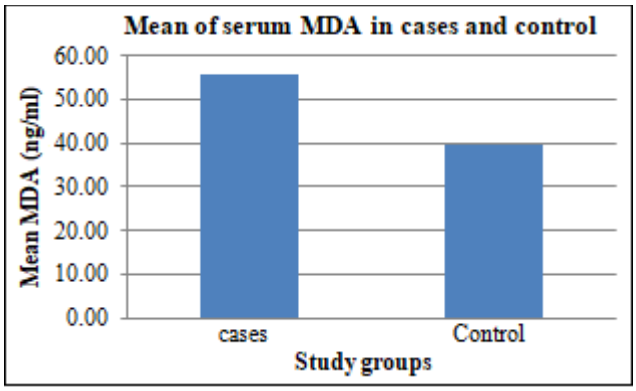


Gender distribution:

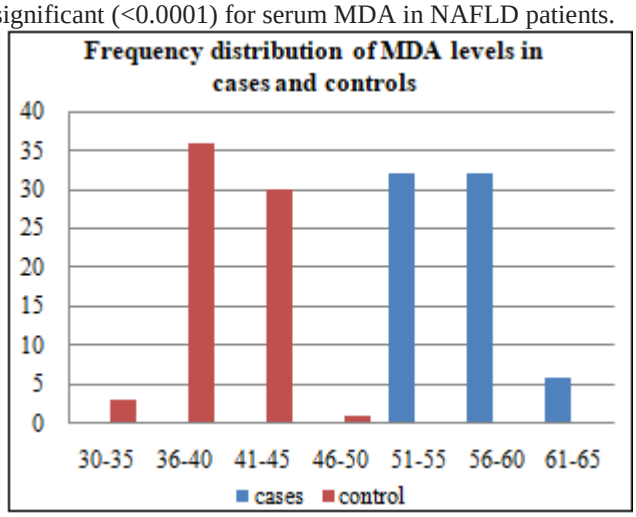




MDA levels in case and control group.



The mean ± SD of MDA level in NAFLD patients was 55.76±2.92 ng/ml and in the control group it was 39.66±2.86 ng/ml (table 5.5). The p value has been found to be highly significant (<0.0001) for serum MDA in NAFLD patients.



It was observed that maximum patients of NAFLD had MDA levels in the range groups of 51 - 55ng/ml (n=32) and 56 - 60ng/ml (n=32).

4. Discussion

Non alcoholic fatty liver disease is a chronic condition encompassing simple liver steatosis, NASH and liver cirrhosis. The prevalence of NAFLD is on the rise worldwide including developing countries like India. Since NAFLD and NASH are asymptomatic and are identified at only advanced stages, there is a soaring need to identify early predictors. Liver biopsy is currently the gold standard in the diagnosis and prognosis of NAFLD; nevertheless it is an expensive and invasive procedure with high sampling error and risk of complications including pain; bleeding and in very rare cases death. Because of poor patient compliance to this invasive procedure, there is an urgent for reliable and non/minimally invasive biomarkers.

The mean ± SD of MDA level in NAFLD patients was 55.76±2.92 ng/ml and in the control group it was 39.66±2.86 ng/ml (table 5.5). The p value has been found to be highly significant (<0.0001) for serum MDA in NAFLD patients. According to our study NAFLD is state of higher oxidative stress evidenced by the higher MDA levels in cases than in controls. Many studies like **Arash A. et al.2021, Zelber - Sagi S et al**, **2020, Kumar A et al.2008**, reported similar findings [(5)] [(6)] [(7)] reported similar findings. The higher oxidative stress marked by increase in MDA levels is seen in NAFLD patients. Modern day lifestyle is responsible for this manifestation. High stress jobs leading to mental disorders like anxiety and depression is often seen to lead to metabolic syndrome. Metabolic syndrome and dyslipidemia hugely overlap with NAFLD and bidirectional causal relationship has been established. General shift in dietary habits from locally grown foods to high carbohydrate diets that are rich in simple sugars like glucose and fructose (corn syrup), transfats have increased free radical mediated injury. Glucose, fructose and cholesterol crystals act as endogenous s triggers in activating various proinflammatory cytokines releasing pathways (activate inflammosomes). Moreover over nutrition, obesity leads to increased production of FFAs that undergo β oxidation. This in turn produces more electrons than required and generates ROS. Increased ROS causes lipid peroxidation that can be detected by its byproducts like MDA.

Limitation of the study:

1) Due to small sample size uniform comparison between the two groups was not possible.
2) Shorter study period

5. Conclusion

In our study we have found that patients with NAFLD have higher serum levels of MDA than in healthy volunteers. NAFLD is a state of oxidative stress and MDA can be used as a biomarker for NAFLD. NAFLD overlaps with many non communicable diseases like T2DM, metabolic syndrome, mental disorders, obesity, cardiovascular diseases etc. In recent years the burdens of these “silent killers” have increased drastically. So estimating MDA as a screening method for oxidative stress can not only help in diagnosis but also prevention of these diseases including NAFLD.

Patients with high oxidative stress status hence screened out can be advised to maintain a healthy lifestyle with better food habits and daily physical exercise. Specific dietary advice like consuming locally grown foods rich in antioxidants (vitamin C, E etc) and microminerals (Cu, Zn etc) can be provided to the patients. If needed micronutrient supplements can also be added. This will act as primary prevention method for these notorious non communicable diseases and hence prevent the burden on health system. This will also allow the government to make better as well as more targeted policies to prevent and detect diseases like NAFLD.

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