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Micronutrient Levels of Non- Alcoholic Fatty Liver Disease.

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ABSTRACT

Oxidative stress is known to play an important role in the onset of Non-Alcoholic Fatty Liver Diseases (NAFLD). Cu / Zn superoxide dismutase counteracts oxidative stress and depends on adequate copper and zinc availability, suggesting a link between copper and zinc availability and antioxidant defences in NAFLD. The multifacetted biological properties of copper appeared attractive to investigate the potential contribution of copper and zinc bioavailability to the development of NAFLD. We aimed to compare serum levels of copper and zinc in patients with NAFLD and normal individuals. Patients with NAFLD (n= 100) were compared to control subjects (n=100). Serum was estimated for copper and zinc levels by atomic absorption spectroscopy Results are presented as mean + standard deviation value. Student's test was used to correlate between serum levels of copper and zinc in patients with NAFLD and normal individuals. A 'p' value of 0.05 or less was considered significant. The mean serum level of copper in NAFLD individuals was found to be higher when compared to normal individuals. Serum copper level in NAFLD individuals was 83.74±8.43 and that of normal was 77.55±7.06. The mean serum zinc levels in NAFLD individuals were64.34±9.21 and that of normal was73.60±11.90. Serum zinc levels in NAFLD individuals were lower when compared to normal individuals. Serum copper levels are higher and zinc levels are lower in NAFLD patients when compared to normal individuals.

Keywords: Non-Alcoholic Fatty Liver Diseases, Oxidative Stress, Copper, Zinc

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INTRODUCTION

Non- Alcoholic fatty liver disease is an increasingly recognized condition that may progress to end-stage liver disease. The pathological picture resembles that of alcohol-induced liver injury, but it occurs in patients who do not abuse alcohol. A variety of terms have been used to describe this entity, including fatty-liver hepatitis, nonalcoholic Laennec's disease, diabetes hepatitis, alcohol-like liver disease, and nonalcoholic steatohepatitis. Nonalcoholic fatty liver disease is becoming the preferred term, and it refers to a wide spectrum of liver damage, ranging from simple steatosis to steatohepatitis, advanced fibrosis, and cirrhosis. Steatohepatitis (nonalcoholic steatohepatitis) represents only a stage within the spectrum of nonalcoholic fatty liver disease. The clinical implications of nonalcoholic fatty liver disease are derived mostly from its common occurrence in the general population and its potential to progress to cirrhosis and liver failure [1-4].

NAFLD is currently the most common liver disease in the United States as well as worldwide. NAFLD affects an estimated 10-39% of the world's population, and in the US upwards of 30 million Americans have NAFLD, while 8.6 million of these persons have NASH.[5] NAFLD occurs in all age groups and it affects all races. NAFLD is reported to occur in 57-74% of obese individuals, and 90% of morbidly obese individuals. Obesity and the cluster of symptoms known as metabolic syndrome are linked to NAFLD. [5]

Oxidative stress is known to play an important role in the onset of NAFLD. When pro-oxidant pathways generate more reactive species than can be consumed by antioxidant pathways (eg, via protein disulfide isomerase or reduced glutathione peroxidase), oxidative stress occurs, with resulting accumulation of reactive oxygen species (ROS, chiefly superoxide and hydroxyl radicals plus hydrogen peroxide).[6-10] Micronutrients also play an important role in health and disease.[11] One of the enzymes counteracting oxidative stress, Cu / Zn superoxide dismutase depends on adequate copper and zinc availability, suggesting a link between copper and zinc availability and antioxidant defense in NAFLD.[12] Moreover, NAFLD is frequently accompanied by perturbations of iron homeostasis [13,14] that are molecularly linked to low copper bioavailability and decreased levels of the copper containing ferroxidase ceruloplasmin.[15,16]. Systemic copper deficiency causes mitochondrial dysfunction in mice and similar morphological and functional alterations have also been described in human NAFLD. [17,18] Given the multifacetted biological properties of copper, it appeared attractive to investigate the potential contribution of copper and zinc bioavailability to the development of NAFLD. We aimed to compare serum copper and zinc concentrations of patients with NAFLD and normal individuals.

MATERIALS AND METHOD

Groups

Control: 100 healthy patients Serum was collected from K S Hegde Hospital, Mangalore.
Study: 100 Patients with Non-Alcoholic Fatty Liver Diseases serum was collected from K S Hegde Hospital, Mangalore.

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Inclusion Criteria

Non fatty liver disease subjects were diagnosed by USG.

Exclusion Criteria

- Alcoholic fatty liver subjects.
- Pateints taking lipid lowering drugs.
- Pateints suffering from hepatitis (ALT 350).

Estimation of Serum Copper and Zinc Levels by Atomic Absorption Spectrophotometer

Sample Digestion

To 100µl of serum, 200 µl of Conc. nitric acid was added and kept over a heating plate till colourless fumes appear. Then the sample was made up to 10ml by adding deionized water.

Estimation

Copper and zinc was estimated by atomic absorption spectroscopy.

Statistical Analysis

Results are presented as mean ± standard deviation value. Student't' test was used to correlate between total antioxidant level and dental caries in study and control groups. A 'p' value of 0.05 or less was considered significant.

RESULTS

The mean serum level of copper in NAFLD individuals was found to be higher when compared to normal individuals. Serum copper level in NAFLD individuals was 83.74±8.43 and that of normal was 77.55±7.06.(Table 1,Graph 1) The mean serum zinc levels in NAFLD individuals was 64.34±9.21 and that of normal was73.60±11.90. (Table 1, Graph 2). Serum zinc levels in NAFLD individuals were lower when compared to normal individuals.

Table 1: Comparison of serum Zinc and Copper levels in normal and NAFLD individuals

Parameters	Normal Mean±SD	NAFLD Mean±SD	'P' Value
Copper	77.55±7.06	83.74±8.43	0.0137(Significant)
Zinc	73.60±11.90	64.34±9.21	0.0075(Significant)

*P<0.05 is statistically significant. Statistical comparison was performed by Student't' test. Data expressed as Mean±SD.

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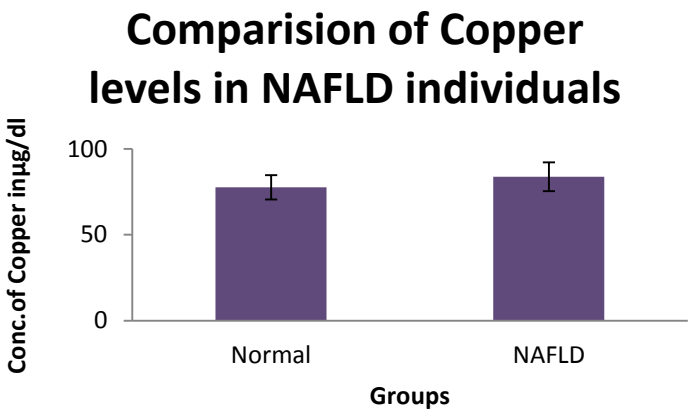
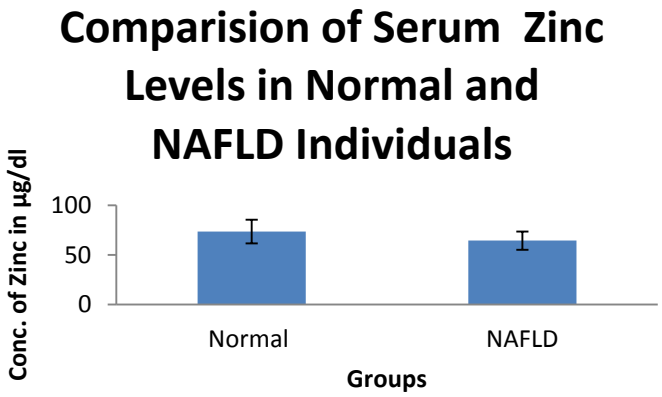
Graph 1: Comparision of serum copper levels in normal and NAFLD individuals



Graph 2: Comparision of serum zinc levels in normal and NAFLD individuals



DISCUSSION

The prevalence of NAFLD is continuously rising and represents a growing clinical problem. NAFLD is an increasingly recognized form of chronic liver condition affecting both children and adults within the wide spectrum of fatty liver diseases. Its incidence and prevalence are increasing, paralleling the increase in obesity and diabetes mellitus. It is well-known that lipid peroxidation and oxidative stress play significant roles in the pathogenesis of various diseases including chronic liver diseases. NAFLD is present in 10% to 24% of the general population in various countries. [2]

Increased oxidative stress is considered a key trigger in the pathogenesis of human NAFLD and one of the enzymes counteracting oxidative stress, copper/zinc (Cu/Zn) superoxide dismutase (SOD) depends on adequate copper availability, suggesting a potential link between copper availability and impaired antioxidant defence in NAFLD[20, 21]. Copper is an essential metal that is an important cofactor for many proteins. The average diet provides substantial amounts of copper, typically 2-5 mg/day; the recommended intake is 0.9 mg/day. Most dietary

copper ends up being excreted. Copper is absorbed by enterocytes mainly in the duodenum and proximal small intestine and transported in the portal circulation in association with albumin and the amino acid histidine to the liver, where it is avidly removed from the circulation. The liver utilizes some copper for metabolic needs, synthesizes and secretes the copper-containing protein ceruloplasmin, and excretes excess copper into bile. Processes that impair biliary copper excretion can lead to increases in hepatic copper content.

In the study it is seen that serum copper level increased in NAFLD individuals when compared to normal individual. This study showed a decrease in serum zinc levels in NAFLD individuals when compared to normal individuals.

This increase is mainly because Cu complexes could be considered as complexes able to scavenge the oxygen-free radicals by enhancing the synthesis of SOD or its SOD-mimetic activity. 19 Moreover, the SOD-mimetic activity of Cu complexes may facilitate de novo synthesis of Cu and zinc-SOD and Cu-manganese-dependent tissue repair enzymes and synthesis of CP, which downregulates NOS and inhibits NADP-dependent NOS where the complex acts as an electron transporter or acceptor. [22, 23].

Obesity, type 2 (non-insulin-dependent) diabetes mellitus, and hyperlipidemia are coexisting conditions frequently associated with nonalcoholic fatty liver disease. [22] There is a direct correlation between the degree of obesity and prevalence and severity of NAFLD. The prevalence of NAFLD increases by 4.6- fold in obese people. [24] with any degree of obesity, type 2 diabetes mellitus significantly increases the prevalence and severity of NAFLD. [1, 25].
Epidemiological studies have reported that low zinc intake and low zinc concentrations in blood are associated with an increased prevalence of obesity and Zinc deficiency increases oxidative stress and the inflammatory response in obese individuals. This study showed a decrease in serum zinc levels in NAFLD individuals when compared to normal individuals.

CONCLUSION

This study will help clinicians to draw different baselines for serum copper and Zinc levels in patients with Non-Alcoholic Fatty Liver Diseases. Serum copper levels are higher and zinc levels are lower in NAFLD patients when compared to normal individuals.

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