International Journal of Biochemistry Research & Review

20(4): 1-5, 2017; Article no.IJBCRR.33499
ISSN: 2231-086X, NLM ID: 101654445

Evaluation of High Levels of Triglycerides in Non-alcoholic Fatty Liver Disease

D. Santha Rao[1*], V. Praveena[1] and Bhukya Veeranna[1]

[1]ESIC Medical College, Sanathnagar, Hyderabad, India.

Authors' contributions

This work was carried out in collaboration between all authors. Author DSR designed the study, performed the statistical analysis, wrote the protocol, and wrote the first draft of the manuscript. Authors VP and BV managed the analyses of the study. Author BV managed the literature searches. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/IJBCRR/2017/33499
Editor(s):
(1) Enrico Sanjust, Associate Professor, Department of Internal Medical Sciences, University of Cagliari, Italy.
Reviewers:
(1) Dhastagir Sheriff, Benghazi University, Libya.
(2) Elvira Bormusov, Technion Institute of Technology, Israel.
Complete Peer review History: http://www.sciencedomain.org/review-history/23151

Short Communication

Received 18th April 2017
Accepted 27th January 2018
Published 12th February 2018

ABSTRACT

Non-alcoholic fatty liver disease (NAFLD) is starting as accumulation of fat in the hepatocytes (steatosis) which is a sub-clinical condition in those who are not consuming alcohol. Non-alcoholic steatohepatitis (NASH) is a condition of steatosis, associated with inflammation of liver cell. This is a clinical form of NAFLD, which is regarded as a major cause of cirrhosis of the liver [1]. This distinction between simple steatosis and NASH is important because the natural history of these categories differs substantially. Patients with simple steatosis usually have a benign prognosis from the point of view of liver disease [2-5]. In contrast, up to 20% of patients with NASH may ultimately develop advanced liver disease [2,4-6]. The prognosis of NASH-related cirrhosis is poor: It results in liver failure or liver-related death in approximately one third of cases [7,8]. Hepatocellular cancer is also a recently recognized complication of NASH-related cirrhosis [7,9].

Keywords: Non- alcoholic fatty liver disease(NAFLD); Non alcoholic steatohepatitis(NASH); cirrhosis; liver failure; Hepatocellular cancer; advanced liver disease.

**Corresponding author: E-mail: santha2035@gmail.com;*

1. PATHOPHYSIOLOGY

NAFLD is considered a spectrum of disease activity. This spectrum begins as fatty accumulation in the liver (hepaticsteatosis). A fatty liver can remain without disturbing the function of the liver, but by the varying mechanisms and possible insults to the liver, may progress to outright inflammation of the liver. When inflammation occurs in this setting, the condition is then called NASH. Over time, up to 20 percent of patients with NASH may develop cirrhosis. However both obesity and insulin resistance likely play a strong role in this disease process. The exact reasons and mechanisms by which this disease progresses from one entity to the next is a subject of much research and debate.

Current concepts suggest that NASH involves two different clinical conditions, in which the initial symptoms deal with macrovesicular steatosis results from insulin resistance and subsequent hyperinsulinemia which leads to alterations in the hepatic pathways through which synthesis of fatty acids occur, and ultimately cause accumulation of lipids in the hepatocytes. These changes make the liver susceptible to get in chance of the second symptoms, resulting in inflammatory response and progress to liver damage. Oxidative stress, mainly as a consequence of mitochondrial dysfunction, and proinflammatory cytokines such as TNF-∞, are thought to play a central role in the progression of simple steatosis to steatohepatitis and cirrhosis and these may be the primary cause of this phenomenon [10]. Recent studies revealed that, adiponectin, are an adipocyte-produced protein & have gained considerable attention as a possible key regulator of liver injury in NAFLD. Adiponectin is secreted by adipocytes in inverse proportion to BMI and metabolically acts to reduce body fat, improve insulin sensitivity, and decrease serum free fatty-acid levels. Finally, hepatocyte apoptosis, a specific form of cell death is characterized by organized nuclear and cellular fragmentation, which has been identified as a potential mechanism in dealing with the NAFLD and its adverse patho-physiological conditions [11,12]. Although much progression has been made, those are revealed in treating the moderate conditions of NAFLD.

Cytosolic TGA accumulation leads to enhance the chances of NAFLD. This arises from an imbalance between lipid acquisition (i.e fatty acid uptake and de novo lipogenesis) and removal from the Cytosolic embedding (i.e mitochondrial fatty acid oxidation and export as a component of VLDL particles). Fatty acid uptake into the liver contributes the steady balance of hepatic triglycerides in the liver, as well as the pathogenesis of NAFLD. The rate of fatty acid uptake from plasma into the cells depends on the fatty acid concentration of plasma and the hepatocellular capacity for fatty acid uptake [13].

2. MATERIALS

2.1 Controls

Men and women who were selected of age between 35 to 65 years with normal levels of triglycerides and no central obesity.(20 controls)

2.2 Patients

For the present study men and women were selected of ages between 35 to 65years with clinical jaundice and fat around the umbilicus.(40 cases)

All patients and controls were asked to come to clinical biochemistry laboratory on overnight fasting at 9 A.M. After brief clinical examination i.e. taking relevant history (No H/o Alcohol intake) and blood sample were taken for the measurement of Total Triglycerides,(TTG).Total triglycerides TTG) upper limit is 150 mg/dl.

Comparative Table of Results-1 : Controls to NASH

Controls	TTG (mg%)
Average	129.8
S.D. ±	11.97
NASH	TTG(mg%)
Average	169.4
S.D. ±	18.2
P value	P<0.001
Significance	Highly Significant

Comparative Table of Results-2 : Controls to cirrhosis

Controls	TTG (mg%)
Average	129.8
S.D. ±	11.97

Cirrhosis	TTG(mg)
Average	167.5
S.D. ±	11.3
P value	P<0.001
Significance	Highly Significant

3. RESULTS

In the present study, 20 Controls and 40 selected cases of jaundice with fat around umbilicus were taken for fasting blood sample for measurement of Total Triglycerides(TTG). A raise in Total Triglycerides (TTG) is highly significant ($P<0.001$) in cases of Non Alcoholic Steato-Hepatitis (NASH) and cirrhosis when compared with controls as shown in the above tables.

4. DISCUSSION

Insulin resistance increases adipose lipolysis, resulting in efflux of free fatty acids (FFA) into the serum, which are then delivered to the liver. The fatty acids supplied, synthesized in liver by lipogenesis are in turn esterified into triglycerides and incorporated into very low density lipoproteins (VLDL). Excess VLDL secretion by the liver leads to hypertriglyceridemia. In addition, insulin resistance inhibits peripheral lipoprotein lipase activity, reducing VLDL clearance and increasing serum triglyceride levels further [14,15]. When VLDL delivery is hampered due to nutritional lack of lipotropic factors from the liver and or hepatic *de novo* synthesis of triglyceride exceeds delivery, fatty liver results. Hypertriglyceridemia is found in 21% to 61% of patients with NAFLD [16,17].

There is increasing evidence that fatty livers are more vulnerable to any factor associated with further hepatic injury. In fact, hepatic steatosis may contribute to this injury by increasing sensitivity to oxidative stress and cytokine-mediated hepatic damage. Nonalcoholic fatty liver disease (NAFLD) has attracted a great deal of attention since the report by Leevy described 270 patients with NAFLD in 1962. It has been reported that NAFLD is related to obesity, [18,19] diabetes mellitus [16,18,20] and dyslipidemia. [16,20,21] However, NAFLD has been found in individuals without such risk factors [16].

5. SUMMARY AND CONCLUSION

NAFLD or NASH appears to be the commonest pathophysiological liver conditions, although the determination of its precision is very uncommon so that the prevalence of the disease remains contant. An increasing number of studies have examined the significance of NAFLD, as it is increasingly prevalence and understood as a complication of liver cirrhosis. The relationship between triglycerides and NAFLD is well known and triglycerides that contribute to increased visceral adiposity might be relevant in the pathogenesis of NAFLD [22]. Although simple fatty liver seems to be a benign condition, some patients may progress to NASH and ultimately to cirrhosis. Whereas the consequences of the disease, that emphasize the importance of the detection of NAFLD at high-risk groups, including obese patients as well as those with evidence of insulin resistance or other components of the metabolic syndrome.

There is a need for screening and surveillance methods should be applied more uniformly, and reliable non invasive techniques are needed for diagnosis of NAFLD as well as detection of progressive liver disease. The diagnosis of NAFLD should prompt management of the metabolic risk factors. Weight loss regimens are thought to be helpful and numerous drugs have been investigated in small studies. Large, randomized clinical trials are necessary to determine the real benefits of these agents. Finally, studies on the pathogenesis of NAFLD may not only improve our understanding of the mechanisms involved in NAFLD progression, but also may lead to potentially generate novel therapeutic strategies to treat this conditions [23].

From this particular study, we have noticed that there are in association of raised triglycerides and NAFLD, as it is known that NAFLD progression to NASH and further cause to cirrhosis if appropriate intervention is not taken. So screening of triglycerides level and there control in high risk groups viz obese subjects to those with insulin resistance is useful in avoiding progression of NAFLD to NASH by life style modification and hypolipemic drugs.

CONSENT

As per international standard or university standard written patient consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

As per international standard or university standard written ethical permission has been collected and preserved by the author(s).

ACKNOWLEDGEMENT

Our sincere thanks to Dr. Dhanalaxmi specialist Dept. of Biochemistry Esic hospital, sanathnagar, for helping in procuring the blood samples.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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APPENDIX

Control	Cirrhosis	Nash
TTG mg%	**TTG mg%**	**TTG mg%**
130	155	145
125	171	190
140	170	160
145	180	165
135	170	190
140	165	120
130	175	195
125	165	170
140	170	200
115	161	170
135	162	175
110	155	150
150	180	178
125	135	180
105	180	160
130	160	170
120	165	165
120	175	170
130	185	165
145	170	170
2595	**3349**	**3388**
129.75	**167.45**	**169.4**
11.973	**11.335**	**18.219**

Peer-review history:
The peer review history for this paper can be accessed here:
http://www.sciencedomain.org/review-history/23151