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Review Article

A Widespread Acquired Ailment, Nonalcoholic Fatty Liver Disease; Its Approaches Related to Nutritional Therapy

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Abstract

NAFLD (non-alcoholic fatty liver disease) is an inherited metabolic disorder characterised by triglyceride buildup in the liver (TGs). The four clinical-pathological categories frequently followed by the NAFLD pathway are non-alcoholic steatosis, steatohepatitis, increasing fibrosis/cirrhosis, and hepatocellular cancer. The prevalence of NAFLD is increased by obesity and insulin resistance. NAFLD is linked to liver disease in both children and adults and is influenced by age, gender, race, and ethnicity. Hyper-caloric diets, especially those high in trans-/saturated fat and cholesterol, as well as fructose-sweetened drinks, seems to enhance visceral adiposity in people of all ages. Reduced calorie intake, increased soy protein and whey consumption, and supplementation of monounsaturated fatty acids, omega-3 fatty acids, and fibre, polyphenolic substances have preventative and therapeutic benefits are the initial steps toward its management. Along with good eating habits, exercise and physical activity that leads to weight loss and a reduction in liver fat buildup are also important. The patient becomes vulnerable to liver transplantation due to poor care (the end stage of NAFLD).

Keywords: Non-alcoholic Steahepatitis; Non-alcoholic Fatty Liver; Fibrosis; Cirrhosis; Type 2 Diabetes; Cardiovascular Diseases; Chronic Kidney Diseases; Nutritional Management; Lifestyle Modifications; Liver Transplant

Introduction

Non-alcoholic fatty liver disease is the most common kind of chronic liver disease worldwide (NAFLD). NAFLD involves adipose (containing adipocytes) tissue deposition in the liver due to advanced hepatitis, fibrosis (fibrotic scarring), cirrhosis (late fibrosis), and sometimes, hepatocellular carcinoma (HCC, or may termed as primary cancer of liver) related steatosis [1]. NAFLD is defined as the accumulation of triglycerides inside hepatocytes (liver cells) that exceeds 5% of total liver weight. NAFLD contains a variety of diseases which may accelerates towards cirrhosis and HCC, from basic steatosis to nonalcoholic steatohepatitis (NASH). Non-alcoholic steatohepatitis (NASH) occurs when inflammation, ballooning and mild fibrotic scarring occur in addition to steatosis; and the development from NASH to cirrhosis and hepatocellular cellular fibrotic [2]. It is basically a developed metabolic disorder categorized by fat accumulation within the liver caused due to metabolic stress. NAFLD is linked with insulin resistance and also genetic vulnerability and has histologically featured that correlate with the alcoholic liver resistance [3].

NASH is defined histologically by the presence of macro vesicular steatosis, lobule edoema, and hepatocellular ballooning. The study is commonly similar to alcoholic fatty liver disease; hence, the diagnosis may be made only if there is no excessive alcohol use, defined as less than 30 grams per day for males and 20 grams per day for females [4].

The progress of NAFLD is associated with the person's lifestyle, such as unnecessary consumption of high caloric foods, in addition with decreased physical activity, exercise and workouts. In these centuries, global urbanization and transformations have been related to unhealthy shifts in lifestyles [5]. Treatment of steatohepatitis and related metabolic comorbidities is the care of people who have NAFLD [6]. Additionally being closely correlated with the production and progression of NAFLD, harmful eating patterns and uneven nutrition are both threats for obesity and errors of metabolism [7].

Changes in the lifestyle such as weight loss along with a healthy balanced diet reduce the risk of fibrosis and non-alcoholic steatohepatitis (NASH) necro-inflammatory changes and is helpful in recovery of the liver tissues and hepatic steatosis in people suffering with NAFLD [8]. So, in addition, a balanced diet has advantages beyond well.

Epidemiology

NAFLD is the common one from all hepatic diseases affecting 20-33% of adults [9]. Around 30% of NAFLD patients develop NASH, which includes the emergence of various phases of swelling and fibrosis, which can develop to cirrhosis in 20-25 percent of cases within twenty years [10].

NAFLD occurrence is 16.9 percent to 23.8% in males and 16.2% of females in industrialized countries - 22.6 percent whereas in boys it is 8.1%-12.9 percent and 8.4 percent-13.4 percent in girls of developing countries [11]. The development of only a minority of NAFLD patients will be Chronic liver disease complications, four to eight percent death from Cirrhosis problems and one to five percent of hepatocellular complications about carcinoma (HCC) [12].

Risk factors

Non-alcoholic fatty liver disease is a very complicated one. It touches many metabolic paths which seem to be controlled by both of the factors i.e. genes and environment. Most of the processes implicated in the development and advancement of non-alcoholic fatty liver disease are expected to be similar to those implicated in the advancement of obesity, metabolic syndrome, T2DM, CVD, and cancer. It is also evident that genetic and environmental interactions affect both NAFLD growth and progression [13].

Other factors include an inactive life, a caloric dense diet, diet high in saturated fat, processed carbs and more consumption of fructose [14]. Besides, heritable, and nutrition variables; other influences include human microbiome, resistance to the insulin, adipose tissue linked hormones, epigenetic resistance [15].

Etiology

Basically, the very simple definition of NAFLD is that fatty acid accumulates in liver even <5 percent of hepatic mass. The reasons of nonalcoholic fatty liver disease are many, but main causes are overweight, T2DM, dyslipidemia, and resistance to insulin that all are basically related to overweight. NAFLD has a pathophysiology that is distinct from typical alcoholic fatty liver disease, and it is only identified when there is no evidence of heavy alcohol consumption (>30 grams per day for men, 20 grams per day for women) [16].

Secondary causes

The secondary causes of NAFLD are following. The first one is the complications of fat metabolism that includes a wide range of complications associated with NAFLD.

Disorders of lipid metabolism

Abeta-lipo-proteinemia (Bassen–Kornzweig syndrome)

Abeta-lipo-proteinemia (ABL) is caused by alteration in the gene that used to form microsomal triglyceride transfer protein (MTTP) and it is an autosomal recessive syndrome. MTTP is an endoplasmic reticulum (ER) protein that is involved in the transfer of triglycerides from hepatocytes to apolipoprotein B-100 (apoB100) and enterocytes to apolipoprotein B-48 (apoB48). This gene mutation prevents the transfer and combining of triglycerides to these lipoproteins, as well as the creation of VLDL and chylomicrons, respectively. The lack of chylomicrons and vLDL results in the accumulation of triglycerides in the hepatocytes, resulting in steatosis [16].

Hypobetalipoproteinemia

(FHBL) Familial hypobetalipoproteinemia is a disease of fat metabolism in which low ranges of LDL and apolipoprotein B found. Like ABL, it is also an autosomal recessive disorder and in this also no formation of VLDL occur that ultimately results in accumulation of triglycerides that is leading cause of macro-vesicular steatosis. Even the clinical signs and symptoms of FHBL is analogous to those of ABL. This disorder treats with fat-limited foods with supplements of vitamin A, D, E and K [16].

Familial combined hyperlipidemia

Familial combined hyperlipidemia (FCHL) is a disease of fat metabolism that results in overproduction of apolipoprotein B-100 (apoB100) and it is an autosomal dominant disorder. This increased production of apoB100 lead towards the increased production of VLDL and increased levels of liver and peripheral lipids. NAFLD is observed in about seventy-five percent of FCHL. This disorder is treats with diet low in fat, weight loss, increased physical activity and cessation of smoking [17].

Glycogen storage disease

(GSDs) Glycogen storage diseases are glycogen metabolism syndromes which caused by the unusual glycogen accumulation. There are twelve kinds, however phosphorylase b kinase deficiency and types 0, 1, 3, 4, 6 are all connected to hepatic diseases. Liver is the main organ for the storage of glycogen and this glycogen used during fasting for the synthesis of glucose but due to altered liver glycogen metabolism both hypoglycemia and hepatomegaly occurred. In adults with GSD, there is a risk of developing hepatic illness, cirrhosis, and potentially the progression of hepatic adenoma. GSD's treatment includes to avoid fasting, the consumption of corn's starch (the glucose that is slowly absorbed) and has sometimes liver transplantation [17,18].

Lipodystrophy

Lipodystrophy chances to occur is 1 in 10 million. It is simply defined an autosomal recessive syndrome and is the uneven rearrangement of adipose tissue in the body and sometimes it's completely loss from the body (lipoatrophy). The clinical signs and symptoms of this syndrome in infants are extreme fat loss, hastened body growth, voracious appetite, and complicated bone age. At childhood stage developed lipodystrophy starts early and late in adulthood even before the individual was healthy. Acquired lipodystrophy can also be caused by long-term use of nucleoside analogues or highly active antiretroviral therapy (HAART) for HIV treatment. Treatment involves the usage of some agents like hypoglycemic medications, insulin, and metformin and if diet low in fat is unable to control serum lipid levels then lower the risk of other metabolic aberrations [19].

Nutritional causes

The nutritional causes for NAFLD are following.

Total parenteral nutrition

TPN means the provision of calories and/or glucose through the intravenous route of administration. Long-term usage of TPN results in many conditions. To begin with, it lowers carnitine levels, which are required to transport free fatty acids from the cytoplasm to the mitochondria for further processing (beta-oxidation). Secondly, it also depletes choline, that is necessary nutrient for the secretion of lipoproteins, and it results in lipid storage in hepatocytes promote. Serious liver injuries and in sometimes the last phase liver disease directly correlates with the duration of TPN administration [20].

Figure 1: TPN related liver injury. Steatosis, cholestasis, and duct proliferation with inspissated bile are shown by the arrow.

Surgical weight loss

(JI) The jejunoileal bypass practice, which is now in practice, has forty percent chances for abnormal LFTs and six percent occurrence of steatohepatitis. Jejunoileal bypass causes the demolition of adipocytes that results in a huge increase in free fatty acids, which then go to the liver. After the operation, for the prevention of developing steatosis the most effective and appropriate ways are lifestyle changes including foods and physical activity.

Starvation

There are several mechanisms that cause steatosis by severe starvation. Due to starvation protein deficiency occur that results in the reduction of apo-lipo-protein production and VLDL formation also decreased that inhibits VLDL transport. In protein-energy malnourished children, the synthesis of VLDL-apolipoprotein B-100 is linked with liver fat levels.

As oxidative stress causes reduced beta-oxidation processing of fatty acids, but extended starvation causes more of the beta-oxidation. This contradiction in two statements shows that during starvation less transport of VLDL plays a more important role in fat accumulation than its role in oxidative stress (Jacob., *et al*. 2012).

Pathogenesis

The liver plays a crucial role in lipid metabolism, absorbing free fatty acids from the bloodstream and generating, storing, and transporting lipids and lipoproteins. Major breakthroughs in our understanding of the disease's pathophysiology have highlighted the disease's intricacy. The 'multi-hit' concept, which incorporates many interlocking mechanisms, innate immune activation, including lipotoxicity, and the microbiome on a background of environmental and genetic variables, replace the 'two-hit' concept. The breadth of this study does not allow for a thorough explanation, although it has been fully examined elsewhere 14 and is described in Figure (James, 2018).

Figure 2

The pathogenesis of nonalcoholic fatty liver disease is depicted in Figure 2, where LPS stands for lipopolysaccharides, FXR stands for farsinoid X receptor, and TLR stands for toll-like receptor (James., *et al*. 2018).

Pathophysiology

Insulin resistance (IR) is a key factor in the buildup of free fatty acids in hepatocytes, which eventually leads to NAFLD. In the adipose tissues, IR reduces lipogenesis (fatty acid production) as well

as the esterification of free fatty acids, but it stimulates lipolysis (fatty acids breakdown, which means increases the influx of free fatty acids in the liver). This is due to an increase in serum free fatty acids (FFA), which are utilised by the liver. Insulin-unregulated transcription factors such sterol regulatory element binding protein (SREBP)-1c and peroxisome proliferator-activated receptor gamma (PPAR) promote increased hepatic TG synthesis in response to increased FFA input. Insulin prevents FFA from being oxidised. Insulin resistance also reduces the formation of apolipoprotein B (apoB) or the function of microsomal triglycerides transfer protein (MTP) that incorporates TG with apo B, resulting in the inhibition of TG transport via very low-density lipoprotein (VLDL) because the production of VLDL is reduced due to the inhibition of TG transport via lipogenesis. As a result, the formation of reactive oxygen species (ROS) rises, and hepatic oxidative stress rises (Claudia., *et al*. 2019).

Figure 3: Pathophysiology of NAFLD (Christopher *et al*., 2015).

Clinical manifestations

As the disease progresses, it may lead to some clinical manifestations. Clinical signs and symptoms of NAFLD include: Frequently asymptomatic, Hepatomegaly (in 50%), High blood pressure, Abdominal right upper quadrant discomfort, Fatigue, Overweight (BMI≥25kg/m^2), Dyspepsia, Vague, and unspecific symptoms, Central adiposity, splenomegaly (in 25%) (Claudia., *et al*. 2019).

Diagnosis

The diagnosis of NAFLD entails identifying steatosis in the absence of a secondary etiology (e.g., alcohol and steatogenic medications). However, regardless of transaminase levels, the diagnosis should be explored in high-risk individuals with type 2 diabetes or metabolic syndrome. CT and MRI scans are both effective in detecting mild to severe fatty alterations in the liver. On ultrasonography, the echogenicity of the renal cortex or spleen is lower than the echogenicity of hepatic fat (James, 2018). It is impossible to tell whether a person has simple steatosis or NAFLD without a biopsy. The use of biopsy screening to distinguish between these two disorders is possible (M. K., *et al*. 2008).

Stages of NAFLD

Hepatic fat deposition (hepatic steatosis), Inflammatory hepatic fat deposition, Fibrosis, and Cirrhosis are the four phases of NAFLD. Hepatic fat deposition, commonly known as non-alcoholic fatty liver fat, is the initial stage of NAFLD. Non-alcoholic steatohepatitis (NASH) is the second stage of NAFLD, which involves hepatic fat accumulation and inflammation. Fibrosis is the third stage of NAFLD, which is defined by the production of scar tissue in the liver and is caused by persistent liver inflammation (hepatitis). Cirrhosis is the fourth and final stage, and it is the most dangerous since most liver cells are replaced by fibrosis, which weakens the structure and function of liver cells, leading to liver failure.

Figure 4: Stages of NAFLD (Kate., *et al*. 2019).

Lipid peroxidation and cyclic ROS by-products are the major pro-inflammatory agents that lead to cause hepatic stellate (HSC) cells, contributing to Hepatic Fibrosis. In this way, three different pathways can be used to progress from steatosis to NASH and fibrosis: lipid peroxidation, proinflammatory cytokine induction, and Fas ligand induction. Diabetes and NAFLD have mutual pathogenetic mechanisms and metabolic derangements may interact with environmental and genetic factors to accelerate the progression of NAFLD in diabetic and insulin-resistant patients [21].

Steatosis

Because of its low cast and great accessibility, ultrasonography has become the diagnostic method of choice for diagnosing steatosis. These tests employ simple clinical data that can be fed into free online algorithms, which would be especially beneficial in contexts where imaging is too expensive and difficult to get.

The controlled attenuation parameter (CAP) is a relatively new feature of transient elastography equipment that employs ultrasonic waves to assess liver fat (Fibroscan TM, Echosens, Paris). Overall, a score of 250 dB/m is an adequate cut-off for confirming the diagnosis of NAFLD (James, 2018).

Fibrosis

The presence or absence of substantial fibrosis is a crucial prognostic characteristic in NAFLD, and it represents a considerable risk. Multiple serological assays for fibrosis diagnosis have been developed using basic biochemical and clinical characteristics that incur no additional expense above regular haematology and biochemistry investigations and may be computed readily using internet resources. Split cut-offs to define the sensitivity or specificity with enhanced capability to identify and diagnose advanced rather than moderate fibrosis are a frequent characteristic of the tests. As a result, a typical method is to detect severe fibrosis using simple serological indicators, which might be an efficient approach to filter referrals from primary to secondary care. Additional risk-stratification technologies, such as transient elastography, can be used to undertake a more complete evaluation in this case (TE). Liver biopsy is a useful method for identifying NASH and fibrosis in people who have been recognised as being at risk of serious illness using non-invasive indicators (James, 2018).

Cirrhosis

For individuals with NASH cirrhosis, appropriate screening for HCC, esophageal varices, and other cirrhosis sequelae is necessary. Decompensation with ascites, variceal haemorrhage, or hepatic encephalopathy should require an early examination by a transplant institution [22].

Relation with other disease

(CVD) Cardiovascular diseases and (CKD) Chronic Kidney diseases

CVD and chronic renal disease are caused by NAFLD. Hepatic/peripheral insulin resistance, which promotes atherogenic dyslipidemia, may be caused by NAFLD, particularly its necro-inflammatory version (NASH). It produces a multitude of pro-inflammatory, thrombogenic, and vasoactive chemicals that contribute to the pathophysiology of cardiovascular and cardiac illnesses, as well as

CKD. Furthermore, obesity-related increases in fatty acid buildup in the heart/pericardium and kidney may have negative consequences, including structural and functional abnormalities of the kidney, myocardium, and vasculature. NAFLD is not only responsible for kidney and vascular/cardiac damage but, may also involves in the significant complications of CVD and CKD. Briefly, NAFLD directly accelerate development and progression of the vascular or cardiac problems through hepatic production of lipids, atherogenic lipoproteins, dys-glycaemia (i.e., increased hepatic glucose production), the establishment of hepatic/peripheral insulin resistance, as well as the release of a slew of potentially harmful mediators into the bloodstream (i.e., pro-inflammatory biomarkers, pro-oxidant molecules, and pro-coagulant and pro-fibro genic factors). NAFLD is the mediator of cardiac biomarkers which increases the pressure on heart and cause heart diseases. CRP (C-reactive protein); FGF-21 (fibroblast growth factor-21); HDL (low density lipoprotein cholesterol); LDL-C (high-density lipoprotein cholesterol); PAI-1 (plasminogen activator inhibitor-1); TNF (tumour necrosis factor) are some of the biomarkers [23].

Figure 5: Relation of NAFLD with CVD and CKD (Christopher., *et al*. 2015).

Unhealthy lifestyle and NAFLD

Overeating and a sedentary lifestyle are the causes of obesity and hepatic steatosis. Increased consumption of fructose, glucose, and saturated fat, as well as subclinical inflammation in the liver and adipose tissue, and insulin resistance in adipose tissue, the liver, and skeletal muscle, all contribute to hepatic de-novo lipogenesis and promote hepatic de-novo lipogenesis. Adipose

tissues increase the secretion of proinflammatory cytokines and dysregulated adipokines, resulting in increased lipid accumulation throughout the liver. Ceramide signalling is also linked to an increased risk of NAFLD. Gut dysbiosis is linked to fat buildup in the liver and the development of NASHIn the context of dysbiosis and a leaky gut, bacteria-derived compounds can promote adipose tissue inflammation, hepatic inflammation, and hepatic steatosis. Finally, a sedentary lifestyle can exacerbate NAFLD [24].

Figure 6: Impact of lifestyle on liver (Norbert., *et al*. 2018).

Relationship of diet with NAFLD

Macronutrients and NAFLD

Independent of energy intake, the inadequate macronutrient composition in a diet may be responsible for NAFLD/NASH. The buildup of triglycerides in the liver, which leads to insulin insensitivity and poor postprandial triglyceride metabolism, is exacerbated by macronutrients and animal proteins in excess. However, MUFA and PUFA-3 fats, as well as plant-based proteins and dietary fibre, may be advantageous to the liver [25].

Fats

Fat may be good or bad; it all depends on the quality of fat consumed. Fats must be used in moderation and should be of good quality. Types of fat in a diet include saturated fats, monounsaturated fats, polyunsaturated fat, trans-fat [25].

Saturated fat

SFAs only have single carbon-to-carbon bonds. Endoplasmic reticulum (ER) stress and hepatocyte damage may result. SFAs cause hypothalamus inflammation, which is linked to metabolic problems and the genesis of obesity. More than 10% of total energy from SFAs may promote insulin resistance, whereas less than 10% of total energy from SFAs lowers plasma TG levels and LDL; however, less than 7% of total energy from SFAs may not improve NASH and may even be harmful [11].

Saturated fat stimulates de novo lipogenesis and adipose tissue lipolysis, and the quantity of free fatty acids in the liver rises as a result of an increase in serum free fatty acids. NAFLD progresses owing to glutathione deficiency, which promotes oxidative stress. Unsaturated fat consumption may minimise lipolysis, limiting fat formation in the liver and, as a result, lowering the risk of NAFLD.

Intake of more than 10% of total energy from SFAs may impair insulin sensitivity, whereas intake of less than 10% of total energy from SFAs lowers plasma LDL and TG levels; however, intake of less than 7% of total energy from SFAs has no effect on NASH.

Monounsaturated fat

In the hydrocarbon of MUFAs, there is only one carbon to carbon double bond. MUFAs lower oxidised LDL, LDL cholesterol, TC, and TG levels while leaving HDL unchanged. MUFAs raise HDL levels while lowering blood sugar and blood pressure. VLDL triacylglycerol and VLDL cholesterol levels are lower in people who eat a diet high in MUFAs [11].

Patients with NAFLD benefit from MUFAs. Fatty liver is improved by consuming extra virgin olive oil. Furthermore, as compared to a diet heavy in carbs and fibre, a MUFA-rich iso-caloric diet resulted in a considerable reduction in liver fat. Furthermore, in individuals with NAFLD, consuming 20 g/day on hypocaloric diets for 12 weeks reduced the degree of fatty liver [25].

Furthermore, in NAFLD men and women, a diet containing 20% MUFAs as an energy source of total daily caloric intake enhances fatty acid oxidation through increased PPARs activity and lowers lipogenesis. A high MUFA consumption significantly lowered hepatic fat accumulation in T2DM individuals, regardless of physical activity. A MUFA-rich diet might help with NAFLD therapy in the liver [26].

Polyunsaturated fat

In their hydrocarbon structure, PUFAs feature two or more carbon to carbon double bonds. PUFAs are advantageous for individuals with NAFLD, since a four-week consumption of 50 grammes of rapeseed/canola oil improved TC, LDL, and liver enzymes. Omega-3 (ω-3) and omega-6 (ω-6) are key PUFAs that have a role in the development of NAFLD. While omega-3 fatty acids are good, omega-6 fatty acids should be avoided since they raise inflammatory indicators. As a result, the suggested ω-3 to ω-6 ratio is 1: 1 to 1: 4. Gene expression, hepatic lipid metabolism, fatty acid oxidation, and decreased expression of pro-inflammatory genes are all affected by omega-3 fatty acids (Rahim., *et al*. 2019).

Docosahexaenoic acid (DHA), linolenic acid (plant oil), and eicosapentaenoic acid (EPA) are examples of omega-3 fatty acids (EPA). -3 fatty acids reduce hepatic steatosis and inflammatory indicators while also improving insulin resistance and cardiovascular disease. Similarly, NAFLD is caused by a decrease in dietary -3 fatty acids and an increase in plasma and hepatic SFAs; hence, lowering SFA intake while increasing -3 fatty acid intake slows NAFLD progression in children. -3 fatty acids enhance markers of NAFLD and the intestinal microbiome. Omega 3 improves insulin sensitivity and hepatic echogenicity in children with NAFLD [27].

Trans fat

Trans-fatty acids are found naturally in foods and have a role in the development of NAFLD. Trans-fat contains a variety of isomers that control human metabolism either directly or indirectly. Cis-9, trans-11 conjugated linoleic acid, and trans-11 oleic acid are the most common trans-fats found in dairy products, and they have no deleterious impact on lipoprotein levels. However, some trans fats, such as trans-10 and cis-12 conjugated linoleic acid, have a beneficial impact on inflammatory indicators, resulting in a drop in HDL and an increase in harmful LDL and total cholesterol. Hydrogenated oils are the most common source of trans-fat. Patients with NAFLD should avoid eating highly processed meals that contain a lot of trans fat.

Protein

Patients with NAFLD should consume a moderate quantity of protein since excessive protein consumption can lead to problems such as intrarenal capillary hypertension, glomerular sclerosis, and eventually renal impairment. Total restriction of protein is not

suggested because its deficiency may be responsible for hepatic steatosis and NASH. Adequate intake of protein along with low carbohydrates diet improve liver steatosis. Animal protein aids in the regeneration of hepatocytes and provides some important amino acids that help to prevent fat buildup in the liver. Moderate intake of protein has no bad effects and involve in the deduction of fat contents in patients with NAFLD [28].

A moderate protein intake with low carbohydrate intake has showed to increase HDL cholesterol and decrease LDL and total cholesterol, AST, TG, GGT, AP and fasting blood glucose, beneficial for NAFLD patients [29]. Soy protein is also advantageous because it lowers plasma cholesterol levels and fat buildup in the body, particularly in the liver. It also lowers TDG buildup in the liver, improves insulin sensitivity, and has antioxidant properties.

Carbohydrates

Reduction of total calories is very important to avoid NAFLD and its associated diseases such as diabetes, obesity. As a result, a high carbohydrate consumption is cause for worry since it promotes the formation of free fatty acids (FFA) in the liver. Excess carbs intake causes the liver to produce 30% more free fatty acids in individuals with NAFLD, although it is only responsible for 5% of free fatty acid generation in healthy people. Low carbohydrates intake leads to reduce weight, intrahepatic TGs contents and lipid or other metabolic profile because low carbohydrate's intake increases HDL cholesterol and decreases LDL and total cholesterol. Thus, reduction in total carbohydrates intake is recommended for NAFLD but reduction for longer period may have adverse side effects. The intake of low carbohydrates containing foods over an extended period like 1 year or more may stimulates the pathogenesis of NAFLD and thus, insulin insensitivity and increases total cholesterol and total LDL cholesterol in patients suffering from NAFLD. Composition of low carbohydrate diet causes weight loss, only if it is consumed for 6-8 months but no significant change in weight reduction occurs when such diet consumes for an extended period such as 1 or 2 years.

Fructose

Fructose, a sweetener, can cause serious alterations or problems in metabolic functions of toddlers suffering from NAFLD as compared to toddlers without the disease because this sweeter is mostly present in jams, jellies, juices and candies. Fructose intake can cause insulin resistance and thus, may be responsible for NAFLD progression. Intake of fructose increases the lipogenesis and TG synthesis and thus cause hepatic steatosis. Furthermore, excess intake of fructose inhibits the secretion of leptin (a fat deriver anorexigenic hormone) and thus, the patients become fail to achieve satiety. By up-regulating the expression of the NF-kB gene and down-regulating the expression/activity of PPAR and hepatic lipid oxidation, fructose consumption in individuals with NAFLD enhances oxidative stress, which leads to hepatic steatosis and fibrosis. Fructose intake leads to down regulation of metabolic pathways especially glycolysis and lipogenesis by interfering with transcription factors and genetic make-upAccording to one study, consuming 3 grammes of fructose per kilogramme of body weight per day causes fat storage in the liver, which raises plasma triglyceride levels and makes the patient with NAFLD insulin resistant. As a result, people with NAFLD should consume less fructose.

Fiber and glycemic index diet

There are two types of fiber: soluble and insoluble fibers. Pectin and gums are soluble fibers. Fruits are the natural source of pectin. Oats, bean, barley, lentil, peas, chickpea are the natural sources of gums. Cellulose, is a fiber that does not dissolve in water, is present in wheat, hemicellulose which is present in grains and lignin which is present in vegetables. Insoluble fiber promotes the feeling of fullness (satiety) and thus, helpful in the reduction for total caloric intake. On the other hand, soluble fiber slows down the stomach emptying rate and reduces the uptake of glucose and cholesterol by the cells of the body especially hepatocytes. Thus, soluble fiber as in oats decreases the total triglycerides content. One study showed that low glycemic index foods and high fiber containing foods might be beneficial for patients with impaired insulin sensitivity and thus beneficial for patients with NAFLD. Consumption of fiber-rich diets decreases plasma free fatty acids (TG levels) and insulin levels following subsequent meals in both males and females. Dietary changes for individuals with insulin resistance, NASH, and other hepatic problems include fiber-rich meals, fermentable starch, and low-GI carbs. In individuals with NAFLD, these dietary changes assist to maintain blood glucose, insulin, and FFA levels [30].

Figure 7: (Rahim., *et al*. 2019).

Micronutrients and NAFLD

Micronutrients vary from macronutrients, since they are only needed in very small quantities by the body. Micronutrients such as vitamins and minerals are vital in avoiding the development and development of NAFLD. Zn, Cu, iron, Se, Mg, vitamin A, vitamin D, vitamin E, vitamin C and carotenoids are micronutrients which have protective role in the progression of the disease because they have antioxidant, immune-modulatory and lipo-protective properties. Thus, these micronutrients reduce oxidative stress in the liver, increase high density lipoproteins, cholesterol, decrease low density lipoproteins and total cholesterol or triglycerides content and thus prevents the deposition of fat in the body. It has been shown that blood levels of Zn, Cu, vitamin A, vitamin C, vitamin D, vitamin E, and carotenoids are lowered in individuals with NAFLD, resulting in weakened immunity and antioxidant activity, both of which have negative impacts on the course of NAFLD. Among vitamins, fat soluble vitamins have direct relationship with NAFLD, and their excess intake led to accumulation of fat in the body. So. Fat soluble vitamins must be consumed in adequate amounts because their limited intake is also associated with the severity of NAFLD. Among fat-soluble vitamins, A, E and C are significant [31].

A dominant antioxidant, Vitamin E leads to reduced oxidative stress in the body which reduces the transaminase level and reduces liver lobular inflammation, thus reduces liver fibrosis and hepatic steatosis. But excess intake of vitamin E has adverse effects as well such as deposition of fat, several cancer or hemorrhagic stroke (Genoveva., *et al*. 2019). Adequate intake of Vitamin A is considered to be beneficial for a patient with NAFLD. Vitamin C also acts an antioxidant reduced oxidative stress and hepatic steatosis. Furthermore, vitamin C also reduces LDL and total cholesterol, thus provides protection against fatty liver. Again, vitamin C also used in an adequate amount according to recommendations for NAFLD patients because excess may lead to toxicity and more complications. Vitamin D involves in genes expression especially those genes that are involved in hepatocytes and glucose and fat metabolism. Thus, Vitamin D deficiency causes NAFLD though the activation of TLRs which lead to liver inflammation, oxidative stress and insulin resistance, excess intake may be harmful [32]. In short, Vitamins along with minerals are beneficial in NAFLD. They must be used in mixture and in adequate amounts [33].

Lifestyle modification

Because obesity and insulin resistance are risk factors for NAFLD, it is critical for people with NAFLD who are obese to reduce weight. But fast weight reduction is not a good idea it may cause inflammation and fibrosis. There is a noticeable improvement in patients of steatosis and NASH by reducing almost 7–10 percent weight in a year. This weight reduction is preferred to be done by lifestyle changes as doing some moderate to vigorous exercises and by diet. For which dietary counseling of patient must be done properly [34]. There are different healthy approaches which include dietary habits alteration, consistent physical exercise, and slow weight reduction for patients with NAFLD. The first and most important step in the treatment of NAFLD is to change one's lifestyle [35].

Diet modification

Diet modification includes adequate intake of fruits and vegetables, low intake of fructose, saturated fatty acids, trans-fats, and total fats. Adequate consumption of fruits and vegetables helps to reduce oxidative stress in patens with NAFLD. Fruits and vegetables contain biologically active substances like phenolic compounds and vitamins which are naturally antioxidant are very helpful. In individuals with NAFLD, increased dietary fructose consumption is the leading cause of obesity and insulin resistance. Foods high in monounsaturated fatty acids and/or omega-3 fatty acids have been reported to reduce the risk of liver steatosis and insulin resistance in NAFLD patients. It has been shown that a lack of dietary omega-3 fatty acids combined with an increase in dietary omega-6 fatty acid consumption raises the risk of developing NAFLD. Hepato-protective benefits of coffee like anti-oxidative, anti-inflammatory, anti-fibrotic effect, and chemo preventive which has some significant effect with chronic liver disease. Behavioral, lifestyle and dietary modifications have significant importance for the management of NAFLD [36].

Hypocaloric diets (a diet contains less caloric energy than the normal) can reduce hepatic triglycerides contents and improve markers of insulin sensitivity [37]. It is not known about the best diet to treat NAFLD. A calorie limited plan (600 Kcal just under a person requires to stay at the very same weight) must be prescribed before more proof is possible, promising to reduce half to one kilograms in 7 days before the weight goal is met. To stop saturated fats, basic carbs and sweetened beverages, patients of NAFLD must be told. Progressive fibrosis in mouse models is consistent with a 'fast food diet'. A Mediterranean diet showed to decrease liver steatosis and increase sensitivity to insulin in persons with no diabetes but NAFLD, relative to a meal low fat and high carbohydrates. In these people Nutritional treatment of one year/ twelve

months is more successful as compared to the routine treatment to lose 5.6 kg of weight as compared to 0.6 kilograms. Previous findings have found that decreased steatosis, hepatocellular damage, and hepatic inflammation have been correlated with >7 percent and >9 percent reduction of body weight [38].

Physical activity/exercise

People with NAFLD engage in less physical activity than their healthy counterparts, and lower levels of steatosis are connected to greater levels of habitual physical activity. Physical activity enhances muscle cell insulin sensitivity and alters one of the key pathophysiological pathways that causes NAFLD (insulin resistance). NAFLD therapy exercise remains uncertain, low intensity workout, training of high intensity and strength workouts have demonstrated increase in the hepatic enzymes and decrease in fat of the liver, without loss in weight, but histology results remain uncertain. Both NAFLD patients should also be cheered to improve their activity routine and to perform daily exercise. One solution, before more data is available, is to prescribe 30 minutes of moderate workout five days per week. However, in practice, a large proportion of NAFLD patients do not agree with these guidelines. The use of pedometers in such patients can be effective and increasing their daily step count to greater than 10 000 steps per day are also advised by the consultant [38].

Figure 8: Impact of exercise on body (Kate., *et al*. 2019).

Weight reduction

The most important threat for NAFLD is obesity so weight loss is primary action to improve this condition to reduce liver fat, improve insulin sensitivity, proinflammatory cytokine secretion, preservation of normal heart function and adipose tissue inflammation. So, 10% weight loss in patient is necessary to improve hepatic histology, cardiovascular risk profile, steatosis and also decrease in liver inflammation, and hepatocellular damage. Probiotic yoghurt is good choice for NAFLD. While a weight reduction of seven to ten percent is considered modest, larger weight reduction results in better improvement in patients with obesity and overweight who have NASH. As a result, weight reduction can improve the following conditions: diabetes/ cardiovascular risk, liver disease to its previous state, NASH resolution, and fibrosis improvement by at least one stage.

The most preferred method of weight loss is modest exercise as aerobic exercise of half hour because activity enhanced by aerobic exercises, antioxidant enzymes expression's also increase and facilitate deduction of dichlorodiphenyltrichloroethane (DDT) that induces oxidative damage in better oxygen accessibility condition (Kate., *et al*. 2019).

Tips how to encourage and support patient for lifestyle modification

- Educate the patient about NAFLD and how it may be reversed with a change in lifestyle; additionally, clarify any misconceptions about alcohol being the cause of NAFLD.
- Describe how variations in body weight are related to energy balance.
- Set a weight-loss goal.
- Make recommendations for suitable interventions e.g., portion control, reduced snacking, regular meal patterns.
- Counseling the patient includes the usage of self- monitoring/ self- regulation tools e.g.
- Taking regular weight measurements. By using a diary, smartphone app or internet website count daily caloric intake to track food intake.
- Pedometers/activity trackers usage.
- Read nutrition information labels to compare and pick healthier alternatives.

Liver transplantation

Cirrhosis can advance to the point where it requires liver transplantation if it is compounded with hepatic failure or HCC. Currently, roughly 3% of all transplants in North America are performed owing to advanced NAFLD; however, those with cryptogenic cirrhosis or those who are unable to undergo transplantation due to comorbidities linked to insulin resistance are excluded from this scenario. After transplantation, steatosis can recur (in sixty to one hundred percent of cases), whereas steatohepatitis can arise in one-third of patients [39].

Conclusion

NAFLD is a metabolic liver disorder caused by the accumulation of TGs in more than 5% of hepatocytes. NAFLD includes anything from basic steatosis to non-alcoholic steatohepatitis (NASH), which can result in liver fibrosis, cirrhosis, and hepatocellular cancer. Because of underlying variables like as insulin resistance, obesity, and many others, overall mortality appears to be increased in NAFLD patients. NAFLD development is aided by high-fat, high-carbohydrate diets. Dietary changes and exercise may help to reverse the clinical manifestations of NAFLD and improve quality of life. NAFLD pathogenesis is prevented by vitamin C, vitamin E, vitamin D, and polyphenols. As a result of poor care, NAFLD progresses to the point where liver transplantation is the only choice.

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