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Research Article

Silent Disease of The Current Scenario – MASH (Metabolic Dysfunction Associated Steatohepatitis)

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ABSTRACT:
Metabolic Dysfunction Associated Steato Hepatitis (MASH) is emerging as the top most liver disease in today's scenario because of the discouraging dietary pattern & poor lifestyle behaviour . MASH is a fatty liver disease and difficult to diagnose because of the symptoms being silent. Obesity, type 2 diabetes, metabolic syndrome and high fat levels in the blood are the common risk factors. Fatigue, unexplained weight loss, general weakness and discomfort in the right hypochondria are the non specific symptoms of MASH. The worst Complication of MASH is cirrhosis of the liver. Cirrhosis can lead onto liver failure & sometimes to liver cancer. Liver function tests, lipid profile, fasting & postprandial blood glucose estimation, abdominal ultrasound, Computed Tomography(CT) scan and Magnetic Resonance Elastography (MRE) will enable to clinch the diagnosis of MASH. Body weight reduction, proper dietary and lifestyle plan, regular exercise, Yoga and drinking coffee will chase the disease away from us. Controlling the blood sugar, quitting smoking and alcohol, regular treatment of health conditions of Hyperlipidaemia and hormonal disorders, vaccinations against Hepatitis A and B, Covid -19, Flu, Pneumococcal infections will undoubtedly enable our population to be free from MASH and its deleterious effects. Resmetirom ,SNP-630, SNP-630-MS and anti oxidants like Vitamin E, selenium, and betaine are therapeutic drugs used in MASH with promising results.Let the Mystery disease MASH become a Maya (Illusion) and a myth by the effective practice of the aforementioned conglomerated preventive measures.

Keywords: Metabolic Dysfunction Associated Steatohepatitis, Liver, Silent Disease, Life Style Changes, Anti oxidant

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Introduction / Background:

Today's Modern era of rat race world is hastening the emergence of new diseases in the silent mode. Symptoms Free Diseases are on the rise and culminating in drastic complications all of a sudden. Earlier the diagnosis and treatment is becoming a remote possibility for these symptomless diseases. Public education and awareness about these silent killers are the need of the hour to keep these diseases at bay. MASH(Metabolic Dysfunction Associated Steatohepatitis) is emerging as the topmost liver disease in today's scenario because of the discouraging dietary pattern and poor lifestyle behavior in day to day life. Metabolic dysfunction-associated steatohepatitis or MASH is a silent liver disease and mimics alcoholic liver disease, but occurs in people who drink little or no alcohol. Metabolic dysfunction associated steatohepatitis (MASH) initially known as Non alcoholic steatohepatitis (NASH) is a fatty liver disease. It is defined as the severe form of Metabolic dysfunction-Associated Steatotic Liver Disease (MASLD), also called as Nonalcoholic Fatty Liver Disease (NAFLD). MASH is difficult to diagnose because of the symptoms being silent or nonspecific. [1,2,3]

MASLD is a benign condition characterized by accumulation of fat in the liver. MASLD has no symptoms of liver disease. About 20% of people with MASLD manifest MASH. MASLD includes a spectrum of liver abnormalities, from metabolic dysfunction–associated steatotic liver (MASL, simple steatosis) to Metabolic dysfunction-associated steatohepatitis (MASH). All these diseases starts with infiltration of fat in the liver (hepatic steatosis). A liver still be fatty without abnormalities in the liver functions (MASL), but by various factors and insults to the liver, it can result in steatohepatitis (MASH), a condition in which steatosis is combined with inflammation and later develop fibrosis.[1,2,3] Steatosis is responsible for the virulent nature of MASH. Infiltration of fat in the liver leads to the increased levels of hepatocyte injury inducers which triggers inflammatory responses and immune cell infiltration into the liver. Fibrosis of the liver sets in through the activation of hepatic stellate cells (HSCs), which are the ultimate sites of fibrogenesis . C-X-C motif chemokine ligand 10 (CXCL10), an important inflammatory mediator, hastens MASH development through the mechanism of impairing autophagy. [4,5]

MASH is becoming the major cause of hepatocellular carcinoma (HCC) in liver transplant candidates. MASH is also the predominant cause of age-related liver cancer deaths globally. Immediate intervention with awareness are mandatory to address the increasing prevalence and major risks associated with MASH. People with MASH often have no clear symptoms, and it is diagnosed during routine blood tests, abdominal imaging or liver biopsy. MASH can occur even in kids but predominantly it attacks the 40 to 60 age group females than the males. [6]

MASH is commonly associated with the risk factors such as obesity, type 2 diabetes, metabolic syndrome and high fat levels in the blood. Usually MASH presents with no symptoms. Other factors as possible candidates of MASH are Insulin resistance,release of toxic inflammatory proteins by fat cells (cytokines) and oxidative stress inside the liver cells. If the MASH progresses, the symptoms indicative of the inflammation and damage done to the liver cells starts appearing in the due course. MASH is also reported in thyroid, pituitary, gonadal disorders, polycystic ovarian syndrome, consistent elevation of liver enzymes, advancing age etc. Majority of these disorders predict the outcome of MASH.

The Common MASH symptoms are tiredness,unexplained sudden weight loss, general weakness and discomfort in the right hypochondria. The reasons attributed for some people getting MASH and experience symptoms are due to genetics, family history and environmental factors.MASH is most commonly seen in the age group of 40 to 60 years old. MASH do occur in people who have none of the aforementioned risk factors.[1,2,3]

The progression of MASH severity can resemble the symptoms of cirrhosis. Jaundice,bruising and bleeding spots in the skin, ascites, pedal edema, enlargement of liver, dilatation of spider like blood vessels under the skin, esophageal varices resulting in blood vomiting, persistent itching of the body (pruritus), mental confusion, drowsiness, slurring of speech and finally leads to Hepatic coma.The drastic complication of MASH is cirrhosis of the liver. Cirrhosis can ultimately results in liver failure and sometimes to liver cancer. MASH can also lead on to the increased risk of coronary artery disease and type 2 diabetes mellitus that are supposed to be the main risk factors for developing Metabolic dysfunction-Associated Steatohepatitis and vice versa.[1,2,3]

Liver function tests for evidence of liver inflammation depicted by abnormal liver enzymes, serum lipid profile, fasting and postprandial blood glucose estimation, abdominal Ultrasound, Computed Tomography(CT) scan, Magnetic resonance Elastography (MRE) combines ultrasound and MRI imaging to create a visual map of the extent of the liver fibrosis. Liver biopsy is the confirmative test.Cytokeratin 18 fragments M30 (CK-18), a marker of hepatocyte apoptosis is an extensively evaluated biomarker for the diagnosis of MASH. Moderate accuracy is the drawback of the CK-18 Biomarker. The dual combination of CK-18 with the liver-derived hormone-fibroblast growth factor 21 (FGF21) will improve the accuracy of MASH diagnosis. It was recently shown that C-X-C motif chemokine ligand 10 (CXCL10), a key inflammatory mediator promotes MASH development through impairing autophagy. [7,8,9]

The usage of drug therapies in combination with lifestyle modifications are essential. Till date, the thyroid hormone receptor beta (THRβ) agonist resmetirom (MGL-3196) approved by the Food and Drug Administration (FDA) in 2024 represents the

first-ever selective treatment for MASH. At present many clinical trials are underway, increasing the possibility of more therapeutic regimens. The drug Resmetirom (Rezdiffra) is considered to treat MASH in combination with lifestyle modifications aimed at diet and exercise. MASH patients may require medications to control high blood sugar or high cholesterol and high triglycerides. SNP-630, a new promising synthetic molecule with varied mechanisms of action, and a combination of two of its active metabolites (SNP-630-MS) inhibit the CYP2E1 expression to prevent Reactive Oxygen Species (ROS) generation, thereby decreasing hepatic triglycerides and chemokine levels.[10]

Anti oxidants like Vitamin E, selenium, and betaine act by reducing the oxidative stress that increase inside the liver in patients with MASH. An experimental clinical trial to treat MASH is the use of newer anti-diabetic medications even in normal persons(non- diabetic).[11] Most patients with MASH have insulin resistance, indicating that the insulin present in the bloodstream is less effective in controlling blood glucose and fatty acids in the blood than it is for the normal individuals who do not have MASH. The newer anti-diabetic medications sensitize the body to insulin and may aid in reducing liver injury in patients with MASH. Studies of these medications including metformin, rosiglitazone, and pioglitazone are under clinical trials.[12,13,14,15]

Reduction of body weight can result in reduced fat levels and inflammation in the liver. A reduction of 3% to 5% of the body weight can cut fat from the liver and also to decrease the inflammation and scarring due to MASH. Reduction of 7% to 10% is mandatory.[16] Slow and steady reduction of body weight is the best. It is vital to monitor the blood sugar level in diabetic patients periodically and to take medications to control the blood sugar levels. A balanced healthy diet low in saturated fats, avoidance of trans fat and rich in monosaturated fats have to be planned. Apt is to practice Mediterranean diet with fruits, vegetables, whole grains and lean proteins. Regular exercise and Yoga helps in managing the weight as well as stress and anxiety which can affect liver health. Gardening, brisk walk, jogging, swimming, dancing and high or low-intensity aerobic exercises for 30 to 60 minutes per day during most days of the week will result in a favourable outcome. [1,2,3]

Lifestyle modifications such as diet, exercise and Yoga can arrest the progression of MASH and in few cases can reverse the liver damage in the early detection of the disease. Drinking coffee daily can help prevent liver fibrosis due to metabolic dysfunction-associated steatohepatitis. More than two cups per day is really beneficial. Exercising every day, eating nutrient-rich foods, controlling the blood sugar, quitting smoking and alcohol, regular treatment of health conditions of Hyperlipidaemia and hormonal disorders, vaccinating against Hepatitis A and B, Covid -19, Flu, Pneumococcal infections will certainly prevent MASH. [1,2,3,17]

CONCLUSION:

MASH is occupying the pinnacle of the silent (symptom less) diseases among the present and the future generations to come. Prevention with awareness is the golden key for keeping this disease at distance rather detecting & treating the same. Proper and healthy dietary practice as daily routine coupled with scientific lifestyle modifications on permanent basis will help the society at large to chase the MASH & remain non existent in the future. MASH Formerly called as NASH if left undetected and not treated because of its silent nature can lead onto the serious health complications resulting in liver cirrhosis, liver cancers, hepatic failure and death.To save the future generation from this (quiet) lifestyle disease MASH let us advocate nutritious diet with above mentioned dos and don'ts and regular exercise and Yoga.

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