

## LIFESTYLE RECOMMENDATIONS FOR PREVENTION AND TREATMENT OF METABOLIC SYNDROME DIET -A REVIEW

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### ABSTRACT

Modern human lifestyle has led to the significant reduction in physical activity, adequate exercise and balanced diet consumption. All these factors are the chief cause of worldwide epidemic of obesity and non-alcoholic fatty liver disease (NAFLD). NAFLD is not only associated with liver-related morbidity and mortality, but also with an increased risk of developing cardiovascular disease (CVDs) and Type 2 diabetes mellitus (T2DM). Obesity and NAFLD associated pathological features are together known as metabolic syndrome (MetS). MetS is considered as a primary risk factor for atherosclerotic complications and deaths. Therefore, MetS become major health problem of 21<sup>st</sup> century and the preventive strategies are very essential to cure this syndrome. The very important preventive methods include lifestyle management programs like regular exercise regimen and healthy diets which have been shown to be a beneficial option on overall metabolism of the body. The pathological hallmark of NAFLD is also linked to dyslipidemia, which is characterized by hypertriglyceridemia, low HDL-C levels, and high LDL-C levels. Lowering the triglycerides and Low-Density Lipoprotein (LDLs) levels thereby increasing the High-Density Lipoprotein (HDL) in the serum has been reported to reduce the risk of CVDs in NAFLD patients. Hence, it is important to identify early metabolic variations and to prevent these diseases and their advancement. This article aims to provide knowledge concerning the role of healthy lifestyle management, proper nutrition and adequate physical activities which have beneficial effects on human health and longevity.

**KEYWORDS:** Exercise, obesity, metabolism, type 2 diabetes, nutrition.

### INTRODUCTION

The emergence of chronic diseases such as coronary heart disease, cancer, arthritis, diabetes and obesity are becoming the leading cause of death globally.<sup>[1]</sup> The changing pattern of lifestyle is an important reason for the development of chronic diseases.<sup>[2]</sup> The incidence of overweight and obesity has amplified from 28.8% to 36.9%, and from 29.8% to 38%, respectively. Obesity gives rise to a spectrum of liver related very common abnormalities like NAFLD. NAFLD ranges from simple steatosis to non-alcoholic steatohepatitis (NASH), which may lead to cirrhosis and Hepatocellular Carcinoma (HCC).<sup>[3]</sup> Oxidative stress leads to lipid peroxidation, DNA and protein damage and eventually leads to cell death. The di-aldehyde produced as a by-product of lipid peroxidation infiltrates the inflammatory cells into the liver and causes production of collagen and fibrosis initiation.<sup>[4]</sup> Studies by Jakicic et al.<sup>[5]</sup> have shown that physical exercise and energy expenditure through various other activities have a positive impact on long term weight control. In order to prevent the morbidity and mortality due to obesity related -T2DM and

cardiovascular disease, mass intervention programs should be strategized on increased physical activity and healthier food patterns. The incidence of hypertension, stroke and CVDs are increased in obese population. The accumulation of fat cells produces a variety of metabolic, hormonal and inflammatory products which cause harm to liver, heart, pancreas, muscle and arteries.<sup>[6]</sup> The adipocytes behave as immune cells and secretes proinflammatory adipokines and cytokines abundantly. All these factors contribute to insulin resistance.<sup>[7]</sup> Many studies have suggested that, there is a strong relation between visceral adiposity, hyperinsulinemia, the MetS are linked to different types of cancer. The abundance of inflammatory cells in visceral adipose tissue triggers insulin resistance and inflammation and increased risk of tumor progression.<sup>[8]</sup>

Chronic inflammatory state is a key feature of abdominal obesity, MetS, T2DM and CVD. In all these disease conditions, there is an increased level of cytokines in the circulation, which are responsible in controlling many functions of the body.<sup>[9]</sup> Exposure to high free fatty acid (FFA) concentrations is a common moderator which is a

consequence of an expanded intra-abdominal fat mass. Weight reduction around 5-10% with proper diet and exercise significantly lowers the risk of MetS, CVDs and T2DM.<sup>[10]</sup> Analysis by Yung *et al.*, have demonstrated that exercise and physical activity favorably modulate the endothelial function, dilatation of the aorta and reduce arterial stiffness of the heart.

### Nutrition

Nutrition is an environmental factor which plays a major role in health and disease.<sup>[11]</sup> Nutrients have the capacity to regulate the activity of many metabolic enzymes and regulates various gene expression by epigenetic modifications. Hawley *et al.*, 2020.<sup>[12]</sup> have reported that modifications in the dietary patterns reduce the impact on incidence of metabolic diseases. An increased consumption of high Glycemic Index (GI) diet causes insulin resistance and leads to the development of T2DM in persons with metabolic syndrome. On the other hand, low-GI and abundant in fiber diet decrease insulin resistance and the risk of developing type 2 diabetes mellitus.<sup>[13]</sup> Intake of fresh fruits and vegetables and avoiding high sugary foods, high salt and sweetened food have negative consequence on healthy life. Therefore, individuals should be encouraged to make healthier food choices to combat current health problems.<sup>[14]</sup>

### Metabolic Syndrome (Mets)

Metabolic syndrome is also called as 'insulin resistance syndrome', 'death quartet' or 'syndrome X. The prevalence of MetS is greater among adult population because of sedentary lifestyle and obesity.<sup>[15]</sup> Approximately 39% of the adult population globally are overweight and more than 13% are obese. Consumption of saturated fatty acids (SFAs) are injurious to health, while monounsaturated (MUFAs) and polyunsaturated fatty acids (PUFAs) are beneficial to improve human health. Adjunct treatments such as pharmaceuticals, surgery and dietary supplement counteracts the adverse effects MetS.<sup>[16]</sup>

### Obesity

According to the World Health Organization, there is an increase in the prevalence of obesity among adults as well as children worldwide.<sup>[17]</sup> Obesity is closely associated with many chronic diseases and contributes to higher rate of morbidity and mortality.<sup>[18]</sup> The three important diseases associated with obesity are cardiovascular disease, Type 2 Diabetes and NAFLD. The accumulation of visceral adipose tissue is also connected with metabolic syndrome.<sup>[19]</sup> The adipokines released from adipocytes cause oxidative stress by the production of reactive oxygen species. The activity of endogenous antioxidant enzymes Superoxide dismutase (SOD), Catalase (CAT) and Glutathione peroxidase (GPx) are down regulated. All these factors indulge in the progression of atherosclerosis and NAFLD.<sup>[20]</sup>

### Type 2 Diabetes

Type 2 diabetes mellitus (T2DM) is a growing global

health problem currently affecting over 170 million people throughout the world and, hypothetically, over 365 million in the year 2030. Very commonly known features and characteristics of T2DM pathogenesis includes Insulin resistance and decreased insulin production along with increased blood glucose level. It is closely connected to the epidemic of obesity.<sup>[21]</sup> The improper functioning of protein IRS-2, PKB, the FOXO protein and p85 regulatory subunit of PI-3 kinase results in insulin resistance.<sup>[22]</sup> Investigations by Hussain *et al.*<sup>[23]</sup> has revealed that a higher FFA level serves as a marker for prolonged development of glucose intolerance and progression to T2DM. Variation in transcription by FFA through their binding to peroxisome proliferator-activated receptors is responsible for compromised glucose metabolism.<sup>[24]</sup> T2DM patients with MetS is associated with a substantial reduction of pro-inflammatory markers such as C-reactive protein and anti-inflammatory markers like adiponectin. The pharmacological strategies can be used to reduce the inflammation.<sup>[25]</sup>

**Cardiovascular Diseases:** Cardiovascular diseases (CVD) are the leading cause of death all over the world. The risk factors for CVDs include hypertension, smoking, type 2 diabetes mellitus, overweight, hyperlipidemia, sedentary lifestyle and family history. Prolonged obesity leads to elevated expression and secretion of pro-inflammatory cytokines (TNF- $\alpha$ , IL-1, IL-4, IL-6 and IL-18) and adipokines (leptin, resistin and visfatin) from adipose tissue and reduced expression of anti-inflammatory cytokines (IL-18 binding protein (IL-18BP), Membrane-bound IL-1 receptor type 2 (mIL-1RII)) and adipokines (adiponectin), resulting in the development of a prolonged inflammatory state. Thus, imbalance in adipokine difference is believed to be a basic event in promoting the systemic metabolic dysfunction and CVD.<sup>[26]</sup> Reducing the body fat compensates the risk of development and progression of CVDs. Physical activity and exercise exert a significant effect on patients with MetS, insulin sensitivity and atherosclerosis.<sup>[27]</sup> Healthy lifestyle management like balanced diet, smoking status, alcohol consumption, and physical activity plays a paramount role in the prevention of CVDs.<sup>[28]</sup>

### NaflD

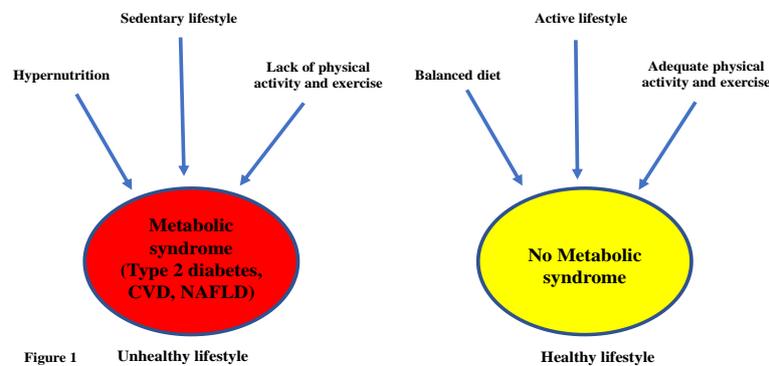
Nonalcoholic fatty liver disease (NAFLD) also known as hepatic steatosis, is one of the most diagnosed chronic liver diseases in the world. It occurs when there is liver fat deposition in the absence of excessive alcohol consumption. NAFLD is strongly related with T2DM, obesity and cardiovascular diseases begins with the accumulation of intrahepatic triacylglycerides.<sup>[29]</sup> There are no approved drugs available for the treatment of NAFLD and alcoholic liver disease (ALD) till date.<sup>[30]</sup> The clinical recommendation is also supporting the lifestyle modifications which include decreased intake of total fat, saturated fatty acids, trans fatty acids and fructose. In contrast, the use of polyunsaturated fatty

acids and monounsaturated fatty acids is advised to reduce the risk of NAFLD progression.<sup>[31]</sup> Routine exercise has also been demonstrated to reduce the prevalence of NAFLD.<sup>[32]</sup>

### Lifestyle Modifications

Lifestyle modifications and dietary interventions for weight reduction through regular practice of exercise have been shown to effectively decrease the visceral and

liver fat.<sup>[33]</sup> Reduction in the energy intake and proper energy expenditure can have beneficial effects to reduce weight and improve obesity and diabetes associated health complications.<sup>[5]</sup> The investigations by Annesi & Unruh *et al.*<sup>[34]</sup> revealed that, regular exercise not only play a vital role in weight reduction but also helps to improve mood changes, body image, self-efficacy, self-esteem among obese individuals.



**Figure 1: Differences between healthy and unhealthy life style and their association with Metabolic syndrome.**

### CONCLUSION

All these elegant studies strongly suggest that sedentary lifestyle and western dietary habit increases the risk of metabolic syndrome. Hypernutrition increases the obesity and type 2 diabetes and long-term progression of obesity and type 2 diabetes will lead to NAFLD and CVD. Healthy and harmonious dietary habit and with proper lifestyle plays a major beneficial role in controlling overall health and longevity of an individual.

### REFERENCES

1. Prasad S, Sung B, Aggarwal BB. Age-associated chronic diseases require age-old medicine: role of chronic inflammation. *Preventive medicine*, 2012; 54: S29-37.
2. Gonzalez K, Fuentes J, Marquez JL. Physical Inactivity, Sedentary Behavior and Chronic Diseases. *Korean journal of family medicine*, 2017; 38(3): 111-5.
3. Friedman SL, Neuschwander-Tetri BA, Rinella M, Sanyal AJ. Mechanisms of NAFLD development and therapeutic strategies. *Nature medicine*, 2018; 24(7): 908-22.
4. Moore JB. Non-alcoholic fatty liver disease: the hepatic consequence of obesity and the metabolic syndrome. *The Proceedings of the Nutrition Society*, 2010; 69(2): 211-20.
5. Jakicic JM, Otto AD. Treatment and prevention of obesity: what is the role of exercise? *Nutrition reviews*, 2006; 64(2 Pt 2): S57-61.
6. Bray GA, Kim KK, Wilding JPH, World Obesity F. Obesity: a chronic relapsing progressive disease process. A position statement of the World Obesity Federation. *Obesity reviews: an official journal of the International Association for the Study of Obesity*, 2017; 18(7): 715-23.
7. Monteiro R, Azevedo I. Chronic inflammation in obesity and the metabolic syndrome. *Mediators of inflammation*, 2010; 2010.
8. Doyle SL, Donohoe CL, Lysaght J, Reynolds JV. Symposium 3: Obesity-related cancers Visceral obesity, metabolic syndrome, insulin resistance and cancer. *Proceedings of the Nutrition Society*, 2012; 71: 181-9.
9. Calle MC & Fernandez ML. Inflammation and type 2 diabetes. *Diabetes & Metabolism*, 2012; 38(3): 183-191.
10. Han TS & Lean ME. A clinical perspective of obesity, metabolic syndrome and cardiovascular disease. *JRSM cardiovascular disease*, 2016; 5: 2048004016633371.
11. Barrea L, Annunziata G, Bordini L, Muscogiuri G, Colao A, Savastano S, et al. Nutrigenetics-personalized nutrition in obesity and cardiovascular diseases. *International journal of obesity supplements*, 2020; 10(1): 1-13.
12. Hawley JA, Sassone-Corsi P, Zierath JR. Chrono-nutrition for the prevention and treatment of obesity and type 2 diabetes: from mice to men. *Diabetologia*, 2020; 63(11): 2253-9.
13. Hoyas I, Leon-Sanz M. Nutritional Challenges in Metabolic Syndrome. *Journal of clinical medicine*, 2019; 8(9).
14. Rush EC, Yan MR. Evolution not Revolution: Nutrition and Obesity. *Nutrients*, 2017; 9(5).
15. Yamaoka K, Tango T. Effects of lifestyle modification on metabolic syndrome: a systematic review and meta-analysis. *BMC medicine*, 2012; 10: 138.

16. Albracht-Schulte K, Kalupahana NS, Ramalingam L, Wang S, Rahman SM, Robert-McComb J, et al. Omega-3 fatty acids in obesity and metabolic syndrome: a mechanistic update. *The Journal of nutritional biochemistry*, 2018; 58: 1-16.
17. Jiang SZ, Lu W, Zong XF, Ruan HY, Liu Y. Obesity and hypertension. *Experimental and therapeutic medicine*, 2016; 12(4): 2395-9.
18. Upadhyay J, Farr O, Perakakis N, Ghaly W, Mantzoros C. Obesity as a Disease. *Medical Clinics of North America*, 2017; 1-21.
19. West-Eberhard MJ. Nutrition, the visceral immune system, and the evolutionary origins of pathogenic obesity. *Proceedings of the National Academy of Sciences of the United States of America*, 2019; 116(3): 723-31.
20. Fernández-Sánchez A, Madrigal-Santillán E, Bautista M, Esquivel-Soto J, Morales-González A, Esquivel-Chirino C et al. Inflammation, Oxidative Stress, and Obesity. *International Journal of Molecular Sciences*, 2011; 12: 3117-3132.
21. Tangvarasittichai S. Oxidative stress, insulin resistance, dyslipidemia and type 2 diabetes mellitus. *World journal of diabetes*, 2015; 6(3): 456-80.
22. Saini V. Molecular mechanisms of insulin resistance in type 2 diabetes mellitus. *World journal of diabetes*, 2010; 1(3): 68-75.
23. Hussain A, Hydrie M.Z.I, Claussen B, Asghar S. Type 2 Diabetes and obesity: A review. *Journal of Diabetology*, 2010; 2(1): 1-8.
24. Sobczak AIS, Blindauer CA, Stewart AJ. Changes in Plasma Free Fatty Acids Associated with Type-2 Diabetes. *Nutrients*, 2019; 11: 1-42.
25. Balducci S, Zanuso S, Nicolucci A, Fernando F, Cavallo S, Cardelli P, et al. Anti-inflammatory effect of exercise training in subjects with type 2 diabetes and the metabolic syndrome is dependent on exercise modalities and independent of weight loss. *Nutrition, metabolism, and cardiovascular diseases: NMCD*, 2010; 20(8): 608-17.
26. Nakamura K, Fuster JJ, Walsh K. Adipokines: a link between obesity and cardiovascular disease. *Journal of cardiology*, 2014; 63(4): 250-9.
27. Ahmed HM, Blaha MJ, Nasir K, Rivera JJ, Blumenthal RS. Effects of physical activity on cardiovascular disease. *The American journal of cardiology*, 2012; 109(2): 288-95.
28. Liu G, Li Y, Hu Y, Zong G, Li S, Rimm EB, et al. Influence of Lifestyle on Incident Cardiovascular Disease and Mortality in Patients with Diabetes Mellitus. *Journal of the American College of Cardiology*, 2018; 71(25): 2867-76.
29. Hodson L, Gunn PJ. The regulation of hepatic fatty acid synthesis and partitioning: the effect of nutritional state. *Nature reviews Endocrinology*, 2019; 15(12): 689-700.
30. Wong VW & Singal AK. Emerging medical therapies for non-alcoholic fatty liver disease and for alcoholic hepatitis. *Translational Gastroenterology and Hepatology*, 2019; 4:53: 1-13.
31. Dongiovanni P, Lanti C, Riso P, Valenti L. Nutritional therapy for nonalcoholic fatty liver disease. *The Journal of nutritional biochemistry*, 2016; 29: 1-11.
32. Keating SE, Adams LA. Exercise in NAFLD: Just do it. *Journal of hepatology*, 2016; 65(4): 671-3.
33. Loomba R, Cortez-Pinto H. Exercise and improvement of NAFLD: Practical recommendations. *Journal of hepatology*, 2015; 63(1): 10-2.
34. Annesi JJ & Unruh JL. Relations of Exercise, Self-Appraisal, Mood Changes and Weight Loss in Obese Women: Testing Propositions Based on Baker and Brownell's (2000) Model. *The American Journal of the Medical Sciences*, 2008; 335(3): 198-204.