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Review Article

View of the Non-Alcoholic Fatty Liver in Non-Obese Patients from MAFLD Perspective

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Abstract

Background: A novel concept consensus by an international panel of experts recommended a change in name for NAFLD to metabolic (dysfunction) associated fatty liver disease (MAFLD). The new definition is a landmark in hepatology bringing a new way of thinking about diseases of the liver that are associated with fat deposition and metabolic dysfunction Importantly, this "MAFLD definition" avoid the dichotomous view of NAFL and NASH, since it is based in "positive" criterion (evidence of hepatic steatosis) instead of "negative" criterion hard to exclude. Lean NAFLD is defined as hepatic steatosis with a BMI < 25 kg/m2 in non-Asian people or BMI < 23 kg/m2 in Asians.

At present, it is not possible to define a phenotype of Metabolic Healthy Obesity (MHO) due to the lack of consensus. This disparity is due to the difference in defining metabolic health found by some authors when studying the phenotypes of subjects with unhealthy metabolic weight. We generally associate the development of NAFLD Patients with Obesity, but in opposition to this, lean patients can also develop this disease, especially when we find visceral obesity associated with a strong genetic predisposition and an altered and unhealthy diet pattern.

Here is the importance of addressing important concepts such as metabolic unhealthy normal weight, MUHO, MHO, as well as the interrelationship that all of them have with the distribution of body fat.

For this reason, for the sake of understanding and finding a clinical-pathophysiological relationship of the disease, I try to follow a route which helps me to better understand said relationship of importance in the study of Metabolic Association of Fatty Liver. It is essential to start from the term MAFLD which follows 2 routes, one in obese patients and the other in non-obese patients.

Conclusion: Adequate understanding of the spectrum of MAFLD in association with non-obese NAFLD constitutes a new line of research which would provide a better and more exhaustive understanding of the relationship between metabolic dysfunction and fatty liver disease, especially in non-obese patients in any of It would be necessary to delve further in non-Asian patients to establish a better characterization of the disease. In another order, it is very important to establish clinical criteria in correlation with the pathophysiological pathways of the disease. This will allow a greater approach and management of the patient with this type of condition, giving us benefits beyond the simple understanding that until now we have had about the fatty liver.

Keywords: *MAFLD; Lean NAFLD; Lean MAFLD; Non obese NAFLD; MHNW and MONW; Metabolic Health and Metabolic Healthy Obese*

Abbreviations

NAFLD: Non- alcoholic Fatty Liver Disease; MAFLD: Metabolic Association Fatty Liver Disease; MHNW: Metabolically Healthy and Normal Weight; MONW: Metabolically Obese but Normal Weight; BMI: Body Mass Index; NFS: NAFLD Fibrosis Score; FIB-4: Fibrosis 4; MH: Meta-

bolic Health; MUHNW: Metabolic Unhealthy Normal Weight; MUHO: Metabolic Unhealthy Obesity; MHO: Metabolic Healthy Obesity; CT: Computed Tomography; MRI: Magnetic Resonance Imaging; DXA: Dual-Energy X-Ray Absorptiometry; BIA: Electrical Bio Impedance; VAT: Visceral Adipose Tissue SAT: Subcutaneous Adipose Tissue

Introduction

Recently, a consensus by an international panel of expert recommended a change in name for NAFLD to Metabolic (dysfunction) Associated Fatty Liver Disease (MAFLD). This recent and new perspective is seen as an advanced way of approaching fatty liver disease, breaking with the old term where NAFLD and NASH were separated, being a positive and inclusive criterion above all [1]. Recently, a high prevalence of MAFLD patients in Western countries has been evidenced, which shows the chronic nature of the disease [2].

The defined criteria for Metabolic Associated Fatty Liver disease are: 1) Waist circumference ≥ 102 cm in men and 88 cm in women. 2) Pre-diabetes Glycated hemoglobin (HbA1c) of 5.7 - 6.4%, or fasting plasma glucose of 5.6 - 6.9 mmol/L, or 2-hour post-load glucose levels of 7.8 - 11.0 mmol/L). 3) Blood pressure ≥ 130/85 mmHg or under antihypertension therapy. 4) High-density lipoprotein cholesterol (HDL-C) 2 mg/L [1,3]. Lean NAFLD is defined as hepatic steatosis with a BMI < 25 kg/m^2 (or < 23 kg/m^2 in Asians) [4].

It is very clear that Metabolic Health (MH) is a well-known term that uses the elements of the metabolic syndrome. With age and decreased physical activity, a redistribution of fat is evident, especially in the gluteofemoral area [5].

It is well known that type of adipose tissue growth, adipose tissue anatomical location, adipose tissue inflammation, ectopic fat accumulation, genetic factors, and lifestyles factors (Diet and physical activity) are determinant factors that can explain the metabolic features of MHO subjects [6].

Individuals with lean/non obese NAFLD, despite not presenting with obesity, have increased visceral adiposity, and sarcopenia is a common feature. Since both characteristics act sinergically, worsening the prognosis, the assessment of body composition could help to identify high risk subjects. Therapeutic management of patient with lean NAFLD is based on life style modifications to address increase visceral fat and insulin resistance [7].

In contrast to non-lean NAFLD, lean patients are likely to have a distinct pathophysiology [8,9].

Due to the importance that the new term called MAFLD reverts to the study of non-obese patients, we should reflect and ask ourselves: How could we approach non-obese patients from the perspective of MAFLD?

MAFLD perspective

In 2020, international consensus guidelines recommended the renaming of NAFLD to MAFLD, supported by diagnostic criteria. There is evidence that MAFLD with its criteria is a step up from its predecessor term, which is more practical and more decisive in discriminating patients with this condition [1,10].

Metabolic fatty liver as an entity has a heterogeneous behavior both for its causes and for its evolution and natural history, so it is influenced by different factors, which we mention as follows [1]:

- **Age:** With increasing age there are several physiological changes such as: decreased hepatic blood flow, altered liver function, alterations in lipid metabolism, especially cholesterol, as well as a significant reduction in the number of mitochondria. Other changes evidenced in close relationship with This condition is the changes in the body constitution with the consequent decrease in body mass, the increase in abdominal adiposity and the abnormal deposition of fat with a considerable increase in Insulin Resistance and the appearance of the Metabolic syndrome [1].

- **Ethnicity:** The disparity according to ethnicity is not fully understood, although some authors try to explain it from the perspective of genetic predisposition, metabolic changes, socioeconomic and cultural factors, dietary and exercise habits, access to the health system, as well as environmental risk. A significantly high prevalence has been evidenced in Hispanics, Intermediate in white people and low in black people. On the other hand, Asian population experiences rising numbers [11].

- **Dietary intake, gut microbiota and bile acids:** There are some factors directly related to metabolism, some of which are specific to the digestive tract and others that are not. Among the first ones we can find: dietary intake, the enterohepatic circulation, gut microbiota and bile acids and their related metabolites. The second option is: the neuroendocrine axis, muscle mass and physical activity. All of them are closely related and widely implicated [1].

- **Obesity and metabolic health:** Obesity is closely related to liver fat, but not all obese patients develop fatty liver. On the other hand, we can classify Obesity in: metabolically healthy obese or metabolically unhealthy obese, which affects 45% of obese patients where it does not exist consensus for metabolic health [12]. This is where it is important to highlight the role that insulin resistance plays in the pathophysiology of fatty liver. On the other hand, 30% of individuals who can be classified as metabolically healthy obese with normal weight have been shown to be prone to considerable cardiometabolic risk and a proportion of these patients are lean [1].

- **Lean NAFLD:** Lean NAFLD is defined as hepatic steatosis with a BMI < 25 kg/m^2 in non-Asian people or BMI < 23 kg/m^2 in Asians [13]. The natural history of patients with Lean NAFLD is not fully defined although it can be associated with a worse picture in these patients, it is said that they have a better metabolic profile compared to obese patients [14], while others suggest no difference or even better outcomes [4].

Impact on the performance of non-invasive assessment of fibrosis

Studies point to a difference between some fibrosis tests such as the NAFLD fibrosis score (NFS) and fibrosis 4 (FIB-4) where there is lower specificity in older adults and lower accuracy in younger adults [15]. Hepatic elastography is very important to take into account especially in the association between ethnic differences and diabetic and obese people. The validation of any future markers must be done in large populations and it is of vital importance taking into account that there are different biomarkers that may replace liver biopsy in the future, so it is suggested that the heterogeneity factors of the disease be taken into account when designing and applying scores.

Histopathology and natural history MAFLD is categorized into two histological types: a) simple steatosis, which includes patients with hepatic steatosis with or without mild inflammation; and b) steatohepatitis, characterized by the presence of inflammation and hepatocyte injury (ballooning) with or without concomitant fibrosis [16,17]. Steatohepatitis which translates as chronic inflation progressing to fibrosis requires the presence of the following histopathologic changes steatosis, ballooning, and lobular inflammation. The diagnosis is usually made on the basis of a finding since most patients are asymptomatic on both laboratory and imaging tests [18].

Elevated aminotransferases are frequent in patients with MAFLD and are sometimes the main cause, but are not excluded when normal values are observed, whereas gamma glutamyl transferase may be elevated and there is a close relationship between this and the fibrosis state according to studies [18].

To establish an accurate diagnosis of MAFLD, it is important to diagnose steatosis with at least diabetes mellitus, obesity or overweight and metabolic dysfunction by ultrasonography. It should be defined that all of the above is important under the condition of having at least two of the criteria mentioned below: Waist circumference ≥ 102 cm in men and 88 cm in women. glycosylated hemoglobin HbA1c: of 5.7 to 6.4%, fasting plasma glucose of 5.6 to 6.9 mmol/L, glucose levels at 2 hours' post-load of 7.8 to 11.0 mmol/L) or Prediabetes 3) Blood pressure ≥ 130/85 mmHg or on antihypertensive treatment. 4) High-density lipoprotein cholesterol (HDL-C) 2 mg/L [3].

Why MAFLD instead of NAFLD?

Strong arguments are given by Eslam., *et al*. in their consensus on the importance of changing the terminology.

Firstly: NAFLD has been established as a condition of exclusion where its diagnosis is established only when there is an absence of other conditions (HBV, HCV, autoimmune disease, alcoholic hepatitis). However, progress in understanding the pathophysiology of the disease is evident that clearly the disease is more a definition of inclusion than of exclusion [1].

Second, there remains debate about the safe limit of alcohol intake. Making a diagnosis of NAFLD without alcohol consumption is clearly impossible and really unclinical as several authors have suggested [19].

Third, Consider hepatic steatosis associated with metabolic dysfunction as well as other hepatopathies with certain degrees of fibrosis without the dichotomous stratification of NASH and non-NASH which improves the pathologic outlook at least in the context of hepatic biopsy [1,20].

Fourth, the heterogeneous nature of fatty liver diseases suggests that they cannot be considered or managed as a single condition with a "one size fits all" approach to therapy. Lack of consideration of heterogeneity impacts and detracts from our ability to precisely define the natural history of fatty liver phenotypes, to appropriately select for clinical trials that are weighted to demonstrate meaningful benefits, and to compare or pool results from the trials. For these reasons, an updated and appropriate nomenclature for the disease is the first step in the long path to deconvolution of disease heterogeneity [1].

Referring to the terms metabolically obese with normal weight and metabolically healthy obese

At present, it is not possible to define a phenotype of Metabolic Healthy Obesity (MHO) due to the lack of consensus. This disparity is due to the difference in defining Metabolic Health (MH) found by some authors when studying the phenotypes of subjects with unhealthy metabolic weight (UHMW). With age and the decrease in physical exercise there is a decrease in the distribution of fats, especially gluteofemoral fats [21,22].

When investigating the body fat distribution phenotypes of subjects with Metabolic Unhealthy Normal Weight (MUHNW) Stefan., *et al*. [5] found that in somewhat differed from the one observed in a subjects with Metabolic Unhealthy Obesity (MUHO). There is a big difference between the subjects with MUNW and MUHO since the former have a low amount of gluteofemoral lean fat while the latter have a high amount of fat in the liver due to the excessive amount of visceral fat.

It is widely accepted that adipose tissue in the gluteofemoral region serves as a healthy sink to store excess fat. This is evidence because there is less lipolytic activity due to the increase in energy consumption, which constitutes a decrease in fatty acids in the circulation with consequent decrease in ectopic fat, such as the pancreas and liver [6].

According to some studies, great genetic variability can be evidenced, firstly because MUHO is characterized by variability in the genes that regulate intake and therefore those with MUHNW are characterized by the genes that regulate adipocytic differentiation. It Also has a crucial impact on pathogenesis genes that regulate lipogenesis [1,21,23].

In many studies, MHO subject is defined as an obese individual (≥ 30 kg/m^2) who does not present metabolic abnormalities, such as insulin resistance or hypertension [24]. Some limitations have this definition because BMI is an imperfect parameter which doesn't not take into account the difference between fat and lean tissue without providing information related to body distribution of fat.

Other studies have included the presence of inflammation markers, such as C-reactive protein (CRP) [25], another interesting criterion to take into account is liver fat content, due to the fact that non-alcoholic fatty liver disease (NAFLD) is more frequent in metabolically

unhealthy obese than in MHO subjects. Finally, several authors have suggested insulin sensitivity as the key to define MHO, even suggesting the term "non-insulin resistant obese" to refer to MHO subjects [22].

It is well known that type of adipose tissue growth, adipose tissue anatomical location, adipose tissue inflammation, ectopic fat accumulation, genetic factors, and lifestyles factors (Diet and physical activity) are determinant factors that can explain the metabolic features of MHO subjects.

Type of adipose tissue growth

White adipose tissue expansion needs the development of vasculature to support the increased demand of oxygen and nutrients. The growth of adipose tissue by hypertrophy leads to inefficient remodeling of extracellular matrix, characterized by impaired vascularization and innervation, that results in hypoxia [26]. This, in turn, increases the release of pro-inflammatory cytokines that facilitate immune cell infiltration in white adipose tissue, as well as phenotypic shifts in resident immune cells. Taken together, these processes contribute to the development of insulin resistance [26]. In other cases, the excess of caloric intake promotes hyperplasia (increase in number), thereby increasing the proportion of small adipocytes. In this situation, extracellular matrix remodeling is correct, and normal adipose tissue function and insulin sensitivity are maintained. In addition, taking into account that apoptosis is a process which also contributes to the number of adipocytes, and considering that apoptosis increases with obesity, potential differences in this process between MHO subjects and obese individuals showing metabolic alterations cannot be discarded.

Anatomical location

White adipose tissue is distributed in two main locations, visceral adipose tissue (VAT) and subcutaneous adipose tissue (SAT), which exhibit specific features related to structure, morphology, and function. The fact that VAT enlarges mainly by hypertrophy and SAT expands by hyperplasia can be explained by greater precursor number and/or activity in the latter. Since an excess of VAT is the main risk factor for the appearance of obesity-related co-morbidities, such as type 2 diabetes and cardiovascular diseases [27].

The location of fat accumulation has also been postulated as determinant to explain the lack of metabolic co-morbidities in MHO subjects despite their increased body weight. This has been explained in some studies where MHO subjects showed reduced accumulation of visceral fat, when compared with obese subject showing metabolic abnormalities [28]. According to Ross, in the study, which matched the subjects according to the distribution of body fat, evidenced insulin tolerance regardless of whether they were matched by VAT or By SAT. In contrast, no improvement was seen in the subjects from whom SAT was removed surgically [26].

Inflammation

White adipose tissue inflammation is considered an important factor in the development of metabolic diseases [29]. Macrophages, the most abundant immune cells in adipose tissue, regulate metabolic dysregulation of adipose tissue in obesity. Macrophages can be divided into 2 main groups: M1 and M2 macrophages. In obese subjects, pro-inflammatory M1 macrophages are associated with adipose tissue inflammation and insulin resistance, whereas in lean subjects, anti-inflammatory M2 macrophages are more abundant [30].

It is clear that in lean and healthy subjects, there is a greater production of anti-inflammatory cytokines (adiponectin, IL-4, IL-13, TGF-β), in its counterpart, obese subjects produce a considerable amount of inflammatory cytokines (leptin, TNF-α, IL-6, resistin, angiotensin II) [31]. Consequently, the largest number of publications where MHO subjects are reported has evidenced MHO subjects with lower concentrations of pro-inflammatory cytokines and higher concentration of adiponectin, as well as of adipokine with clear anti-inflammatory effect.

Ectopic fat accumulation

White adipose tissue is specialized in triglyceride storage but an appropriate plasticity and expandability capacity of the adipose tissue depots is crucial to prevent metabolic dysfunctions associated to this fat accumulation [26].

Nevertheless, further research is still needed on this topic, mainly concerning genetic background. Another important field of research is the treatment of MHO subjects because nowadays they do not receive a specific and personalized treatment; by contrast, they follow the same lifestyle recommendations than obese subjects with metabolic alterations [22].

For the management of fat deposits, it is necessary to study the body composition. Body composition as a test accurately determines a better way to measure of individual body components including muscle mass, lean mass and, most importantly, the percentage of adipose tissue, the knowledge of which, together with the BMI value, can be used as a screening tool [32].

Body composition can be assessed by various methods: computed tomography (CT), magnetic resonance imaging (MRI), dual-energy X-ray absorptiometry (DXA), electrical bio impedance (BIA), hydrostatic plethysmography, isotope dilution techniques, and skinfold method and air displacement plethysmography [33]. The most common methods are CT, DXA and BIA.

Increased visceral fat is characterized by an increase in adipose tissue in people with MONW [34]. Abdominal fat deposit is one of the causes of insulin resistance. The information related to the percentage of fat is insufficient. Therefore, as conclusion, it is necessary to determine a cut off value that's shoes the existence of metabolic disorders [33].

Lean non-alcoholic fatty liver disease

Lean NAFLD as a condition predisposes to a worse metabolic prognosis and consequently an increase in mortality. Therefore, it is vitally important to focus on studies that evaluate the progress and prevalence of NASH, advanced liver fibrosis or compensated cirrhosis. This condition is frequently associated with sarcopenia so proper management of both would allow risk to be identified and severity to be determined. In view of the above, we see it important to modify lifestyle [7].

NAFLD with its heterogeneous character is closely associated with obesity and comorbidities. Instead lean NAFLD is determined by genetic factors, unhealthy dietary habits as well as visceral obesity. Patients with lean NAFLD have a better metabolic profile, which does not rule out the possibility of a worse prognosis, taking into account that classification in lean or obese only takes into consideration BMI and not the evaluation or visceral fat. Thus, the use of MRI as a reliable and quantitative diagnostic tool for evaluating the presence and severity of abdominal obesity in NAFLD patients might be useful. Currently, lifestyle interventions including weight loss, physical activity and a healthier dietary pattern seem to have beneficial impact on lean NAFLD. The study, management and treatment of patients with lean NAFLD leads to a great challenge because its pathological mechanism together with its natural history have not been widely studied and addressed by physicians [2].

Patients with lean NAFLD had lower prevalence of female sex, type 2 diabetes mellitus (T2DM), nonalcoholic steatohepatitis and advanced fibrosis; they were also younger and had lower blood glucose and triglycerides levels, but higher blood low density lipoprotein cholesterol level than non-lean individuals with NAFLD at baseline [35].

Patients with lean NAFLD shared comparable incidences of T2DM, liver decompensation, cardiovascular events, liver and non-liver cancers, and mortality with non-lean NAFLD counterparts. The occurrence of long-term events was not associated with longitudinal body mass index (BMI) change or PNPLA3 genotype, and advanced fibrosis was the only independent predictor of outcome mortality, especially in lean individuals with NAFLD. Practical significance. Lean NAFLD should be regarded as a 'metabolically diseased and progressive' status. It can be diagnosed as metabolic associated fatty liver disease (MAFLD) if at least two metabolic risk abnormalities or T2DM are

present. BMI-driven approaches for NAFLD should be replaced by better diagnostic tools emphasizing assessment of metabolic disorders and advanced liver fibrosis [35].

The onset of the disease marked by insulin resistance and dyslipidemia is determined by other factors that are not yet exhaustively studied, such as the intestinal microbiota and genetic factors. In patients with lean NAFLD, changes in the dietary pattern have been associated, sometimes with excess cholesterol in the diet. Altered cholesterol metabolism, limitations in adipocyte numbers in childhood, or differences in mucosal immunology [8,9].

In fact, high risk can be found in those patients who change from one weight to another, that is, from normal weight to obese and vice versa than those who remain obese and overweight [36,37].

Non-obese from MAFLD perspective

It is important to note that in 2020 when a group of experts led by Mohammed Eslam proposed the term MAFLD, which is more than all very inclusive and encompasses the spectrum of fatty liver metabolic dysfunction as well as all subtypes of the aforementioned. As Eslam itself points out, it has strong advantages, although it does not fail to show some weaknesses that as a new concept have finally been ironed out over the years, as well as the definitive replacement of the old term and the realization of a greater number of studies. Here is something very important as scientists are still attached to NAFLD instead of making full use of the term MAFLD.

From another perspective, I think we should use the term metabolic dysfunction associated with fatty liver, since metabolic dysfunction, to a lesser or greater degree, is an important element associated with this type of patient who suffers from this condition. On the other hand, it is essential to assess the chronicity of this disease and keep in mind that it has a great heterogeneity with marked risk factors, which makes it peculiar in diagnosis but at the same time difficult in management and long-term prognosis.

With the advent of the new term According to Eslam, greater importance is given to histopathological changes, which gain marked importance, but at the same time the importance of markers, tests, and non-invasive liver function values that are faithful predictors of the state is highlighted and prognosis of each patient. It is worth noting here the relationship that exists between ALT/AST/GGT/CRS/Ferritin and, on the other hand, the predictors that evaluate the issue of fibrosis, such as Elastography in any of its modalities and the predictive indices of fibrosis such as FIB 4, NAFLD Fibrosis Score among others.

Having said all of the above, one cannot speak or use the term MAFLD without first keeping in mind metabolic health and all the consequences that this entails when it is altered. At the same time, the lack of consensus in this field can mean that there are no elements or points relationship in common as to what metabolic health entails.

Here is the importance of addressing important concepts such as metabolic unhealthy normal weight, MUHO, MHO, as well as the interrelationship that all of them have with the distribution of body fat. Understand the pathophysiological changes that occur in patients with this type of metabolic dysfunction. They are very important in determining the course and severity of the disease as well as the development of safe and effective lines of treatment. Well, in one way or another, all of the above is being well addressed by the scientific community at present and is maintaining a good pace.

For this reason, it should be pointed out and here the purpose of our article where there is a very important element that is often ignored and not studied since the most frequent is that this entity occurs in the course of obese/overweight patients, which is the most common in western countries.

Here the importance of asking: Will fatty liver in non-obese patients have an incidence and a tendency to increase in this type of patients in the world?

Well, it is important to define that the category of metabolic fatty liver does not only include obesity and that a large number of researchers pay more attention to the changes in obesity and forget that in this case, lean patients have a great alteration in metabolic function and it is associated with a high risk as well as its counterpart.

This is its essential importance since changes such as sarcopenia can be associated with metabolic changes such as insulin resistance and chronic inflammation. It is vital to note that some authors point out that fatty liver in thin patients has a worse prognosis but a better metabolic profile than in obese but all this based on the BMI which is an imperfect measure and not on the visceral fat mass evaluation.

For this reason, for the sake of understanding and finding a clinical-pathophysiological relationship of the disease, I try to follow a route which helps me to better understand said relationship of importance in the study of Metabolic Association of Fatty Liver. It is essential to start from the term MAFLD which follows 2 routes, one in obese patients and the other in non-obese patients. The first is divided into Patients Metabolic Unhealthy Obesity and Metabolic Healthy Obesity. In the second category called non-obese we will not only include lean patients but we will also include overweight patients who do not fall into the other category. Within lean patients we will include a subcategory where we will divide Metabolically Healthy and Normal Weight and Metabolically Obese but Normal Weight. This subcategory would imply 2 routes based on ethnicity where we will divide it into Type 1: Asian People and Type 2: Non-Asian People which corresponds to white and Hispanic and non-white. To this would be added that everything has the genetic factor, gut microbiota plus the associated comorbidities that may or may not be frequent. This interrelation allows to associate the BMI with the indices of body

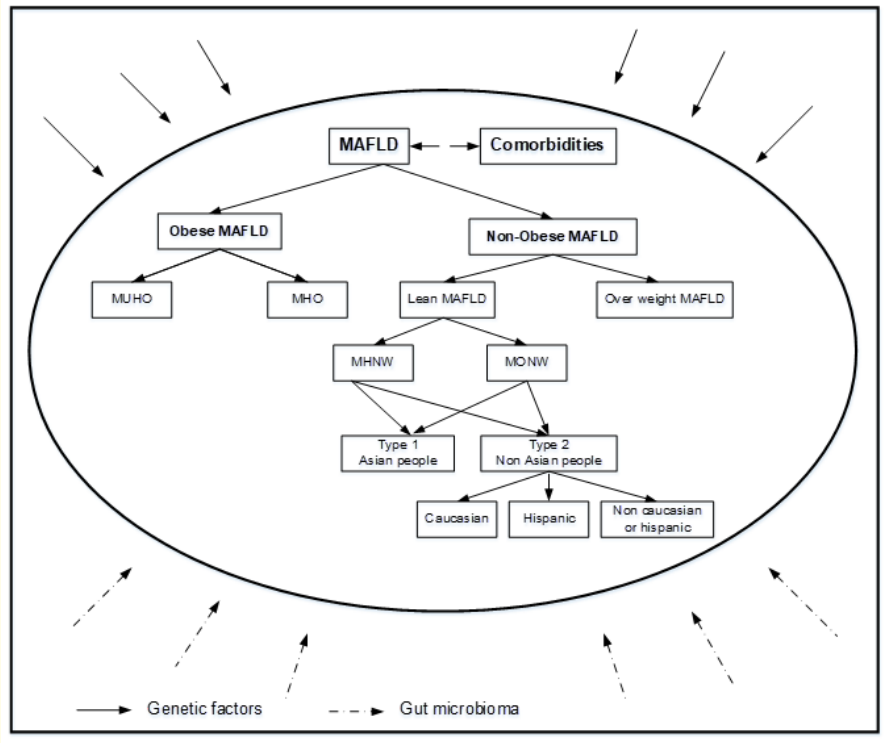

Figure 1: *Diagram showing the clinic pathophysiological pathway that is followed by MAFLD disease. Source: Author.*

fat composition (Figure 1).

As a climax, according to Eslam in his new article, it is important to understand the genetic phenomena that act on this disease in non-obese patients, since it seems to be one of the elements that conditions its appearance, development and prognosis, as well as its interrelation with the gut microbiota.

Conclusion

The use of the term MAFLD as an inclusive criterion and as part of it, non-obese patients should have greater clinical significance. Researchers should pay more attention to it in Western countries. The genetic predisposition of these patients tends to be a crucial element in the understanding and development of the disease.

Adequate understanding of the spectrum of MAFLD in association with non-obese NAFLD constitutes a new line of research which would provide a better and more exhaustive understanding of the relationship between metabolic dysfunction and fatty liver disease, especially in non-obese patients in any of It would be necessary to delve further in non-Asian patients to establish a better characterization of the disease. In another order, it is very important to establish clinical criteria in correlation with the pathophysiological pathways of the disease. This will allow a greater approach and management of the patient with this type of condition, giving us benefits beyond the simple understanding that until now we have had about the fatty liver.

Conflict of Interest

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