

# Current Opinion on Food Sustainability for Liver Associated Health Problems: Facts and Myths with Case Study

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**Abstract.** The liver is the second-largest organ in our body which separates the nutrients and waste as they move through our biological process system and it additionally produces bile, a substance that carries toxins out of your body and aids in digestion. There are several myths associated with liver spread amongst masses. It is a vital necessity to make society devoid of such myths and aware of the real scenario. This review aimed to summarize the different facts and myths associated with health problems of liver and highlight the importance of food sustainability approach with the help of some case studies. A comprehensive literature search was conducted using various databases between 2006 and 2022 that focused on the various facts and myths associated with liver related health issues. Myths create nothing but false notions and fear amongst people. Some case studies were summarized to clear all the conflict statements commonly related with liver diseases in the society. Myths like nothing other than water is considered a good beverage for the liver, but recent studies have proven that measured quantities of coffee and herbal tea intake is healthy for the body. Additionally, coffee has a protective effect on the organ liver. Similarly, hepatitis can spread through casual contacts. Although it is proven that hepatitis B, C and autoimmune hepatitis, do not spread on having casual contact or sharing food and drink. A substantial myth states that blood tests can detect problems associated with the liver, but doctors rarely suggest blood tests for liver functioning. This review is focused to resolve several myths associated with the liver which are often considered true by masses.

## 1 Introduction

It is a widely known reality that the liver is the most important organ in our frame that's accountable for Major capabilities which includes putting off pollutants from the frame's blood deliver. The liver is placed within the pinnacle proper hand a part of the stomach, on the summit of the belly, right kidney, and intestines, and under the diaphragm. It is a deep red, cylinder organ that weighs about 1 kilo. There are reasserts about the delivery of blood to the liver that they are: (a) the hepatic artery carries oxygenated blood and it transfers oxygen-rich blood to the liver, pylorus, pancreas, and duodenum, (b) Nutrient-wealthy blood which flows in from the hepatic portal vein. There are numerous capabilities of the liver like manufacturing of Bile (Bile is a critical fluid because it allows excrete cloth now no longer excreted with the aid of using the kidneys and aids the production of bile salts and acids to aid in the absorption and digestion of lipids. Hepatocytes are used to create bile, which is mostly made from water, ions, bile pigments, bile acids, fat, bile pigment, bilirubin, and phospholipids in addition to other compounds) [1]. The liver has four anatomical lobes: the proper, left, caudate, and quadrate. The quadrate lobe is placed at the inferior floor of the proper lobe. The liver synthesises critical proteins which includes fibrinogen, albumin, prothrombin, and different amino acids in addition to modifies proteins into enzymes and peptide hormones. The liver receives a dual blood supply, with the portal vein providing between 75 and 80 percent of the blood volume and the hepatic artery providing between 20 and 25 percent. The portal triad, which is included inside the hepatoduodenal ligament, is formed by joining the right hepatic artery, a portion of the celiac trunk, and the common bile duct. Generally speaking, the right lobe of the liver must be harvested in order to perform partial liver transplants. It is important to take into account any viable variations that may exist within the liver's physiology. Trans-hepatic portosystemic shunt (TIPS) surgery is used to help patients with portal hypertension due to liver damage or portal vein blockage. These users are provided linking the inferior vena cava, which drains blood from the liver, and the portal vein, which delivers blood to the liver. This provides a technique through which blood can avoid the damaged hepatic device and reduce portal venous congestion. Trans-hepatic portosystemic shunt (TIPS) operation is used to treat people with hypertension due to liver damage or portal vein blockage. This procedure comprises joining the inferior vena cava, which removes blood from the liver, and

the portal vein, that supplies the liver with blood. This provides a technique through which blood can avoid the damaged hepatic device and reduce portal venous blockage [2].

For most species, the distribution of load on the inside of the liver and the blood pressure in sensory arteries are approximately similar. It is believed that the pressure inside the hepatic artery, which originates from the celiac trunk and the descending aorta, is similar to aortic tension. This is characterised by an increased pulsatile pressure around 122 and 88 mmHg with a frequency like the cardiac heart rate. Once At the cyclical level, the stress falls to around 2.5 mmHg and the pulse frequency goes to zero. On the other hand, pressure within the portal vein, which originates from digestive system capillaries, has no pulsing and a pressure of 10–12 mmHg. Each portal vein and hepatic artery pressure in the sinusoids is 3 to 5 mmHg. As a result, the liver's internal pressure dips within the portal venous system are far lower than those within the arterial system. The pressure drop from the accumulating critical veins to the vena cava then is between one and three mmHg, scarcely varying with breathing [3].

The caudate lobe is positioned among the left and proper lobes in an anterior and advanced area manufacturing of cholesterol (sure natural molecules referred to as lipids) and particular proteins to assist supply fats at some point of the frame, preventing infections by producing defensive factors, controlling blood coagulation, and doing away with microorganism from the bloodstream, clearing the blood from medicinal drug and extraordinary poisonous substances, and it's far the constructing blocks of proteins through law of blood tiers of amino acids. The liver controls the amino acid attention withinside the frame, as extra amino acids which want to be excreted safely. The frame is not able to keep proteins or amino acids. In the liver ammonia is fashioned through the deamination of amino acids. It is distinctly poisonous and cannot be allowed to build up withinside the frame [4]. This research suggests that each chronically and acutely, alcohol reasons discounts in skeletal muscle protein synthesis, in addition to of skin, bone, and the small intestine. Chronically, animal research additionally displays expanded urinary nitrogen excretion and lack of skeletal muscle protein [5].

Out of more than one current diseases, liver ailment is one of the distinguished one. There are more than one styles of liver ailment which incorporates Hepatitis (Hepatitis method infection of the liver) [6], Cirrhosis (a critical ailment of the liver prompted specially through ingesting an excessive amount of alcohol) [7], Liver cancers (Several styles of most cancers can shape withinside the liver. The maximum not unusual place sort of liver most cancers is hepatocellular carcinoma, which starts off evolved withinside the primary sort of liver molecular hepatocyte) [8]. Other styles of liver most cancers, along with intrahepatic cholangiocarcinoma and hepatoblastoma, are tons much less not unusual place.), Liver failure Ascites (Abdominal swelling resulting from accumulation of fluid, most usually associated with liver ailment.) [9], Gallstones (Gallstones are hardened deposits of digestive fluid that could shape on your gallbladder [10].

## **2 Literature review**

We had achieved our objective through the literatures work which was based on a systemic, meta-analysis reviews as well as reported clinical trial case studies. This review has been mostly covered the literatures reported in the past fifteen years (i.e., from 2006 to 2022) which were collected from different online databases like PubMed, SCOPUS etc. There were total 103 articles selected for the study and finally 32 out of these articles reviewed for the preparation of our report. All the related articles were filtered as per the topic of interest given in PRISMA report (Fig. 1).

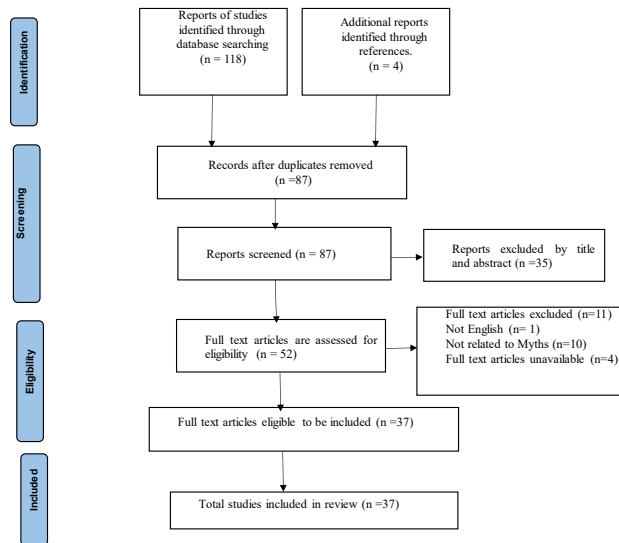


Fig. 1 PRISMA flow diagram for the selection of studies

## 3 Types of Liver Diseases

### 3.1 Hepatitis

Inflammation of the liver is Hepatitis. Inflammation is swelling of tissues in the body that are injured or infected by the foreign parasites which can damage the liver. The function of the liver can be affected by swelling and damage. Hepatitis might be a short-term or a long-term (chronic) infection.

Hepatitis comes in a variety of forms and has several causes:

- The most common type of hepatitis is viral hepatitis. Hepatitis virus A, B, C, D, and E are the major causes. The most frequent hepatitis in the USA are A, B, and C.
- Alcoholic hepatitis is caused by drinking alcohol in high volume.
- Certain poisons, chemicals, medicines, or supplements can be a common cause of Toxic hepatitis.
- A typical chronic condition where the immune system of the body targets the liver is the cause of this episode of autoimmune hepatitis is unknown, however there is a chance that the surroundings and heredity may be to blame.

Viral hepatitis spread through the contact of food and water that was touched or used by an infected person. The person who is in constant in unprotective sex and having a drinking problem in large amount.

**Symptoms:** Fever, loss of appetite, dark urine, joint pain, vomiting, abdominal pain, Nausea.

Hepatitis diagnosed by many ways:

- Checking the medical history of the patient and asking the symptoms.
- By conducting a physical exam
- By taking blood test and viral hepatitis
- Ultrasound, imaging tests, CT scan, MRI is also done.
- In case of liver damage liver biopsy is done to clear the diagnosis.

#### **Treatments of hepatitis:**

Different types of hepatitis have different treatments:

- Often acute viral hepatitis goes away on its own (to feel a relief doctor suggests to take a lot of rest and drink plenty of water) but if the symptoms are serious then treatment in hospital is done.
- Different types of chronic hepatitis are treated by different medicines, other surgeries and medical procedures. Patients of alcoholic hepatitis need to stop drinking alcohol, and liver cancer and liver failure which occurs from chronic hepatitis needs a liver transplant.

**Prevention of Hepatitis:**

Not drinking too much alcohol, and there are vaccines for the prevention of hepatitis A and B but sadly there is no prevention for Autoimmune hepatitis [11].

**3.2 Cirrhosis**

A late stage of fibrosis (scarring) of the liver is called Cirrhosis because of different types of liver diseases and conditions, like chronic alcoholism and hepatitis. The damage done by cirrhosis to the liver is irreversible. If the diagnoses are done in early stages, then the cause is treated, because later on the damage is unlikely to be revisable.

There are different causes for Cirrhosis:

- Chronic alcohol abuse
- Formation of fatty tissues in the liver
- Formation of large iron in the body
- Genetic digestive disorder
- Destruction of bile ducts

**Symptoms:** Nausea, swelling in your legs Fatigue, easily bleeding or bruising, Loss of appetite, feet or ankles, Weight loss, Itchy skin.

**Risk factors:** there are 3 risk factors in Cirrhosis:

- Excessive consumption of alcohol is a major risk factor, and it damages the kidney very fast.
- Being overweight is also a cause that leads to cirrhosis.
- Having viral hepatitis.

Complications of cirrhosis can include:

- Veins that carry the blood to liver are often noticed with higher blood pressure (portal hypertension)
- There is a swelling in the legs and abdomen which is caused by the accumulation of fluid.
- Smaller veins might carry a large amount of blood that was directed from the larger veins because of Portal hypertension which can lead to explosion of the small veins. In the stomach (gastric varices) which can lead to life-threatening bleeding.
- In case of cirrhosis that is difficult in fighting infections.
- Bone strength also decreases which in future leads to a risk of fracture.
- If there is a person with cirrhosis, they have a high chance of getting liver cancer.

Prevention to reduce the risk of cirrhosis and steps to take care of liver:

- Stop drinking alcohol if a person is having cirrhosis.
- Keeping a proper track of food and eating healthy food to reduce fat storage in the body and eating less fried food.
- Keeping a proper track of the weight.
- Not having unprotective sex and sharing needles can make a huge impact [7].

**3.3 Liver cancer**

In liver cells the beginning of liver cancer is started. The liver is the football-sized structure in the upper right part of the abdomen, directly underneath the diaphragm and over the stomach. There are several types of cancer that occur in the liver. The most prevalent kind of liver cancer, hepatocellular carcinoma, begins in the primary liver cell (hepatocyte). Intrahepatic cholangiocarcinoma and hepatoblastoma are the less common types of cancer that occurs in the liver.

**Causes of Liver Cancer :** When there is a mutation in the liver which changes the DNA. Mutation of the DNA causes a growth of tumour.

**Symptoms:** Abdominal swelling, Upper abdominal pain, losing weight without trying, Loss of appetite, nausea and vomiting, General weakness, and fatigue.

There are multiple risk factors:

- Infection with hepatitis B virus or hepatitis C increases a huge number of chances for cancer.
- When Cirrhosis causes scar tissues it increases the chances of liver cancer.
- Blood sugar can also lead to Diabetes which can lead to liver cancer.
- The presence of too much fat in the liver can also lead to liver cancer.

- Consumption of excessive alcohol is not good for the liver which in future can lead to liver cancer.

Prevention to reduce the risk of liver cancer and steps to take care of liver:

- Drinking alcohol in limited quantities can help lower down the risk of cancer in the liver.
- Maintaining a healthy weight and exercising daily can help in a huge amount to reduce the chances of liver cancer.
- Getting vaccinated against hepatitis B can help to prevent liver cancer and it can be given to all the patients including infants, older adults.
- Making sure that the patient partner is not infected with HBV, HCV or any sexually transmitted infection.
- Using a clean needle and making sure that the needle used in hospital is not used before.
- Going to the hospital for liver cancer screening if any symptoms are observed [8].

### 3.4 Ascites

Ascites happens in the stomach there is too much fluid formation. Mainly happens to the people who might be suffering with the cirrhosis of the liver. Peritoneum is the sheet of tissue layer that covers the abdominal organs, with stomach, bowels, kidney and liver.

**Causes of Ascites:** Ascites is mostly brought on by cirrhosis, but it can also be brought on by heart failure, renal failure, infection, and tumour.

**Symptoms:** if your ankles swell difficulty breathing, digestive problems like indigestion, constipation, bloating, abdominal pain, and lack of appetite a backache, sitting with difficulty Fatigue.

There are multiple risk factors:

- Hepatitis B: It is a type of infection that causes inflammation (reddening and swelling) that ultimately leads to liver damage.
- Hepatitis C: The type of infection that causes liver infection which spreads when its contact with the blood.
- Genetic liver illness can result in hemochromatosis, Wilson disease, and alpha-1-antitrypsin deficiency.
- If abdomen and pelvis have cancer, then it can also lead to ascites.

Prevention to reduce the risk of ascites :

- The best way is to eat healthy and exercise daily.
- To limit the consumption of alcohol.
- Stop smoking can also help in prevention of ascites.
- Limiting the usage of salt consumption can also help [9].

### 3.5. Gallstones

In the gallbladder the hardened deposit of digestive fluid forms the stones which are called the Gallstones. The gallbladder is a pear-shaped organ that is situated underneath the liver on the right-hand side of the belly. The gallbladder stores bile juice, which is discharged into the small intestine.

There are two types of gallstones:

- Cholesterol gallstone: this is the most common type of gallstone; these gallstones mainly consist of undissolved cholesterol.
- Pigment gallstones: When there is the formation of brown or black stones which contains too much bilirubin.

**Causes of Gallstone:**

- If the bile contains too much cholesterol, then it can lead to crystals and even formation of stone.
- If there is a presence of too much bilirubin in bile which can cause infection to the liver.
- Dysfunction Ing of gallbladder when it is not empty correctly, which can lead to very concentrated, which can form gallstones.

**Symptoms:** You may experience abdominal pain in the upper right corner, in the middle, or below your breastbone.

Risk factors for Gallstones:

- Being at the age of 40 or above,
- Being overweight
- Pregnancy.
- Eating a diet heavy in fat, cholesterol, and fibre, or having a family history of gallstones.

**Prevention for Gallstones:**

- Eating proper meals which can help in lowering the risk of having gallstone.
- Eating high fibre food can also help such as fruits, vegetables, and whole grain food.

- Drinking a lot of water and not consuming alcohol can also help.

Other, common causes of liver disease are: 1. Chronic alcohol abuse, 2. Fat collection in the liver (non-alcoholic fatty liver disease), 3. Fat collection in the liver (non-alcoholic fatty liver disease), 4. Fat collection in the liver (non-alcoholic fatty liver disease), 5. Fat collection in the liver (non-alcoholic fatty liver disease), 6. Certain prescription or over-the-counter medications [10].

#### 4 Certain Unknown Facts About Liver Disease

- You may be born with liver ailment, settle it from a virus, increase it from what you consume and drink, increase it after publicity to numerous pollutions or be afflicted by it for unknown reasons.
- Liver ailment can influence everybody at any age from toddlers to seniors.
- You may have liver ailment and now no longer understand it due to the fact there can be no symptoms. If you've got symptoms, they might take the shape of fatigue, nausea, darkish urine, or jaundice (while your pores and skin or the whites of your eyes flip yellow).
- Cirrhosis is the period used for scarring of the liver that could take place while any shape of liver ailment reaches a sophisticated stage. It isn't always best associated with alcoholic liver ailment.
- Liver most cancers may be the give up result of many kinds of liver ailment.
- When your liver begins to fail, pollution can lower back up into your mind inflicting a circumstance much like dementia.
- The main reason for liver transplants in Canada is hepatitis C however can also additionally quickly get replaced via means of non-alcoholic fatty liver ailment that is intently related to weight problems and diabetes.
- There are vaccines that could save you hepatitis A and B however no vaccine for hepatitis C yet.
- An individual with severe liver ailment can also additionally bleed or bruise effortlessly considering that a failing liver produces fewer proteins that assist clot the blood.
- A liver transplant isn't always a remedy for liver ailment. Some liver illnesses will assault a newly transplanted liver [11].

#### 4.1 Myth and facts about Cirrhosis

Myth	Fact
Not drinking alcohol does not cause cirrhosis.	Cirrhosis is essentially severe liver scarring brought on by several "injuries" over time. These injuries might be caused by a variety of conditions, include hepatitis B or C, hereditary iron or copper deficiency problems, immune system-related liver illnesses, non-alcoholic fatty liver disease, or excessive alcohol consumption[12, 13].
Despite having Cirrhosis there's no need for medication, since liver cells heal naturally.	The liver is a regrowing organ, but only if it is in a healthy condition enough to do so and do not have a lot of scar tissue. Cirrhosis will stop your liver's ability to regenerate. Because of this, cirrhosis can seldom be reversed[14].
Cirrhosis is associated with Liver cancer.	Cirrhosis can cause a variety of problems, including liver cancer. As early detection of many malignancies is vital, your doctor would want you to undertake routine testing utilising plasma and radiologic imaging if you have cirrhosis. Based upon your condition, the site, and the size of the tumour, surgical therapy or transplanting may be able to cure early-stage liver cancer[15].
Gaining weight is advantageous for Cirrhosis.	If you consume too many calories and lose weight as a result, your liver may develop excess fat that might cause severe damage. If water retention is the source of your weight loss, this may be an indication that your liver is failing. It's crucial to have a balanced diet when you have cirrhosis in order to provide your body the nutrients it needs and prevent muscle mass loss[16].
Liver transplant is always necessary in case Cirrhosis is detected.	Your liver can also additionally nonetheless be capable of carrying out all its ordinary capabilities on each day foundation for an extended

	<p>time. However, having cirrhosis method you could enjoy the formerly referred to signs and symptoms and feature a chance for growing liver in most cancers. You may require a liver transplant if your symptoms are not well controlled by medical treatment or if you have early-stage liver cancer that cannot be removed with surgery[17].</p>
<p>A Liver transplantation is a permanent cure for Cirrhosis</p>	<p>Liver transplants are difficult surgical operations that are sometimes a patient's last resort for recovery. Headaches from the surgery can happen, despite the best intentions and attempts of your treatment team. To prevent liver rejections, you'll also need to take medications for life. Moreover, these medications may have side effects such as diabetes, high blood pressure, high cholesterol, renal disease, or neurological issues. Additionally, the new liver might eventually develop relapses of liver diseases such as cancer, autoimmune disease, number one sclerosing cholangitis. Although while a healthy liver is your best opportunity to get back to a normal life if you have severe cirrhosis migraines, the best course of action is to keep it healthy enough to avoid the need for a liver transplant in the first place[18].</p>

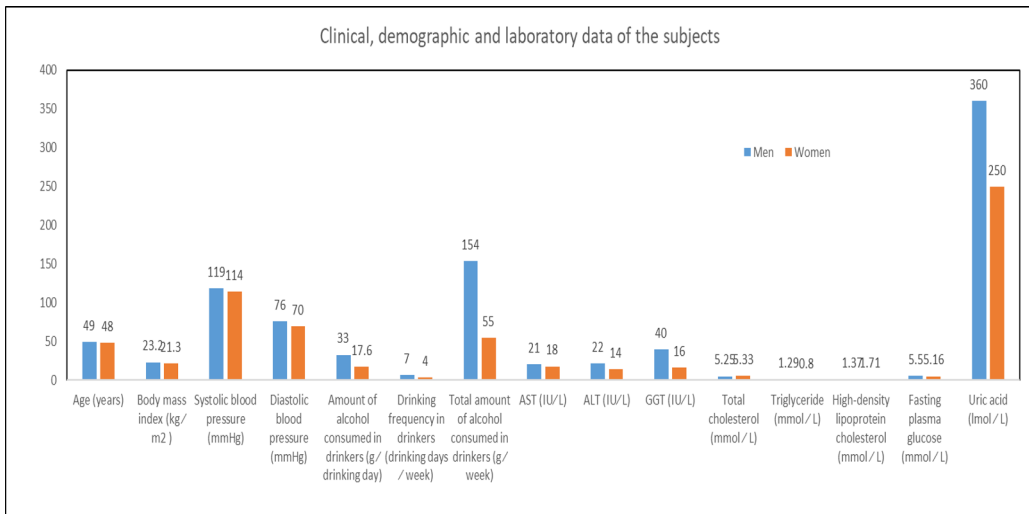
## 5. Case Study

### 5.1 Drinking habits and liver condition of Japanese men and women

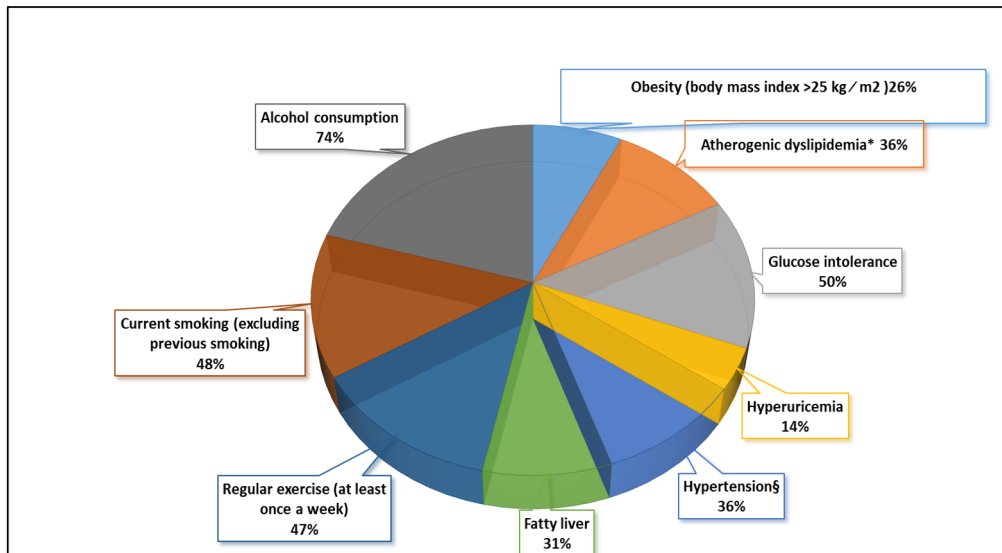
Moriya et al. directed a survey on “Alcohol consumption appears to protect against non-alcoholic fatty liver disease” in the year 2010 with the aim of finding out the drinking pattern and fatty liver in Japanese men and women. The study was conducted in order to gain information about alcohol consumption that was recorded to protect against non-alcoholic fatty liver disease [19].

The 7894 Japanese subjects (5548 men and 2346 women) data included the age, sex, height, body weight, blood pressure, 782 individuals were removed those data didn't match up, only 7112 eligible subjects were given the privilege to participate in the study (4957 men and 2155 women). All the test subjects asked their life-style information like alcohol consumption, smoking history, physical activity and background medical history was obtained by questionnaire. A skilled professionals performed a real-time ultrasonography to find vascular blurring, profound attenuation, and better liver echotexture when evaluating the kidneys for fatty infiltration. Finally, experts validated the data and determined that a fatty liver was present.

It has been concluded that drinking alcohol in moderation may help prevent non-alcoholic fatty liver disease. **Fig.2A** represented all the clinical, demographic, and laboratory data along with the association between alcohol intake and fatty liver. The gender wise metabolic syndrome-related factors are shown in **Fig.2B** and **Fig.2C**, The Individual and multivariable analyses of factors associated with fatty liver is shown in **Fig.2D**. The total consumption of alcohol drink up per week is shown in **Fig.2E** and **Fig.2F**, Comparison of non-drinker and the test subject is shown in **Fig.2G** and **Fig.2H**.

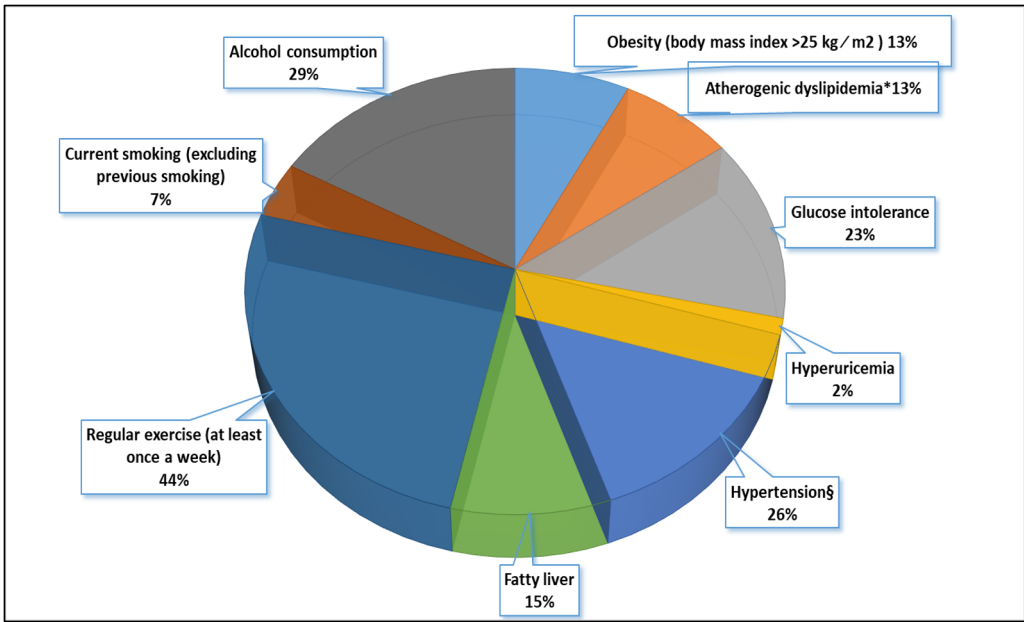


(A)

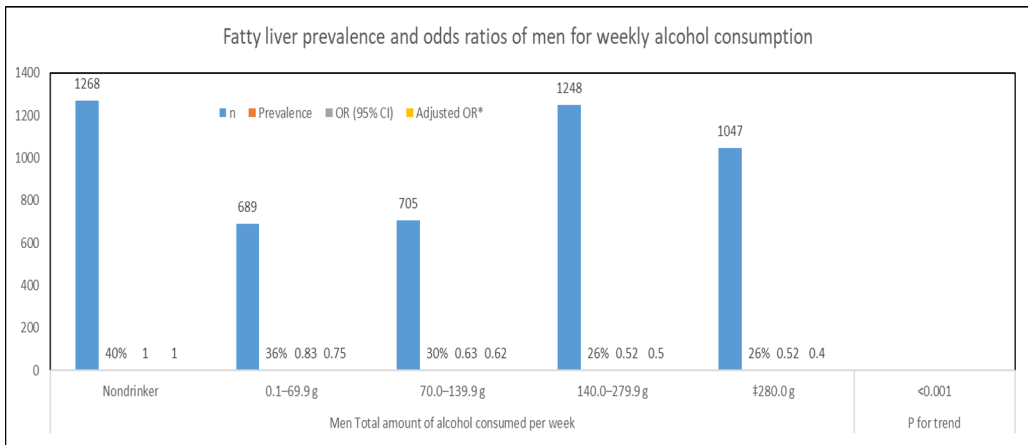


(B)

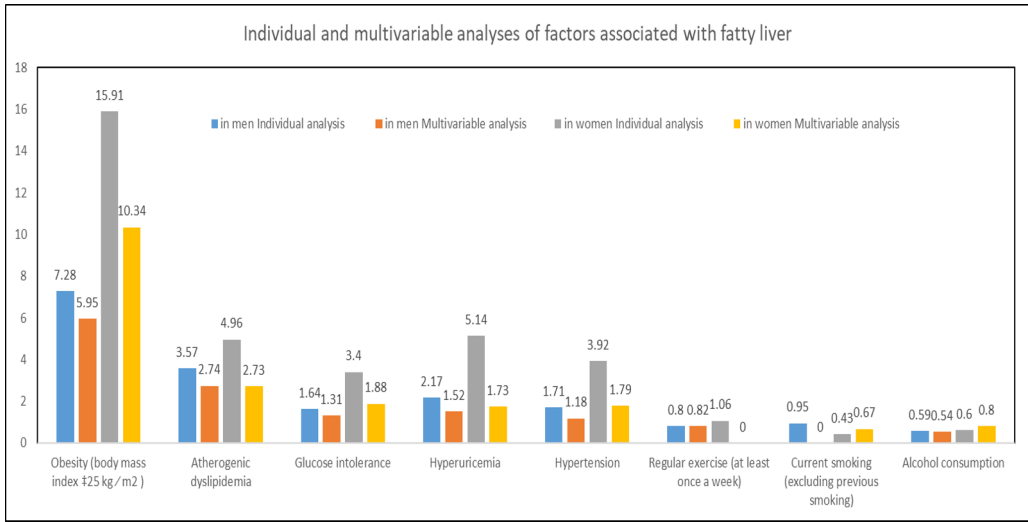




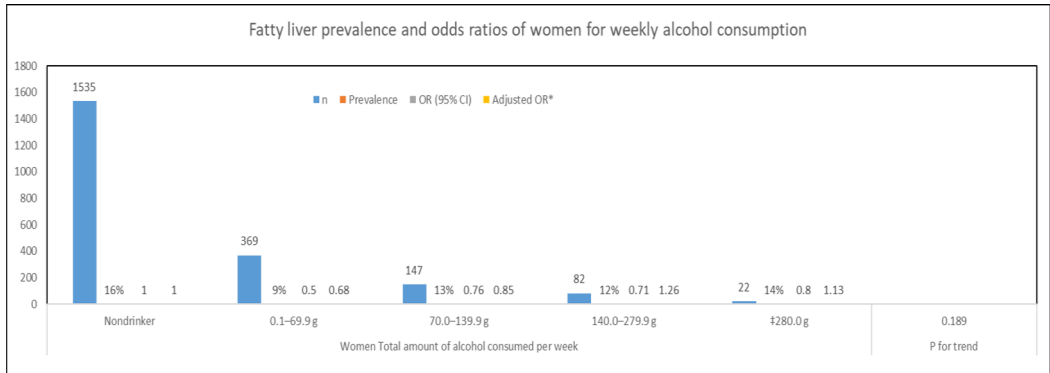
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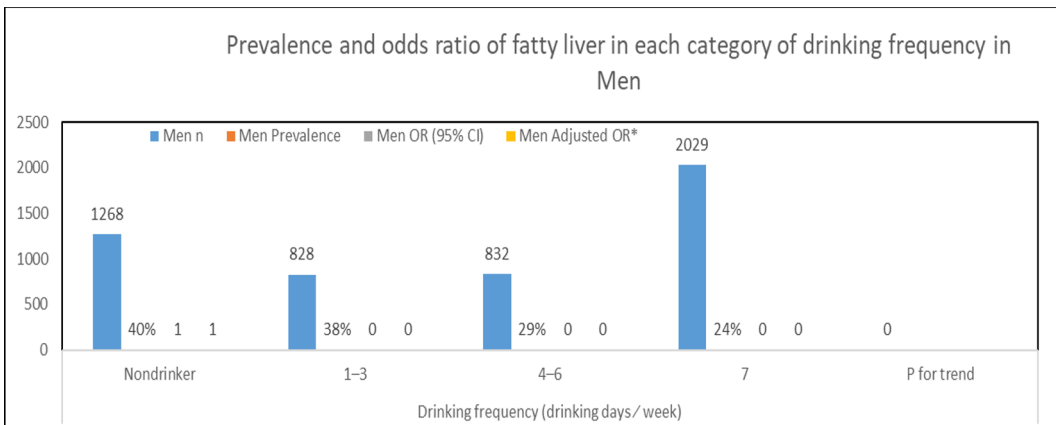
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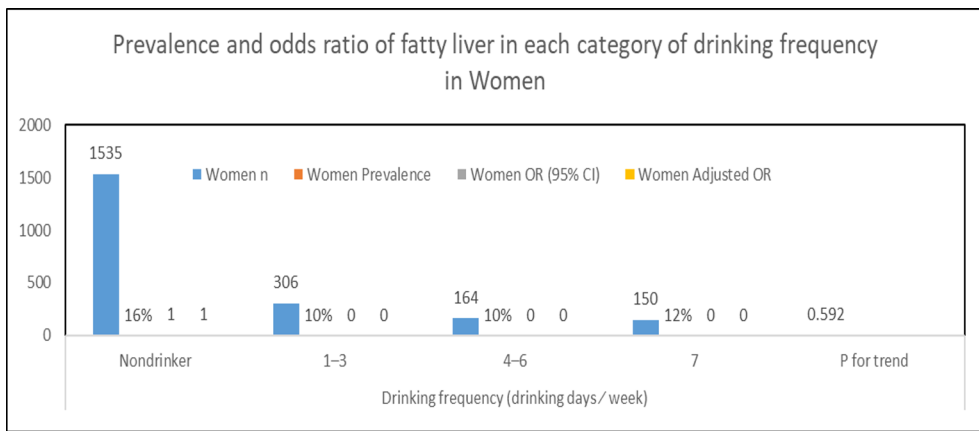
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(F)



(G)



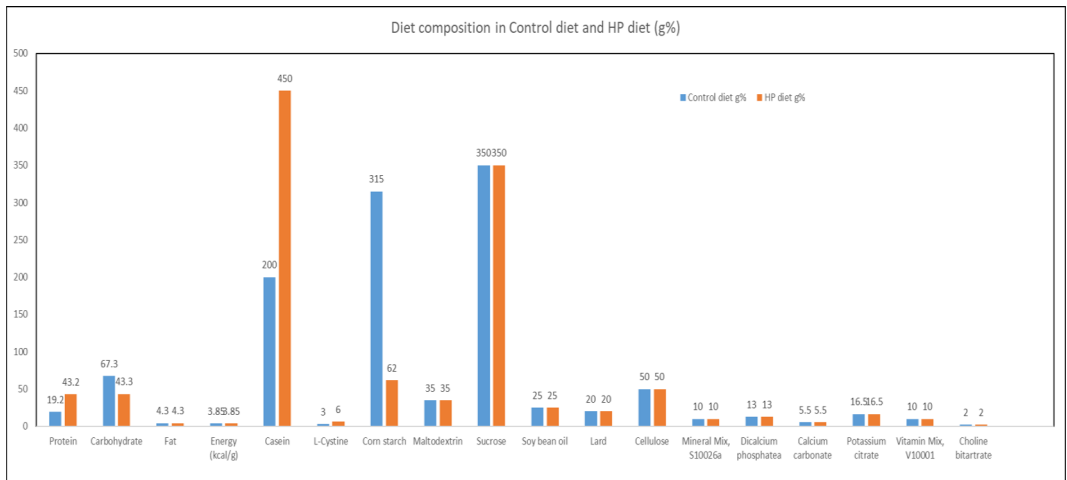
(H)

**Fig.2** (A) Clinical, demographic and laboratory data of the subjects; (B) Metabolic syndrome risk factors prevalent in men; (C) Metabolic syndrome risk factors prevalent in women; (D) Assessments of each individual and combination of elements that contribute to fatty liver; (E) Fatty liver prevalence and odds ratios of men for weekly alcohol consumption (Quantity wise); (F) Fatty liver prevalence and odds ratios of women for weekly alcohol consumption (Quantity wise); (G) Fatty liver prevalence and odds ratios for each type of alcohol consumption in men. (Frequency wise); (H) Fatty liver prevalence and odds ratios for each type of alcohol consumption in women (Frequency wise).

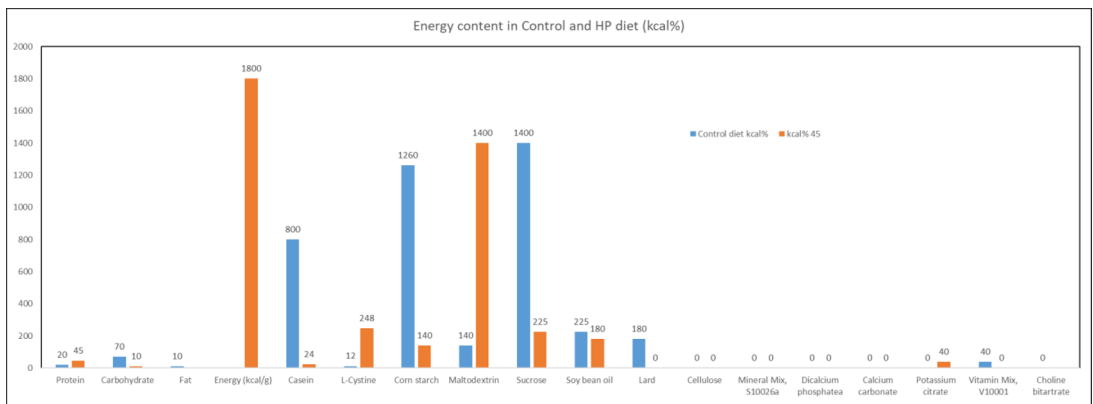
## 5.2 Rats' hepatic symptoms and signs of injury as a result of long-term ingestion of a high-protein diet

Rubén Díaz-Rúa directed a survey on “Long-term consumption of a high-protein food plan will increase liver triacylglycerol deposition pathways and hepatic symptoms and symptoms of harm in rats” in the year 2010 with the aim of finding out the damage caused by protein to the liver in rats as rats are the most closely related to human beings. Consuming high-protein (HP) foods as a daily nutritional workout and/or as component of a lifestyle pattern has become more popular in recent years [20]. HP diets were associated with significant metabolic benefits, including the control and normalisation of several risk factors for metabolic syndrome, such as hyperglycaemia, high cholesterol, and hypertriglyceridemia in obese individuals [21, 22]. The study has also confirmed that eating a lot of protein is linked to a higher risk of weight gain and an increased risk of both fatal and non-fatal consequences [23]. This study adhered to ethical guidelines for the use and care of laboratory animals, as approved by the University of the Balearic Islands Bioethical Committee. 6-year-old male Wistar mice were single-housed at 22°C and put on a twelve-hour light/dark cycle, with the light coming on at 8:00 PM. The rats came from Charles River Research in Barcelona, Spain. age of two months, the rats were divided into two groups based on body weight: a control group (n=7) and a high-protein group (HP, n=6) that was pair-fed as part of a larger animal study [24]. The sample size was chosen in accordance with earlier experimental research that had shown its suitability for identifying statistical differences. The control group was given a normal lipid diet consisting of 70% carbohydrates, 20%, proteins and 10 % fats, while the experimental group was feed high-protein diet with 45% carbohydrates, 45% proteins, and, 10% fats mainly from casein. Both diets, which are isocaloric and had detailed compositions in table 7 you can see the food were bought from Brogaarden and used for four months. Body weight was measured every three days, and food consumption was tracked daily to compute calorie intake. The experimental group ingested 2.3 times as much protein as the control group, a level of protein overconsumption comparable to that observed in people following high-protein weight-loss regimens [25].

The cumulative dietary acid load was determined by two methods, are shown on the diet composition shown in Fig. 3A and Fig.3B. The first method was the Net Endogenous Acid Production (NEAP) calculation, which was derived from the potassium and protein content of the diet using the formula provided by Frassetto et al [26]. (NEAP (mEq/day) = (54.5 x protein (g/day) / potassium (mEq/day)) - 10.2). Potential Renal Acid Load (PRAL) is the second method that is used in this study, by using the Remer et al we estimated the daily intake bu using this method. The high-protein (HP) and control diets came from Experimental Diets, which was bought from Brogaarden in Gentofte, Denmark. Both diets were given as dry pellets and gave with information on the percentage of macronutrients in grams and calories and the energy content in kcal/g. Moreover, the g/kg and kcal/kg constituent compositions are presented [27].



(A)



(B)

**Fig.3** (A) Diet composition in Control diet and HP diet (g%); (B) Energy content in Control and HP diet (kcal%)

The key differences between the two diets are highlighted in bold font. The high protein diet was heavy in casein while the control diet was high in corn starch and other vitamins. The same vendors provided the same amounts of sugar, fats, fibre, minerals, and ions for both diets. Both diets provide 2.96 grams of phosphorus, 6.3 grams of potassium, 0.5 grams of magnesium, & 0.2 grams of calcium per kilogramme [23].

We know that  $0.49 \times \text{protein (g/day)} + 0.037 \times \text{phosphorus (mg/day)} - 0.021 \times \text{potassium} - 0.026 \times \text{magnesium} - 0.013 \times \text{calcium (mg/day)}$  is equivalent to PRAL (mEq/day) [28]. The liver tissue samples were prepared for light microscopy by embedding them in paraffin blocks and cutting 5-µm-thick sections that were mounted on slides and stained with hematoxylin/eosin. By inspecting the full 2 cm<sup>2</sup> region of the histologically stained liver slices from various situations and looking for the existence of fatty vesicles, the existence of hepatic steatosis was determined. Following the manufacturer's instructions, 15-µm cryostat slices were set for 1 hour in 4% paraformaldehyde, rinsed in distilled water, and coloured with the Oil Red O Staining Kit from Abcam, Cambridge, UK, to highlight lipids. The slices were counterstained with Mayer hematoxylin, treated with Oil Red O for 6 minutes, rinsed in distilled water, and mounted in aqueous media (Mount Quick aqueous from Bio-Optica, Milan, Italy). The examination was conducted in a blind manner for all groups [29]. For the microarray analysis, 13 liver RNA samples from both control (n=7) and HP (n=6) groups were used. Samples were randomized and all arrays were processed simultaneously. The labeling and microarray processing steps, including hybridization, washing, and scanning, were performed following a previously described method [30]. Each sample's 1 grams of reverse-transcribed RNA was tagged with Cy5 in half and Cy3 in the other. All Cy3-labeled cRNA samples were blended equimolarly after purifying and measurement. The Cy3 pool was then hybridised with the Cy5-labeled individual samples using 4x44K G4131F rat whole genome Agilent microarrays (Agilent Technologies) [28].

The standard error mean (SEM) is used to display the information for weight gain, adiposity, serum parameters, and microarray findings. The student’s t-test was used to evaluate differences across groups., as specified in the corresponding tables. The normal distribution of the data was confirmed, and the analyses were conducted using SPSS for Windows (version 20) with a significance level set at  $p < 0.05$  or as indicated. The different category on Microarray data processing includes a discussion of the microarray data analysis [28].

## 6 Results& Discussion

The dietary acid load is estimated as the quantity of acid that must be removed by the kidneys in order to keep acid-base balance depends significantly on diet [30]. Based on the combined consumption of the 2 diets during the entire trial period, the predicted dietary acid load was computed to reflect the influence of food on endogenous acid generation [31]. NEAP and PRAL are the two indices of estimated dietary acid load, when compared to animals on the control diet, were discovered to be almost two times higher in rats on the HP diet (Table 1).

Table 1 provides a summary of the weight gain, adiposity, and serum component data that were used in this investigation [24].

The popularity of high-protein consumption is widespread in every country, particularly in relation to weight management, maintenance of weight loss and fitness programs. However, the knowledge about these protein diets is limited and the health consequences. So, we thought it was essential to use healthy animals to look at the effects of prolonged exposure to a high-protein diet. Due to its high nutritional value relative to other protein sources and its abundance of important amino acids and great digestion, our study employed a casein-rich high-protein diet [32].

**Table. 1**Body weight, adiposity, dietary acid load and circulating parameters of the control

Parameters	Control group	HP group
Body weight (g)	500±13	455±12
Adiposity index (% of fat)	8.43±0.70	8.31±1.07
Body fat content (% of fat)	17.8±1.6	18.3±1.7
Cumulative caloric intake (kcal)	10,227±182	8971±495 *
Daily food intake (kcal)	73.2±3.4	69.0±3.4
Cumulative NEAP (mEq)	53,624±0	120,668±0 *
Cumulative PRAL (mEq)	260±5	514±28 *
<b>Circulating parameters in fed state</b>		
Glucose (mg/dl)	97.1±4.4	91.5±3.0
Insulin (µg/l)	1.23±0.22	2.12±0.27 *
HOMA-IR index	2.17±0.49	1.85±0.65
NEFA (µM)	0.62±0.07	0.52±0.05
TG (mg/ml)	7.08±0.63	6.93±1.02
Cholesterol (mg/dl)	200±27	103±27 *
TNF-alpha (pg/ml)	2.64±0.55	13.3±5.7 *
C-reactive protein (ng/ml)	53.1±0.9	76.6±7.0 *
Aspartate transaminase (U/l)	416±29	544±58 *
Urea (mg/dl)	5.08±0.26	8.10±0.68 *

\* $p < 0.05$  where  $n=3$

Liver composition: Table 2 shows that animals on the HP diet had 75% higher levels of liver TG ( $P=.06$ , t-test). However, there was no increase in total lipid content and with no clear signs of macro vesicular lipid presence were observed in haematoxylin/eosin-stained section of the tissue. In sections stained with Oil Red O, diffuse internal fat macrovesicles were seen (data not shown). Although the liver weight remained unaffected, it was larger when expressed as a proportion of the total body weight. The diet had no effect on the amount of hepatic glycogen.

In order to look at potential metabolic changes brought on by the HP diet, they used liver transcriptomics. The microarray research showed that a prolonged HP diet changed the expression of some liver genes. Based on a significance threshold of  $p < 0.001$ , t-test, 148 probes representing 133 distinct genes (110 recognised and 23 unknown) displayed differentially expressed genes between the high protein and control subjects. Just 16% of the known genes were down-regulated, while 84% of them were up-regulated [33].

**Table. 2** Liver composition in animals of the control and HP groups

Parameters	Control group	HP group
Liver weight (g)	13.9±0.4	13.9±0.3
Liver/body weight ratio (%)	2.83±0.05	3.16±0.10 *
Liver glycogen content (mg glycogen/g tissue)	25.3±1.5	22.3±3.9
Liver lipid content (mg lipid/g tissue)	42.6±3.3	38.8±1.3
Liver TG content (mg TG/g tissue)	22.7±3.1	39.9±6.8 *

\*p&lt;0.05 where n=3

The hepatic TG content unexpectedly changed, rising by 75percentage points in the experimental group (HP) versus the control group, despite the experimental group consuming less calories overall. This is essential because the development of non-alcoholic fatty liver disease is thought to be significantly influenced by a build-up of lipids, particularly in the form of TG (NAFLD) [34]. Although there was no obvious evidence of macro vesicular fat accumulation in the test group (HP-fed rats), an increase in the levels of the liver injury markers AST and C-reactive protein indicated hepatic damage. Moreover, heat shock protein HSP90, which has been connected to persistent alcohol-induced hepatic steatosis and hepatocellular cancer, was found in higher quantities in the liver tissue of the HP group [35-37].

It has been concluded that the consumption of a high-protein diet high in casein over an extended period can have a significant effect on liver metabolic pathways, resulting in increased TG deposition, inflammation, and disruptions in pH and oxidative stress levels.[38] While following a high-protein diet for a lengthy term, it's crucial to use caution, especially for people who already have diseases like diabetes, liver disease, or renal disease since they may be more susceptible to its possible side effects.[39] While a significant increase in the protein to starch proportion in the eating plan can help people lose weight, our research indicates that a severe and prolonged increase in protein intake can disrupt the body's natural processes and have unfavourable effects like increased AST levels, inflammation markers, liver TG content, and liver weight.[40] This study is the first to demonstrate that a high-protein diet consumed on a regular basis can significantly raise hepatic HSP90, a sign of liver injury.[41,42]

## 7 Conclusion

The liver very vital organ that works a crucial role in maintaining the health of the body. Despite its importance, there are many misconceptions about liver diseases, and it is essential to distinguish between the facts and myths. It is important to be informed about the myths and facts surrounding liver diseases so that we can make informed decisions about our health and well-being. Early detection and treatment are crucial for the successful outcome of liver diseases, and making lifestyle changes can greatly reduce the risk of developing liver diseases.

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## 9 Declaration of Interest

The authors declare no conflict of interest financial or otherwise.

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