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A Review on the Role of Low Glycemic Index Foods for Glycemic Control in Chronic Liver Disease

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Abstract

Liver is an essential organ that maintains fasting and postprandial blood glucose response via various metabolic pathways. The liver function gradually deteriorates in chronic liver disease (CLD) due to inflammation and destruction of liver parenchyma. The development of glucose intolerance and hepatogenous diabetes (HD) in patients with CLD is an inevitable event. Diabetes and CLD can coexist, and function synergistically to cause unfavorable clinical consequences, including poor treatment outcomes and frequent hospitalization. The complications associated with liver disease (malnutrition, hypoglycemia, acute kidney injury, lactic acidosis, etc.) and lack of guidelines limit pharmacological management of HD. Dietary recommendations by The European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines (2019), suggested weight reducing hypocaloric diet along with adequate branched-chain amino acid (BCAA) and micronutrient consumption to improve steatosis and insulin sensitivity in patients with CLD. Dietary glycemic index controls prognosis of obesity, non-alcoholic fatty liver disease (NAFLD) and diabetes. The importance of low GI diet in reducing fasting blood glucose, hepatic glucose influx and fat accumulation, thereby improving weight loss and NAFLD score, is being published in patients with diabetes or liver disease. Several countries have already incorporated GI into their national health policies, for identification of the nutrient value, resulting in establishment of worldwide GI and glycemic load tables for specific food items. However, the apparent complexity of GI and lack of low GI meal choices need to be resolved in order to enhance patient's quality of life, health and well-being. Low GI nutritional supplements, comprising of balanced proportion of carbohydrate, protein, BCAAs, fibers and micronutrients, may reduce the complexity related to dietary management of HD. The review summarizes the importance of nutritional management in HD with focus on low GI diet in people with CLD.

Keywords

Chronic Liver Disease, Cirrhosis, Hepatogenous Diabetes, Low Glycemic Index, Non-Alcoholic Fatty Liver Disease

1. Background

The liver plays an essential role in maintaining blood glucose homeostasis through regulation of glycogenesis and lipogenesis after having a meal, and glycogenolysis and gluconeogenesis during fasting [1]. In chronic liver disease (CLD), the liver function gradually deteriorates over time due to continuous process of inflammation and destruction of liver parenchyma [2]. Non-alcoholic fatty liver disease (NAFLD), the most common form of CLD may develop to more severe conditions like non-alcoholic steatohepatitis (NASH), fibrosis and cirrhosis [3]. The complications associated with CLD are fatigue, anorexia, weight loss, variceal bleeding, ascites, spontaneous bacterial peritonitis, jaundice, hepatic encephalopathy, hepatorenal and hepatopulmonary syndrome and hepatocellular carcinoma; signs and symptoms can be non-specific and complication-dependent [2]. The treatment of choice for CLD is pharmacological and non-pharmacological therapy including weight reduction, physical activity, dietary changes, avoidance of driving factors (alcohol abstinence) and liver transplantation (for NASH management) [4] [5]. The global prevalences of NAFLD and NASH are estimated to be 25% and 1.5% - 6.5%, respectively. In India, 38.6% adults and 35.4% children have been found to suffer from NAFLD [6].

Approximately 54% patients with NAFLD and 65.26% with NASH are reported to develop type 2 diabetes mellitus (T2DM) [7]. Diabetes, occurring due to liver disease is termed as "Hepatogenous diabetes or HD", which is a separate entity from T2DM, with different risk factors and complications [8]. Pharmacotherapy for HD is limited due to the presence of serious comorbidities like hypoglycemia, hypoalbuminemia, lactic acidosis, poor renal function and slow renal clearance of the drug metabolites [9]. This highlights the importance of dietary modifications or role of nutritional management towards preventing or treating HD. The significant health benefits of low glycemic index (GI) foods for lowering body weight, blood glucose level and postprandial glucose (PPG) response are reported in this patient population [10] [11] [12] [13]. Though clinical dietary recommendations exist for management of NAFLD [14] [15] [16] but specific guidelines for preventing or treating HD are still lacking. This review will summarize the role of nutritional management with focus on low GI diet in patients with CLD.

2. Chronic Liver Diseases and Diabetes Mellitus: A Viscious Cycle

There is a strong relation between NAFLD and T2DM; often, NAFLD and

T2DM coexist and function synergistically to cause unfavorable clinical consequences [17]. Non-alcoholic fatty liver disease raises the risk of future development of T2DM [18], whereas diabetes worsens NAFLD, leading to more severe forms of steatohepatitis, progressive fibrosis, cirrhosis, and hepatocellular carcinoma along with cardiovascular incidents and overall mortality [19] [20]. Also, T2DM was noted to be responsible for poor treatment outcomes and frequent hospitalization in people with cirrhosis because of both cirrhosis and non-cirrhosis related reasons [21]. Nevertheless, CLD as a whole can cause diabetes, a condition known as HD. Improvement in insulin resistance is observed following a successful liver transplant, suggesting that HD is directly related to loss of liver function [22]. Hepatogenous diabetes can even be considered as a marker for advanced stage of liver disease [23] [24].

A recent cohort study by *Vasepalli et al.*, found glucose intolerance in more than 90% of patients with cirrhosis, among whom 42.98% had HD and 47.93% had impaired glucose tolerance [23]. Another cross-sectional study reported HD in 12.5% patients with cirrhosis while glucose intolerance accounted for 21.6% [24]. An Indian study found 12.9% prevalence of diabetes in patients with CLD and higher mortality (20.0%), compared to non-diabetic patients with CLD [25]. In another prospective observational study, 59 cases of HD were recorded among 116 Indian patients with diabetes mellitus and cirrhosis [26]. A study from Central India reported 90.91% (110/121) cases of decompensated cirrhosis, of which 49 patients had HD [23].

2.1. Pathophysiology of Hepatogenous Diabetes

Insulin resistance and pancreatic β-cell dysfunction are the two major reasons for HD development (**Figure 1**). Insulin resistance occurs due to decreased liver mass and functional impairment of portosystemic shunts in the damaged liver [23]. Decreased insulin clearance by the damaged liver leads to hyperinsulinemia, potentiated by increased levels of glucagon, insulin-like growth factor, growth hormone, cytokines and free fatty acids. The persistent hyperinsulinemia reduces insulin receptor affinity and down-regulates their action over target cell membranes. Slow hepatic clearance of toxic advanced glycation end products results in increased oxidative stress and chronic inflammation, further compounding insulin resistance [27]. Insulin resistance stimulates the pancreas to secrete more insulin to fulfill the metabolic effects, and this over-exertion of β-cells leads to β-cell dysfunction and an eventual decrease in β-cell mass [28]. In patients with advanced cirrhosis, systemic hypoxia occurs due to liver fibrosis, vascular resistance and portal hypertension, which increases blood flow resistance and leads to pancreatic β-cell dysfunction [27]. Death of pancreatic β-cell, in chronic hepatitis, occurs through molecular mimicry of hepatitis C virus proteins with glutamic acid decarboxylase [27]. β-cell damage in alcohol-related liver disease and hemochromatosis disease is caused by ethanol and excessive iron deposition, respectively [27].

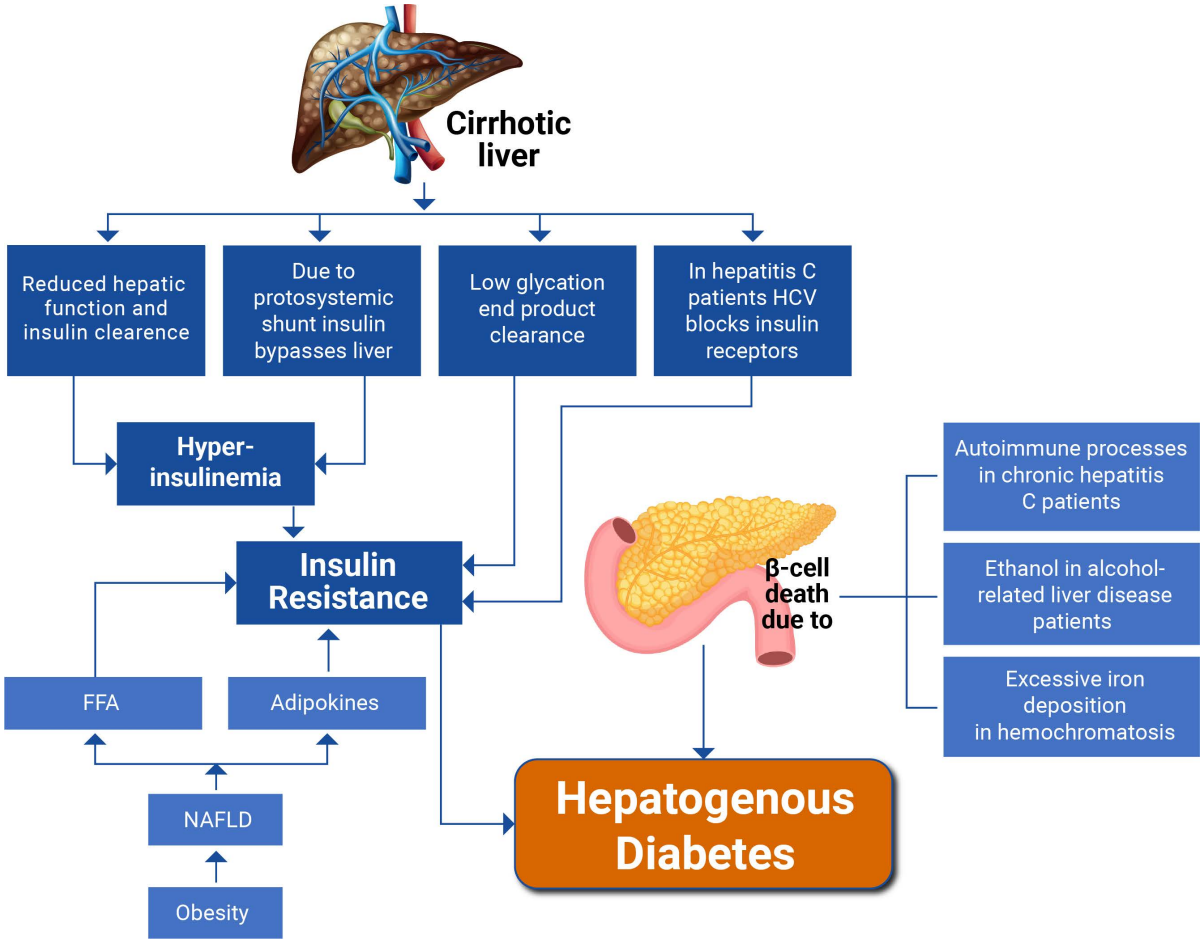

Figure 1. Pathophysiology of hepatogenous diabetes in patients with liver cirrhosis. FFA: Free fatty acids; HCV: Hepatitis C virus; NAFLD: Non-alcoholic fatty liver disease.

2.2. Clinical Difference between Hepatogenous Diabetes and Type 2 Diabetes Mellitus

The bidirectional nature of the relationship linking glucose metabolism inefficiency to chronic liver damage makes it difficult to distinguish HD from T2DM [29]. Both T2DM and HD are observed among people with CLD, yet their clinical features are vastly different [30] [31] [32]. The differences are necessary to understand for better selection of a treatment regime (**Figure 2**).

3. Management of Hepatogenous Diabetes

Papazafiropoulou & Melidonis (2019) have listed three challenges with diabetes management in patients with CLD: 1) presence of serious comorbidities like hypoglycemia, poor renal function, hypoalbuminemia, and lactic acidosis; 2) susceptibility to develop acute kidney injury, resulting in failed renal clearance of the drug and its metabolites; and 3) presence of malnutrition due to impaired metabolism of carbohydrate, protein, lipid, vitamin, and minerals in the liver [9]. Despite these limitations, a particular diabetes management approach must be established in order to reduce the rate of end-stage liver transplantation and

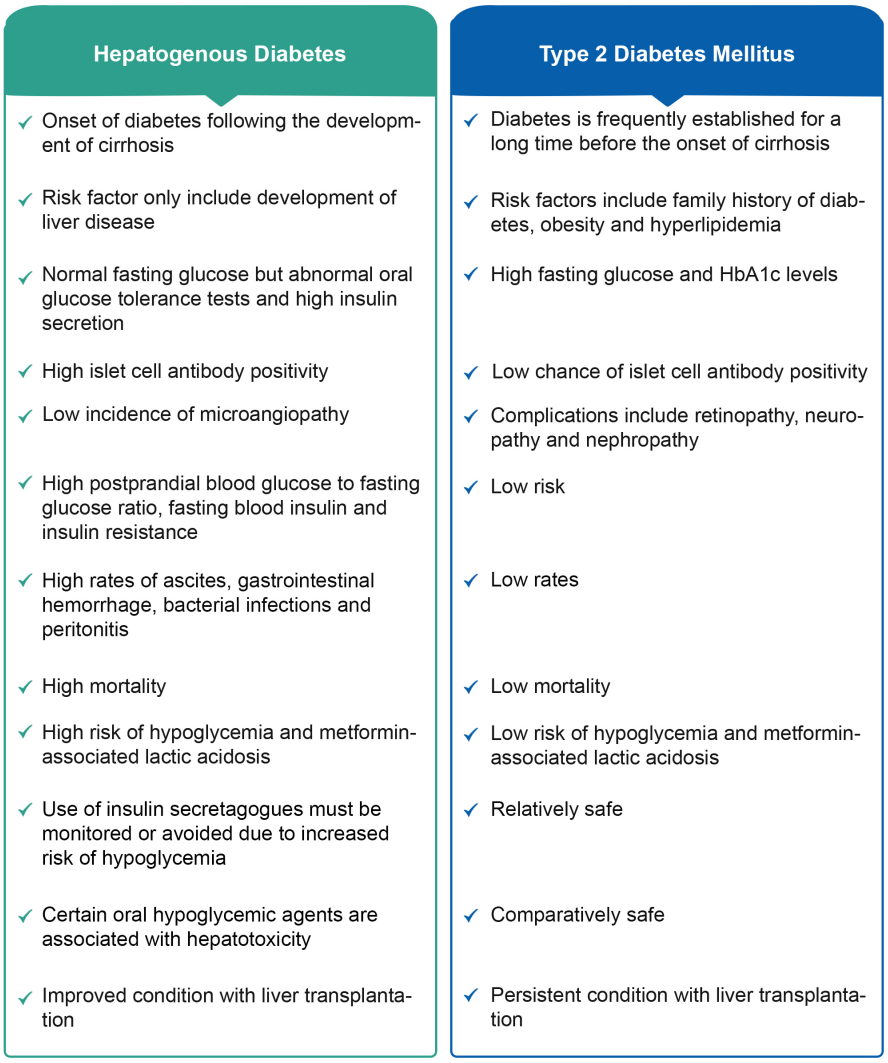

Figure 2. Difference between hepatogenous diabetes and type 2 diabetes mellitus.

mortality in patients with CLD.

3.1. Pharmacological Management of Hepatogenous Diabetes: A Challenge

Pharmacological management of HD is difficult as patients with cirrhosis develop acute kidney injury, leading to slow clearance of drugs/metabolites, resulting in hepatotoxicity. In addition, malnutrition causes protein deficiency-associated hypoalbuminemia, due to which protein-bound drug concentration is increased in blood and results in toxicity. Also, insulin resistance reduces insulin degradation in such patients, and leads to hyperinsulinemia and hypoglycemia that must be considered before initiating pharmacological treatment [33]. There is no direct guideline for HD management; hence anti-hyperglycemic therapy must be used after considering the CLD-related complications and not only diabetes-related complications. Metformin is the first-line therapy for patients with diabetes and cirrhosis, but assumed to increase the risk of lactic acidosis [27]. However, in

other studies, metformin was reported to decrease body mass index (BMI), hepatic fat, hepatic enzymes, glycated hemoglobin or HbA1c [34] [35], all-cause mortality [36], and hepatic encephalopathy [37]. American Diabetes Association (ADA) has declared acarbose safe and well-tolerated in patients with CLD, but it increases the risk of hyperammonemia in patients with advanced hepatic impairment [9]. Sulphonylureas, another oral hypoglycemic agent must be avoided in people with cirrhosis due to reduced hepatic clearance, and risk of hypoglycemia, hypoalbuminemia and acute liver decompensation [38]. A longitudinal cohort of Taiwan's National Health Insurance Research Database (>1 million patients with compensated cirrhosis) reported higher risk of mortality and decompensation with metformin [39], decompensated cirrhosis, variceal bleeding and hepatic failure with dipeptidyl peptidase-4 inhibitor [40] and higher risk of all-cause mortality with insulin use [41].

3.2. Nutritional Management

The major challenges associated with pharmacotherapy directed the clinicians to select non-pharmacological strategy like nutritional intervention in CLD patients. Few evidence-based guidelines are available for nutritional and metabolic management of CLD. A total of 85 dietary recommendations were made by European Society for Clinical Nutrition and Metabolism (ESPEN) guidelines for patients with acute liver failure, alcoholic steatohepatitis, liver cirrhosis, NAFLD, nutrition associated liver injury, and patients undergone liver surgery or transplantation [15]. Some of the recommendations include increased physical activity along with weight reducing/Mediterranean diet to improve insulin resistance, steatosis, liver enzymes and histology in NAFLD or NASH patients; and gluten free diet in patients with celiac disease and NAFLD/NASH, to prevent progression to cirrhosis. The guidelines also recommend use of branched-chain amino acid (BCAA), vegetable protein diets, immunonutrition with arginine supplementation, vitamin A, D and K, thiamine, folate and pyridoxine in alcoholic steatohepatitis, and late evening snacks or nocturnal supplements to reduce the duration of starvation in cirrhosis [15]. The recommended nutritional and lifestyle interventions for management of NAFLD in clinical practice guidelines by ESPEN, European Association for the Study of Liver (EASL), European Association for the Study of Diabetes (EASD) and European Association for the Study of Obesity (EASO) or EASL-EASD-EASO, and American Association for the Study of Liver Diseases (AASLD) [14] [15] [16] are summarized in **Table 1**.

Evidence on Nutritional Management

Besides pharmacotherapy, weight loss can be achieved following recommended dietary plan for CLD patients. In such patients, the nutritional status must be routinely monitored to identify malnutrition and to prevent nutritional deficiency. Carbohydrates are the basic diet in people with cirrhosis, covering up to 50% - 60% of their non-protein daily needs, hence foods rich in complex carbohydrates must be considered [42]. Consumption of complex carbohydrates like

Table 1. Recommendations for patients with non-alcoholic fatty liver disease.

Nutritional and lifestyle interventions	EASL-EASD-EASO (2016)	AASLD (2018)	ESPEN (2019)
Ideal body weight	7% - 10% total weight loss target in overweight/obese NAFLD cases	7% - 10% total weight loss	• 7% - 10% weight loss in obese patients • >10% to improve fibrosis
Energy consumption	500 - 1000 kcal/day	No specific recommendations	Hypocaloric diet (according to current obesity guidelines)
Macronutrient	• Low-to-moderate fat and moderate-to-high carbohydrate intake • Low-carbohydrate ketogenic or high-protein diets • Macronutrient should be adjusted according to Mediterranean diet	No specific recommendations	Mediterranean diet to improve steatosis and insulin sensitivity
Micronutrients	Short-term treatment with vitamin E (800 IU/day) for non-cirrhotic non-diabetic NASH cases	vitamin E for patients with advanced fibrosis and without diabetes mellitus	Specific vitamins, including vitamin A, D and K along with thiamine, folate and pyridoxine to correct deficiency
Fructose	Avoid	No specific recommendations	No specific recommendations
Alcohol	Strictly keep alcohol below the daily risk threshold (30 gm in men; 20 gm in women)	• Men: 21 standard drinks/week • Women: 14 standard drinks/week	Abstain, to reduce risk for comorbidity and to improve liver biochemistry and histology

beans, legumes and whole grains along with fiber intake of at least 25 gm improves insulin resistance and hepatic steatosis [43]. Carbohydrate restriction in patients with NAFLD reduces liver inflammation, hepatic fat accumulation, liver enzyme levels and hepatic *de novo* lipogenesis [43]. Another major macronutrient is protein that provides 10% - 15% of total calories along with the 20 naturally occurring amino acids, including 9 essential amino acids [44]. In patients with liver cirrhosis, an energy intake of 35 - 40 kcal/day/kg body weight and protein intake of 1.2 - 1.5 gm/day/kg body weight is recommended [45]. Daily intake of this amount of protein is helpful in preventing sarcopenia, but should be avoided in case of moderate-to-severe renal insufficiency [46]. Consumption of isocaloric diet, comprising of moderate total fat and low saturated fat lowers the risk of NAFLD [47]. Fast foods, vegetable oil, cakes and pastries contain trans-fatty acids, while fatty meat, butter, full fat dairy products, and tropical oils (palm and coconut oil) contain saturated fatty acids, therefore must be avoided. Moreover, polyunsaturated fatty acids, found in rapeseed oil, soy, walnuts and flaxseed oil improves low-density lipoprotein cholesterol and insulin sensitivity than monounsaturated fatty acids, found in olive oil, rapeseed oil, soy, avocados, certain nuts and fish oils [48]. However, consumption of a diet rich in 27% monounsaturated fatty acids with prescribed aerobic exercise have been shown to

lower liver fat [47]. Mediterranean diet comprising of high amount of bio-active phytochemicals, antioxidants, 44% fat (>50% monounsaturated), 36% carbohydrate, 17% - 20% protein and up to 5% alcohol has favorable benefits on insulin sensitivity [49]. Patients unable to follow these dietary proportions may benefit from readymade supplementations, available in the market.

According to the World Health Organization, for a healthy adult the daily requirements of BCAAs, valine, leucine and isoleucine are 26, 39 and 20 mg/kg body weight, respectively [50]. In patients with NASH-related cirrhosis, prolonged use of BCAA improves glucose tolerance, indicating its long-term use for NASH treatment [51]. Branched-chain amino acid therapy (3 packs of a BCAA nutrient orally, 4.15 gm/pack) for 12 weeks, reduces HbA1c concentrations and improves insulin resistance in patients with chronic hepatitis C and insulin resistance [52]. As per MEDIGENE program (the database of Romanians, Turkish and Albanians) the highest BCAA content is found in cheese (30.41%), followed by red meat and poultry (29.73%), fish and seafood (17.57%), lunch meats (7.43%) and organ meats (5.41%) [53].

Micronutrient deficiencies in liver illness are associated with hepatic function abnormalities and reduced reserves, as well as insufficient food intake and/or malabsorption as the disease progresses [54]. The water-soluble vitamins (particularly group B vitamins), zinc and selenium deficiencies are common in cirrhosis, especially that of alcoholic origin [42]. Minerals like zinc and selenium are responsible for normal cell functioning; zinc is required for cell growth and differentiation, and selenium has antioxidant functions [54]. Vitamin B1 is essential for glucose and amino acid metabolism, and vitamin B2 is a cofactor to be involved in energy metabolism and antioxidant responses [54]. According to a retrospective research, the majority of patients with liver disease undergoing liver transplantation have vitamin A and D deficits [55]. Vitamin A (retinol) has a major role in ocular retinoid metabolism, immunity and tissue repair, and vitamin D has a role in bone homeostasis, cell proliferation and differentiation, immunomodulation and inflammation reduction [54] [56]. Food intake and nutritional state can be indirectly enhanced by improving dysgeusia using zinc and vitamin A supplements [57]. The ESPEN recommends that micronutrients should be given to cirrhotic patients to treat confirmed or clinically suspected deficiency [57]. Moreover, the deficits also can be corrected with nutritional supplementations [46].

4. Glycemic Index: Quick Measure of Carbohydrates in Foods

A new approach to measure the quality and quantity of carbohydrates in a food is by estimating the GI value. The glycemic load of a food is the GI multiplied by the available carbohydrate (gm) in the serving, divided by 100 [58]. A GI of ≤55 is considered as low, 56 - 69 as medium, and ≥70 as high, based on a glucose scale [59]. Multiple factors including proportions of available carbohydrates, types of sugars, the botanical source of starch, the particle size of the food, lipid-

and protein-starch interactions, fiber matrix and presence of viscous fibers play a role in determining the GI of a food [60].

Several organizations concerned with health promotion, such as the ADA, Canadian Diabetes Association, and Diabetes UK have expressed support for this concept. A few countries, such as Australia, Sweden and France have incorporated GI into their national health policies. This has resulted in the establishment of worldwide GI and glycemic load tables for specific food items, such as various varieties of boiled rice, breakfast cereals, bread, noodles, legumes, vegetables, fruits as well as fruit products, dairy and snack products, and sweets [61]. These tables, however, cannot be applied to the Indian context, because the foods consumed in India are diverse, consisting of various components with significantly different source of carbohydrates [61]. Hence, a table of GI value as well as the carbohydrate content for the Indian foods is necessary.

4.1. Sugar Restriction Can Be Achieved with Low Glycemic Index Foods

People are not well-aware about the nutritional value of their regular dietary choices. An Indian study on 140 obese patients with NAFLD reported that choice of full cream milk (60.0%), daily consumption of high sugar (59.3%) along with honey, and/or jaggery, sugar-sweetened beverages and fruit juices (thrice/week) (32.0%), and regular consumption of fast food, bakery products (55.0%) and fried Indian savory snacks (44.3%) are very common [62]. Consumption of excess refined sugar and high-fructose corn syrup lead to increased liver fat, and development of NAFLD [63]. Fructose elevates the risk of fat accumulation in the liver and increases hepatic *de novo* lipogenesis in a dose-dependent fashion, which is poorly regulated in patients with NAFLD [64]. However, a randomized clinical trial has reported a significant improvement in hepatic steatosis in adolescent boys with NAFLD, after 8 week restriction of dietary glucose, fructose, and sucrose (used to consume through sweetened foods and beverages) [64].

Dietary GI offers long term health benefits by controlling prognosis of obesity, NAFLD and T2DM [65]. Low GI diet reduces daily blood glucose level and PPG response in healthy individuals as well as increases the fat oxidation [10]; thereby enhances the overall health and prevents risk of certain chronic diseases. Hypocaloric diet with lower number of calories helps to maintain the intrahepatic triacylglycerol, and improves markers of insulin sensitivity/glycemic control in patients with both NAFLD and T2DM [66]. The overall effect of Low GI diet is summarized in **Figure 3**.

4.2. Benefits of Low Glycemic Index Foods: Clinical Evidences

Clinical studies on low GI diet targeting HD management in patients with CLD remain limited. In spite of this lack of information, the available findings on low GI foods are discussed here to outline its beneficial role. As per the data of Nutrition Examination and National health survey in patients with NAFLD and concomitant diabetes, target weight loss (3% - 5%, 7% - 9% and ≥10% for hepatic

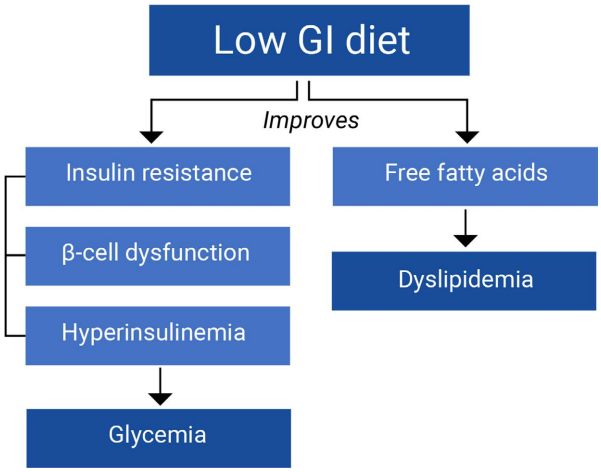

Figure 3. Effect of low glycemic index diet.

steatosis, inflammation and liver fibrosis respectively) can be achieved by lifestyle and dietary modifications [67]. Low GI diet is the proposed lifestyle intervention for NAFLD and CLD, as it reduces hepatic glucose influx and *de novo* lipogenesis [68]. Additionally, it may lower hepatic fat mass and alanine aminotransferase in people with NAFLD [69]. A recent meta-analysis found higher effect of low GI diet in controlling BMI than ADA-recommended, Mediterranean, modified Mediterranean, high GI, low fat, low GI Mediterranean, low carbohydrate, high cereal fiber, low glycemic load and high glycemic load diets [13]. However, Curci *et al.*, recorded improvement in metabolic-associated fatty liver disease with a low GI Mediterranean diet and a combined exercise program for 12 months [70]. Other studies on low GI Mediterranean diet in patients with moderate or severe NAFLD also reported reduction in NAFLD scores [71] [72]. In obese children with hepatic steatosis, low glycemic load diet decreased liver fat and resulted in moderate weight loss within 6 months by diminishing the postprandial glycemia and hyperinsulinemia [11]. In older and obese prediabetes patients, low GI diet and aerobic exercise for 12 weeks reduce inflammatory markers, especially TNF-α, which has a significant role in development of insulin resistance and T2DM [73]. After 1 month consumption of low GI diet, a decline in levels of TNF-α along with IL-6 and non-esterified fatty acids are also found in T2DM patients of another study [74].

Among adults, low carbohydrate and low GI diets have provided preliminary evidence of treatment efficacy for fatty liver and related metabolic diseases [11]. Low GI breakfast and evening snacks were reported to improve the 24 hour glycemic profile and energy balance, and reduced the food intake in healthy Chinese males [75]. A recent study reported that a high protein and low glycemic diet led to a significant controlled attenuation parameter remission, body weight or fat reduction, and improved metabolic markers in patients with metabolic fatty liver disease [12]. Another study also recommended low glycemic and low calorie diets for diabetes management in patients with concomitant liver disease [76]. A previous meta-analysis found reduced levels of fasting insulin and fat

free mass with long-term intake of low GI/low glycemic load foods that might help in prevention of obesity-associated diseases [77]. A systematic review and meta-analysis of randomized controlled trials has suggested improved glycemic control, blood lipids, adiposity and inflammation with low GI/low glycemic load diet in patients with diabetes [78].

In comparison to high GI diet, low GI diet together with exercise for 12 weeks was reported to reduce cardio-metabolic risk factors in older (66.2 ± 1.1 years) adults [79]. A systematic review and meta-analysis showed that low GI diets have a more beneficial effect on glycemic control in terms of HbA1c than high GI diets in patients with T2DM [80]. Sevastianova *et al.*, reported that liver fat was increased during 3 weeks of high GI carbohydrate overfeeding, but decreased with weight loss [81]. Hepatic fat accumulation was reported in healthy males after consuming high GI diet for 7 days in a previous study, and the authors concluded that low GI diet should be followed in NAFLD, obesity and related metabolic disorders [65]. Details of some of the intervention studies are summarized in **Table 2**.

Table 2. Intervention studies assessing the effect of low glycemic index diet.

Reference	Study type	Sample	Intervention	Results
[72]	Randomized clinical trial	• n = 144 with moderate or severe NAFLD • Age: >30 to <60 years • BMI: ≥25 kg/m^2	Low GI Mediterranean diet with aerobic activity program	Reduced NAFLD scores after 45 days of treatment
[70]	Observational	• n = 54, suffering from metabolic dysfunctions • Age: 53 ± 10 years • BMI: 32 ± 5 kg/m^2	Low GI Mediterranean diet and low-intensity aerobic exercises, accompanied by easy to perform strengthening exercises	• Statistically significant direct effect on BMI • Statistically significant direct effect on Homeostatic Model Assessment for Insulin Resistance or HOMA-IR • Improved status of metabolic-associated fatty liver disease
[12]	Randomized controlled trial	• n = 63 with metabolic-associated fatty liver disease • Age: 39.3 ± 8.9 years	High protein and low GI diet for 12 weeks	• Loss in body weight • Reduced body fat percentage • Improved visceral fat and blood glucose-related indicators
[13]	Meta-analysis	n = 2002, having either obesity, diabetes, metabolic syndrome or cardiovascular disease	Low GI diet	• Reduced BMI ($p < 0.05$) • Improved BMI after interventions of >24 weeks • Controlled fasting blood glucose and HbA1c
[74]	Randomized controlled parallel trial	• n = 20 with T2DM • Age: 42.4 ± 5.1 years • BMI: 29.2 ± 4.8 kg/m^2	Low GI test meals (breakfast and afternoon)	• Reduced body fat • Reduced negative metabolic and inflammatory responses
[78]	Systematic review and meta-analysis	n = 1617 with type 1 and 2 diabetes	Low GI/glycemic load diet	• Reduced HbA1c, fasting glucose, triglycerides, body weight and BMI • Improved glycemic control, blood lipids, adiposity, and inflammation beyond concurrent pharmacotherapy

The above-mentioned evidences indicate the importance of promoting low GI foods for management of metabolic complications in patients with CLD. Understanding the GI values of food or beverage can assist dieticians in formulating and advising customers to choose appropriate low GI diets that are expected to minimize the rate of obesity, T2DM, liver disease and HD, especially in developing nations like India.

4.3. Analytical Approach to Healthy Food Choices

The inclusion of low GI foods in diet of patients with liver disease can enhance quality of life, health and well-being by reducing the disease progression to advanced stage. However, the apparent complexity of GI has been identified as the barrier to GI utility on numerous occasions. The following three impediments or complaints frequently reinforce the conclusion that the GI concept is overly complex: GI education contradicts current dietary standards, GI nomenclature is perplexing, and GI education materials are scarce [82]. Furthermore, consumers do not embrace the low GI diet because it restricts their meal options, as parboiled or basmati rice is suggested over processed rice; olive oil, ground nut oil and butter over white bread or rice; coarse grains over refined flour; and to add meat, fish, egg, cinnamon, vinegar, ginger, legumes and high fiber vegetables to the diet [83]. Other barriers include "forgetfulness", "lack of choice when dining out" and "lack of ideas for cooking" [82]. All these roadblocks need to be resolved in order to provide a better diet choice.

Public awareness on dietary issues can be increased by GI food labeling and therapeutic dietary recommendations [65]. Labeling options that a multicomponent food contains complete food ingredients that are intact or reconstituted to their native amounts are commonly allowed [84]. Food labeling to highlight the presence of a broad category of quality carbohydrates (e.g. whole grains inside the food) that fit with consumer conceptions of a healthy dietary pattern and dietary guidelines can be a useful consumer labeling tool [84]. The importance of low GI for glycemic control makes it essential to declare GI values of all the foods available in the market. Furthermore, low GI nutritional supplements comprising of balanced proportion of carbohydrate, protein, BCAA, fibers and micronutrients, suitable for CLD patients must be prepared to reduce the complexity and difficulty related to dietary management of the disease.

5. Conclusion

In CLD patients, insulin resistance and pancreatic β-cell dysfunction lead to development of HD *i.e.*, a state of impaired glucose regulation due to loss of liver function. Pharmacological treatment of HD is challenging because of lack of proper guidelines, as well as poor renal clearance, and events of hypoglycemia and lactic acidosis. Dietary and lifestyle changes appear to improve the glycemic response and quality of life in patients with CLD. This review has summarized the available evidences on importance of low GI diet in reducing hepatic glucose

influx and fat accumulation, and improving weight loss and NAFLD score. In addition, advantages of consuming high protein, low saturated fatty acids, and BCAA, micronutrient and complex carbohydrate enriched diet are also outlined. In conclusion, dietary modification with low GI food/supplement is the cornerstone for preventing or treating metabolic complications in people with CLD.

Authors' Contributions

Bhoite R conceptualized, reviewed, and approved the final manuscript; Joshi NA reviewed and approved the manuscript; Pratti VL conceptualized and reviewed the manuscript; Satyavrat V reviewed and approved the final draft of the manuscript.

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Conflicts of Interest

The authors declare no conflicts of interest regarding the publication of this paper.

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