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A Narrative Review Article

Contemporary directions in fatty liver disease in light of low-carbohydrate approach: a review by public health India

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Abstract

This study aims to equip health professionals with essential directions for their practice and research in fatty liver disease. In fatty liver disease, excess fat is accumulated in the liver cells, and it mainly has two types: Alcoholic Fatty Liver Disease (AFLD) and Non-Alcoholic Fatty Liver Disease (NAFLD). AFLD is widely accepted to be associated with excessive alcohol consumption. However, in NAFLD's case, although the name acknowledges that it is not associated with excessive alcohol consumption, the exact cause of NAFLD remains ambiguous. Furthermore, for almost four decades, without specialised treatments and prevention strategies, NAFLD has constantly increased, affecting more than a quarter of the world's population. Meanwhile, although the current dietary recommendations for NAFLD patients orbit around the conventional High-Carbohydrate Low-Fat diets, mounting evidence advocates the broader benefits of Low-Carbohydrate High-Fat (LCHF) diets in this regard.
Therefore, focusing on the databases such as PubMed, Cochrane Library, and Google Scholar, the authors have carried out an advanced literature search reporting on the efficacy of LCHF diets on NAFLD. After a comprehensive search—using appropriate "keywords and Boolean operators" and "inclusion & exclusion criteria"—the authors selected a potentially relevant set of existing peer-reviewed articles for this narrative review. After critically investigating the LCHF-NAFLD theme, the authors found that LCHF diets may significantly decrease liver fat and may even reverse the disease by targeting the key causes of hepatic fat storage, i.e., high insulin levels, excessive calorie consumption (mainly from carbohydrates), and excessive consumption of refined carbohydrates. Additionally, LCHF diets may provide a comprehensive health benefit beyond liver health. The authors conclude that the LCHF-NAFLD theme represents a rich vein of research opportunities. The authors encourage and call researchers, doctors, nutritionists, dieticians, and related-health professionals to engage more with the LCHF-NAFLD theme.

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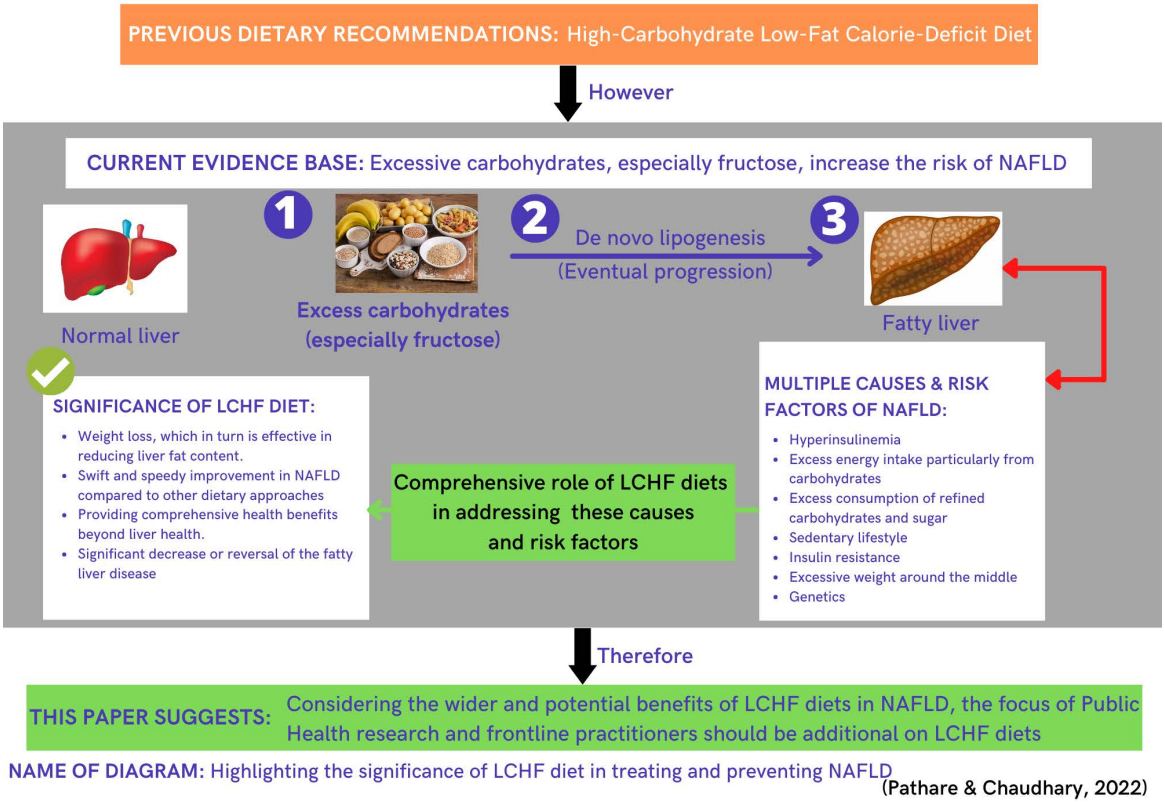
Graphical abstract



(Pathare & Chaudhary, 2022)

Keywords: non-alcoholic fatty liver; hepatic steatosis; nonalcoholic steatohepatitis; liver cirrhosis; low carbohydrate diets; high fat diets; dietary guidelines; public health; weight loss; obesity; exercise; public health research; frontline practitioners

1. Brief statement of purpose

"Public Health India"—a health advocacy and research organisation—publishes this review to spotlight a rich vein of nutritional research that potentially may solve—and even may reverse—fatty liver disease. This review performs this by bringing together—and highlighting—the work of leading researchers across the globe dissecting the effect of diet on fatty liver disease. The supplementary information regarding "Public Health India" is provided in appendix-A.

2. Introduction

2.1 Introduction to fatty liver disease

In Fatty liver disease, excess fat is accumulated in the liver cells. A healthy liver contains a small amount of fat (Petaja & Yki-Jarvinen, 2016) [27]; however, in fatty liver disease, the fat percentage in the liver cells accounts for more than 5% of the liver's weight (McPherson *et al.*, 2015) [21]. Mainly there are two types of fatty liver diseases—first, Alcoholic Fatty Liver Disease (AFLD), and second, Non-Alcoholic Fatty Liver Disease (NAFLD). Historically, as explicated by Ayonrinde (2021) [2], fatty liver was almost solely associated with persons consuming substantial amounts of alcohol. This alcohol-induced fatty liver disease is called AFLD.

On the other hand, as the name suggests, NAFLD is caused primarily by factors other than alcohol. The name also suggests that the exact cause of this disease is still unclear because—

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unlike AFLD—the cause is not mentioned in the name. NAFLD was first described in 1980 (Ludwig, Viggiano, McGill, & Oh, 1980) [16], and it shares the same histological features of AFLD except for alcohol consumption, as this disease is evident even in the population consuming little to no alcohol.

2.2 Current public health challenge

Without specialised treatments, the number of individuals with NAFLD is constantly growing and the disease already affects more than a quarter of the world's population. This collectively suggests that despite the passage of 40 years—since 1980—our understanding of this disease remains imprecise. Additionally, increased fat build-up in the liver is a significant risk factor for Type 2 diabetes, one of the most significant contemporary public health challenges (Taylor, 2008) [35].

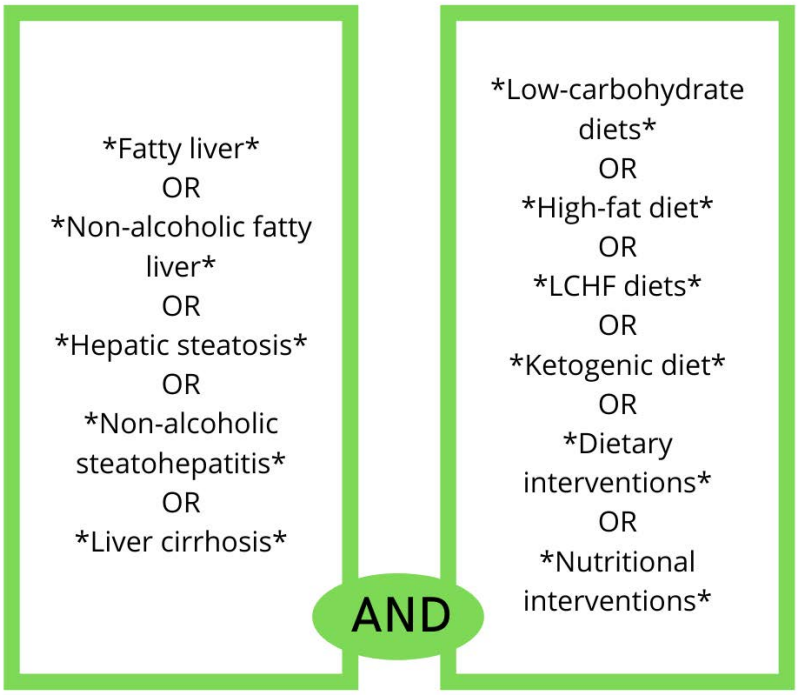
2.3 Significance of this review

The data discussed so far powerfully signal public health and medical researchers to address the NAFLD treatment and prevention strategies urgently. Therefore, to help researchers, this review by "Public Health India" highlights a potential research-theme worthy of studying. This review—acting as a compass—intends to equip health professionals with an essential direction for their practice and research in NAFLD.

3. Methodology

3.1 Data sources and search method

The authors have carried out an advanced literature search reporting on the efficacy of Low-Carbohydrate High-Fat (LCHF) diets on NAFLD. Authors—for exploring the studies dealing with the effects of LCHF diets on NAFLD—have focused on the following databases: PubMed, Cochrane Library, and Google Scholar. The combination of keywords used for this review is as follows: ("fatty liver" OR "non-alcoholic fatty liver" OR "hepatic steatosis" OR "non-alcoholic Steatohepatitis" OR "liver cirrhosis") AND ("low-carbohydrate diets" OR "high-fat diet" OR "LCHF diets" OR "ketogenic diet" OR "dietary interventions" OR "nutritional interventions"). Please refer to figure-one for the diagrammatic representation of the keywords and Boolean operators used. After a comprehensive search, a potentially relevant set of existing peer-reviewed articles is selected for this narrative review. The inclusion and exclusion criteria used are explained in the following section.



(Pathare & Chaudhary, 2022)

Fig 1: Strategy of using keywords in combination with Boolean operators

3.2 Inclusion and exclusion criteria

Studies published only within the last 15 years—available in English language—have been considered. Therefore, the range of years of publication is applied from 2006 to the present date. However, few studies before 2006 had been evaluated and included for two reasons: first, to understand NAFLD's origin and history; second, few studies—before 2006—are present in existing literature whose topic deals with LCHF diets and NAFLD, carrying a potential relevance for the topic of this study. Thus, they potentially may bring a comprehensiveness to this study. In order to ensure the reliability of the studies, only peer-reviewed studies are included. However, peer-reviewed literature does not necessarily signify the study's reliability, especially concerning the question (topic) of the research. Therefore, a critical manual assessment and evaluation have been carried out. In order to capture the role of LCHF dietary approach in NAFLD comprehensively, authors have included studies from diverse methodologies—Randomised Controlled Trials (RCTs), Systematic Reviews and Meta-analysis—and did not restrict the inclusion criteria to one particular method.

4. Main body

4.1 Causes and risk factors of NAFLD

NAFLD is a multifactorial condition, and a range of researchers have still been struggling to comprehend the causes of hepatic fat accumulation. According to the current understanding, NAFLD may cause mainly due to—but not limited to—the following factors:

a) Hyperinsulinemia (Browning *et al*., 2011; Stefan, Kantartzis, & Haring, 2008) [4, 33];
b) Excess energy intake regardless of the source of energy (Parry & Hodson, 2017; Wehmeyer *et al*., 2016) [24,40], and particularly from carbohydrates (Gao, Hua, Hu, & Wang, 2021) [6];
c) Excessive consumption of refined carbohydrates (Schwarz, Linfoot, Dare, and Aghajanian, 2003; Sevastianova *et al*., 2012) [30, 32] and sugar (Basaranoglu, Basaranoglu, & Bugianesi, 2015; Maersk *et al*., 2012; Schwarz *et al*., 2015; Ter Horst & Serlie, 2017)

[3, 18, 31, 37]

d) Sedentary Lifestyle (Kim, Vazquez-Montesino, Li, Cholankeril, & Ahmed, 2020; Rector & Thyfault, 2011) [13, 28].

Furthermore, the risk factors of NAFLD are—but are not limited to—as follows: insulin resistance (Kitade, Chen, Ni, & Ota, 2017) [14]; carrying excessive weight around the middle (Pang *et al*., 2015) [23]; and genetics (Eslam & George, 2020) [5].

4.2 Current interventions in brief

To alleviate or avoid NAFLD, people frequently avoid high-fat food and prefer high-carbohydrate diets (particularly starchy carbohydrates) to lower calorie intake and achieve satiety (Gao *et al*., 2021) [6]. Since many people with NAFLD are overweight, they are frequently advised to follow low-calorie or low-fat diets and exercise.

The rationale for these low-calorie/low-fat/high-carbohydrate diets and exercise interventions is, mainly, to lose weight to help reduce NAFLD. However, this may not be the best option for many people; as Pathare (2021) [25] argued, calorie-reduced low-fat high-carbohydrate diets, due to their hormonal impact (especially on inulin), may not necessarily solve obesity even when combined with physical activity. Although exercise has broader benefits on metabolic health, excessive consumption of carbohydrates—especially the refined one—can likely outrun the benefits of exercising, argues Pathare (2021) [25].

Interestingly, as this review will discuss now onwards, the Low-Carbohydrate High-Fat (LCHF) dietary approach, despite being almost opposite to the conventional recommendations, seems to be gaining reasonable attention of researchers worldwide, as it may help to reverse the NAFLD's process (Perez-Guisado & Munoz-Serrano, 2011; Tendler *et al*., 2007; Vilar-Gomez *et al*., 2019) [26, 36, 39]. LCHF diets achieve this by number of—but not limited to—benefits, such as reducing insulin levels, addressing insulin resistance, normalising appetite, improving heart health markers, and promoting abdominal—and overall—fat loss.

4.3 Significance of a Low-Carbohydrate High-Fat (LCHF) diets in NAFLD

While several weight-loss diets can help with fatty liver, this review will discuss studies showing that LCHF diets may be more helpful than Low-Fat High-Carbohydrate calorie-restricted diets. While weight loss is effective for reducing liver fat content, there is evidence that the benefits of LCHF diets on this front may be—at least, to some extent—independent of it (Gepner *et al*., 2019; Guess, 2018; Holmer *et al*., 2021; Luukkonen *et al*., 2020; Unwin & Tobin, 2015) [7, 9, 11, 17, 38]. Moreover, significant improvements may be achieved through carbohydrate restriction rather than calorie restriction alone (Browning *et al*., 2011; Holmer *et al*., 2021) [4, 11].

Additionally, in NAFLD, research indicates that improvements in responsiveness to LCHF diets can occur swiftly, speeding up the results compared to other dietary approaches (Mardinoglu *et al*., 2018) [20]. This suggests that the LCHF dietary approach may significantly help address NAFLD regardless of weight loss, although still LCHF diets, as explained by Pathare (2021) [25], are likely the most optimal and healthy way to lose unproductive weight. This, collectively, implies that the LCHF dietary approach in NAFLD may provide a comprehensive health benefit beyond liver health.

When compared to other nutrients, excessive carbohydrate consumption may be particularly damaging to the liver (Browning *et al*., 2011; Stefan *et al*., 2008) [4, 33], with the excess being converted to fat via “de novo lipogenesis” (Sanders & Griffin, 2016) [29]. Additionally, sugary carbohydrates may be particularly detrimental because the majority of fructose consumed by an individual can only be digested in the liver before it can be stored or used by other cells

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(Tappy & Le, 2010) [34]. As a result, the capacity of LCHF approach to reduce liver fat accumulation is probably unsurprising, as they can target the key causes of hepatic fat storage, i.e., high insulin levels; excessive calorie consumption, mainly from carbohydrates; and excessive consumption of refined carbohydrates. This suggests that the LCHF dietary approach can significantly decrease liver fat and may even reverse the disease.

5. Implications on current public health dietary guidelines

As recommended by the World Health Organization (WHO, 2020) [41], the Indian Council of Medical Research National Institute of Health (ICMR-NIH, 2020)'s [12] food pyramid prioritises carbohydrates—whole grains, legumes, fruits, and vegetables—and encourages people to consume no more than 10% of their calories from saturated fat. This clearly suggests that current recommendations for healthy eating emphasise a high-carbohydrate, moderate-protein, and low-fat diet. However, as this review discussed, high carbohydrate diets may be detrimental to liver health. This does not imply that the Indian public health guidelines are causing the epidemic of NAFLD; however, it implies addressing the dietary guidelines, and prevention & treatment of NAFLD in light of the LCHF dietary approach.

Notably, acknowledging the multifactorial nature of NAFLD, the authors of this review admit that LCHF diets may not be the only interventions that would work; thus, they may be needed to be combined with several other interventions, such as follows: considering the usage of curcumin or turmeric (Akbari *et al*., 2019; Goodarzi, Sabzian, Shishehbor, & Mansoori, 2019; Mansour-Ghanaei, Pourmasoumi, Hadi, & Joukar, 2018; Mousavi, Milajerdi, Varkaneh, Gorjipour, & Esmaillzadeh, 2020) [1, 8, 19, 22]; regular physical activity (Hashida *et al*., 2017) [10]; and inclusion of fatty fish in diet (Lu *et al*., 2016) [15].

Most importantly, although NAFLD is a multifactorial issue, considering the potential benefits of LCHF diets—and the detrimental role of carbohydrates on the liver—in NAFLD, it appears that the focus of public health research and front-line practice should be additional towards LCHF diets.

6. Conclusion

This review finally concludes that the LCHF-NAFLD theme is not only worthy of study but also represents a rich vein of research opportunities. "Public Health India"—via this review—encourages and calls researchers, doctors, nutritionists, dieticians and related-health professionals to ingrain more engagement towards the LCHF-NAFLD theme. It is worthwhile to concentrate exclusively on the LCHF-NAFLD theme, as it may potentially not only solve NAFLD but may also reverse it, with added comprehensive health benefits beyond the liver. Therefore, the public health importance of focusing more on the LCHF-NAFLD theme is enormous.

7. Limitations and resulting need for future research

Every research study has its limitations, and this article may not be an exception. Due to the resource and words constraints, this article has not provided comments critically evaluating the designs and methods of the included studies. Of course, a more detailed and comprehensive argument could have been delivered by commenting on the methodological areas of the included studies. However, since our main aim was to develop an overview of the topics already covered by NAFLD-related research in relation to the LCHF approach, we consider this methodological decision justifiable. Therefore, a critical evaluation of the design and methodology employed by the included studies could be a potential topic for prospective review.

8. Funding details

This work is funded by the Indian health research and advocacy organisation, "Public Health India", also known as PHI for short. PHI funded this work under the SOLPHI Program, where SOLPHI stands for "Spotlight on Longstanding Public Health Issues". Through SOLPHI, PHI intends to identify important research themes dealing with longstanding public health challenges such as Diabetes, Obesity, and a range of metabolic problems.

9. Author contributions

AVP contributed to the conception, design, interpretation, and manuscript writing. ABC revised the article and made an intellectual contribution. Both authors were involved in carefully proofreading content and approval of the manuscript for publication.

10. Appendix A: About Public Health India (PHI)

Public Health India (PHI) is an Indian health advocacy organisation dedicated to reducing the individual, economic, and social costs of Obesity, Diabetes, and related metabolic diseases by improving the quality of nutrition research. The purpose of PHI is solemn and revolutionary, which is "changing lives by informing Public Health".

PHI believes "obesity is not a personal issue". Indians may suffer from Obesity and Diabetes, not necessarily—or solely—due to their conscious unhealthy food choices, but also due to the misinformed and poorly tested guidance they receive from several platforms regarding what to eat. It may be reasonable to consider that, due to excessive workload, even Doctors and health professionals may get misinformed in today's "age of information overload", resulting in unintended misguidance to their patients and clients. To address this issue, PHI tries to disseminate unbiased and evidence-based information on optimum nutrition to Doctors, health organisations, the public, and healthcare providers.

Most importantly, PHI is not accusing any Doctor or health professional, and PHI is significantly away from the "*blaming approach*." Instead, PHI believes in a whole system approach. PHI respects and appreciates Doctors' and health professionals' role in today's public health, and PHI do not suggest that the public is deliberately misinformed. Instead, PHI highlights how the public—and possibly several Doctors and health professionals—may be chronically misinformed by poor science/research and food politics.

In the rigorous process of trying to explore the most trustworthy scientific literature on health, PHI believes in looking for solutions and not the "*blame game*". PHI acknowledges that the Obesity epidemic is a multifactorial issue; however, the dietary factors are likely the most influential. Healthy scepticism, trustworthiness, goodness, simplicity and inspiration are the core values of PHI.

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