We thank the reviewers for their comments which we have tried to address point by point below:

Reviewer #1

<u>Specific Comments to Authors:</u> This manuscript stated shared mechanisms underlying IBS and NAFLD, however, these mechanisms are not very specific. In other words, what do you think about are there any more direct connections between them. And maybe it will be better to summarize the treatment of both have in common.

Thank you for your comments. To date, evidence shows similar pathophysiological pathways in IBS and NAFLD with overlapping aetiological factors. However, high quality data on a direct connection between both conditions remain limited and not fully elucidated. The common therapeutic strategies for management of both conditions have been included in the discussion.

Reviewer #2:

Specific Comments to Authors: 1.This article identifies a possible association between IBS and NAFLD through a systematic review of the retrieved relationships between IBS and NAFLD, and hypothesizes that the mechanism of action: a.The brain-gut-liver axis and microbiome; b. Chronic Inflammation and Immune System Activation; c. Bile acids; d. Small Intestinal Bacterial Overgrowth (SIBO); e. Intestinal Permeability; f. Obesity and Metabolic Syndrome; g. Poor sleep. Authors need to understand whether their study is aimed at clinical populations or basic research workers, and there should be a core salient and focused part of the mechanism that provides strong evidence. Does the endocrine system play a more important role? Correlation or causation can be pointed out in the discussion section. 2.Both the search and evaluation work inside the systematic review need to be done by two or more people. Is there a missing search formula? You can combine it with free words to check the omissions.

3.The content of Table 2 should be streamlined, and important information should be further organized and presented in the text. The basic information of the five included papers should be more comprehensive, such as location, study population, gender, etc. Other information can be used as supplementary materials in the attached table.

We appreciate the reviewer's valuable comments and will address each point accordingly. Aim of the study: our study is aimed at clinician scientists or research workers. Thus, we focused most of the discussion on potential mechanisms involved in the association between IBS and NAFLD. Core mechanism: We also agree with the reviewer's suggestion to identify a core mechanism that provides strong evidence for the association between IBS and NAFLD. We will focus on the role of increased mucosal permeability as well as the highlight the potential role of lubripostone in both treatments.

2. The literature search for relevant papers was done by two persons. The search terms were relooked at and have been revised accordingly to be more comprehensive in the methodology section with inclusion of two new papers.

3. We have streamlined and revised Table 2 to include the new papers and relevant information.

Reviewer #3:

Specific Comments to Authors: The study is relevant given the high prevalence of both NAFLD and IBS. The authors confirmed the link between NAFLD and IBS and made a practically important conclusion that patients with one of these diseases should be screened for the presence of the other. In the future, this may lead to the development of new therapeutic strategies aimed at both diseases. Patients with overlapping IBS and NAFLD had more metabolic risk factors, including high BMI, hypertension, dyslipidemia, and diabetes. This may be important to develop strategies to prevent such overlap. The authors also discussed in detail the similar characteristics of IBS and NAFLD. The tables and illustrations are well done and reflect relevant content. In conclusion, the manuscript can be recommended for publication after a minor revision. It is recommended to add references to publications 2021-2022 (for example, 1) Purssell H, Whorwell PJ, Athwal VS, Vasant DH. Non-alcoholic fatty liver disease in irritable bowel syndrome: More than a coincidence? World J Hepatol. 2021 Dec 27;13(12):1816-1827. doi: 10.4254/wjh.v13.i12.1816. 2) Franco L, Jones-Pauley M, Tamimi O, Neshatian L, Nguyen D, Graviss E, Quigley EM, Victor D 3rd. Irritable Bowel Syndrome Symptoms in Nonalcoholic Fatty Liver Disease Patients Are an Indicator of Depression and Anxiety. J Clin Gastroenterol. 2022 Oct 10. doi: 10.1097/MCG.000000000001770.) Reference to the Figure 3 (Postulated Pathophysiology) should be given in the text of the manuscript.

We have edited and included the two recent references in the manuscript. Figure 3 has been referenced accordingly in the manuscript at the beginning of the discussion.