Reviewer #1:

1.The manuscript title uses "spondyloarthropathy," while the body of the text alternates between "spondyloarthritis (SpA)" and "spondyloarthropathy." This inconsistency in terminology could confuse readers, and consistency should be maintained throughout the manuscript. It is recommended that the authors choose one consistent term and provide the full definition upon its first mention, then use this term consistently throughout the text. The more commonly used term internationally is "spondyloarthritis," and it is suggested that the authors follow the naming conventions of the European League Against Rheumatism (EULAR) and the Assessment of SpondyloArthritis international Society (ASAS).

Response: We appreciate the reviewer's insight and agree that consistency is crucial. We have now standardized the terminology to "spondyloarthritis (SpA)" throughout the manuscript and ensure it aligns with EULAR and ASAS conventions.

Modification: Updated all instances of "spondyloarthropathy" to "spondyloarthritis (SpA)" and introduce the full definition upon first mention.

2.The manuscript lacks a description of the development of microbiome sequencing technologies. It is recommended to provide an overview of metagenomic sequencing techniques in the introduction section. Specifically, it should be explained why metagenomic sequencing is particularly valuable for studying the relationship between the gut microbiome and spondyloarthropathy. Metagenomics can provide functional information about microorganisms rather than just taxonomic information, detect unculturable microorganisms, and reveal alterations in metabolic pathways. This will provide readers with better background understanding and enhance the academic depth of the manuscript.

Response: Thank you for highlighting this gap. We have now included a section in the introduction providing an overview of metagenomic sequencing techniques and their relevance in studying the gut microbiome's role in SpA.

Modification: Added a paragraph discussing how metagenomics provides functional insights, detects unculturable microorganisms, and reveals metabolic pathway alterations.

3.In Table 2, the symbols "*" and "-" are used for risk of bias assessment but are not explained in the figure legend. This makes it difficult for readers to understand the content of the table. It is suggested to add a note below the table explaining the meaning of these symbols, or alternatively, consider using more intuitive symbols such as "√" and "×" to represent the presence or absence of items. Clear figure legends are essential for readers to understand the results of the study assessment.

Response: We acknowledge the issue and have now provided a clearer legend below the table defining the symbols used for risk assessment.

Modification: Added explanations for "*" and "-" in Table 2.

4.There are formatting issues in the "Bacterial profile of AS patients" section. Specifically, the sentence "Similarly, in a study conducted by..." raises a question regarding its position—should it start a new paragraph or be a continuation of the previous one? The authors are advised to revisit the text structure, ensuring that each paragraph focuses on one central idea and that there is logical coherence between paragraphs. A well-structured paragraph will help readers better understand the connections and differences between the research findings.

Response: We appreciate the reviewer's concern and have ensured better paragraph structuring for logical coherence.

Modification: Restructured the section to maintain clarity, ensuring each paragraph centers around a distinct idea.

5.This review has noticed the omission of a highly cited article, "Quantitative metagenomics reveals unique gut microbiome biomarkers in ankylosing spondylitis." This article has significant impact in the field, and its exclusion could weaken the comprehensiveness and authority of the review. The authors are requested to explain the reason for excluding this article or to include this important study in the revised version.

Response: Thank you for pointing out this relevant study. We have incorporated its findings to enhance the comprehensiveness of our review.

Modification: Integrated key insights from “Quantitative metagenomics reveals unique gut microbiome biomarkers in ankylosing spondylitis” into relevant sections.

Reviewer #2:

1. Please provide a schematic diagram to facilitate a clear understanding for the review content.

Response: A schematic diagram is now included to enhance the visualization of key concepts and relationships discussed.

Modification: A schematic diagram illustrating gut microbiome interactions with SpA pathogenesis is added.

2. The article mentions that for AS patients, TNFi treatment is more effective than non-steroidal anti-inflammatory drug treatment and can improve the patient's gut

microbiome. It is recommended to expand other effective treatment methods besides TNFi.

Response: We acknowledge this suggestion and have expanded the section to discuss other emerging therapeutic strategies beyond TNFi.

Modification: Included discussions on DMARDs, IL-17 inhibitors, and microbiome-targeted interventions.

3. The article emphasizes the importance of the gut microbiome, however the discussion on how to translate these findings into clinical applications is somewhat lacking. Further exploration of potential therapeutic approaches targeting specific microbes or metabolic pathways is warranted, such as the development of novel probiotics, prebiotics, or therapies related to microbial metabolites.

Response: We have added a section discussing translational research and potential clinical applications, including novel probiotics and microbial metabolite therapies.

Modification: Expanded the discussion on therapeutic strategies targeting specific microbial pathways.

4. In the discussion section, it is suggested to further strengthen the critical analysis of the research results. For example, a more detailed discussion on why certain specific microorganisms is enriched in SpA patients, and whether these microbial changes have a causal relationship or are merely accompanying phenomena of the disease state.

Response: We appreciate this suggestion and have now strengthened our analysis on the potential causality of microbial alterations in SpA.

Modification: Provided a deeper discussion on whether microbial changes are a cause or consequence of SpA.

5. Although the article mentioned some key microbial and metabolic changes, the mechanism of how these changes specifically affect the immune response and disease progression of SpA was not explored thoroughly. It is suggested to further elaborate how specific bacteria trigger SpA related inflammatory responses through molecular mimicry or immune activation.

Response: We agree that this aspect needs elaboration. We have now discussed mechanisms like molecular mimicry and immune activation pathways associated with specific bacterial strains in SpA.

Modification: Expanded sections detailing microbial interactions with immune response pathways.