Reviewer 1.

Thank you very much for the kind words of appreciation of our paper. Concerning the comments:

1.The abstract section is good; need to add a focus point in the abstract section.
Response: Thank you for your comment. We have revised our abstract section.

2. In the abstract section, rewrite the sentence: "NDRG1-3 may be the promising biomarker for the diagnosis and prognosis of HCC and may provide promising new targets and strategies for HCC treatment". Need to make those lucid and clear.
Response: Thank you for your comment. We have revised this sentence.

3. The introduction section is inapplicable and redundant. Try to include the existing research limitations also, how the present research unravels those limits.
Response: Thank you for your comment. We have included limitations of the existing research.

4. Also need some more insights on the NDRG1-4.
Response: Thank you for your comment. We have revised our discussion section and included some insights into NDRG1-4.

5. Also, the aim of this study need to separate into a single paragraph in the introduction section.
Response: Thank you for your comment. We have included the aim of the study in the last paragraph of the introduction section.

6. Delete I, we, our throughout the manuscript.
Response: Thank you for your comment. We have deleted "I", "we", "our" in the introduction, method, results sections.

7. NDRG based prognostic signature generation and Mutation and DNA hypomethylation analysis: no references?
Response: Thank you for your comment. We have added several references in the method section for signature generation, mutation and DNA hypomethylation analysis.

8. Tumor microenvironments analysis: Elaborate with valid references.
Response: Thank you for your comment. We have elaborated tumor microenvironments analysis with valid references.

10. Correlation between tumor infiltrating immune cells and expression of NDRG members: Not well-written. Need to add some more insights.
Response: Thank you for your comment. We have revised the correlation between tumor-infiltrating immune cells and the expression of NDRG members.

12. The discussion is feeble. Please, include the data from other sources about related works. Also, delete the subtitles for the discussion. A sound discussion includes principal, relationships, and generalizations supported by the results.

Response: Thank you for your comment. We have revised our discussion part.

14. Conclusion has to be improved by including more points (personal recommendation, limitation, etc.).

Response: Thank you for your comment. We have revised our conclusion part.

15. Spacing, punctuation marks, grammar, and spelling errors should be reviewed wholly. English is poor. The authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.

Response: Thank you for your comment. We have reviewed and corrected errors in the manuscript.

17. Originality of the work should be improved by the author (either in the conclusion or introduction section).

Response: Thank you for your comment. We have revised our manuscript carefully.

Reviewer 2.

Thank you very much for the kind words of appreciation of our paper. Concerning the comments:

1. Authors should finalize with one main title as Page 1, Line 1 reads it as "NDRG family genes expression in patients with hepatocellular carcinoma" whereas submission reads it as "Prognostic and Biological Role of the NDRG Family in Hepatocellular Carcinoma".

Response: Thank you for your comment. We have finalized the main title as "Prognostic and Biological Role of the NDRG Family in Hepatocellular Carcinoma".

2. Please reframe the abstract of the article as a single paragraph, and try to avoid so many abbreviations within the abstract.

Response: Thank you for your comment. We have reframed the abstract of the article.

3. Authors should check the abbreviation. For example, in the abstract text, authors refer to "GEPIA" and "TCGA", or well recognized "RNA-seq" etc. For the first usage of GEPIA, TCGA, OS, DNMIVD etc., the abbreviation should be given. Please check carefully for this, as readers belong to diverse research backgrounds and may not be aware of terminology that looks much known to us. In the text, the authors give both "MS" and "Mass spectrometry". This is not proper. For the first usage of the MS, the abbreviation should be given.

Response: Thank you for your comment. We have given the abbreviation for the first usage.

4. In the text, the authors give both "N-myc downstream-regulated gene" and "N-Myc downstreamregulated gene". This is not proper. Please be uniform throughout the manuscript, either use small/capital 'm' while writing N-myc downstream-regulated gene.

Response: Thank you for your comment. We have used "N-myc downstream-regulated gene".

5. Add space while indicating two-member protein between like: NDRG1, 2.

Response: Thank you for your comment. We have used added space between NDRG1 and 2.

6. While indicating "multivariate Cox analyses", 'C' should be in the capital letter as Cox (name of the scientist, by whom this model is being proposed).

Response: Thank you for your comment. We have used "Cox" in our manuscript.

7. Throughout the manuscript, authors should clearly indicate whether they are explaining about NDRG gene or protein. For instance: "NDRG1-4 are four members of the N-myc downstream-regulated gene (NDRG) family and they are located on different chromosomes. The five amino acids at the C-terminus represent conserved residues and four members have different sequences among the N- and Cterminal regions [7].", here is quite unambiguous. Also, in the second sentence, it is not contradictory in itself that whether or not the C-terminus region is conserved.

Response: Thank you for your comment. The sequence differences between NDRG1–4 are located in the N- and C-terminal regions, except for 5 amino acid residues in the C-terminal.

8. In the methods section, "…were used for expression of the NDRG family (NDRG1-4)." is not a proper phrasing. Please rephrase it and elaborate on what kind of expression data have been collected from mentioned databases. Again, in the next sentence "The RNA-seq data and related clinical information of liver hepatocellular carcinoma", please explicitly mention what related information. (Or authors can add the data in a supplementary document while providing an in-text citation for the supplementary document).
Response: Thank you for your comment. We have provided some detailed information in our methods section.

9. "The DNA methylation of cg sites in the gene promoter regions": CG should be in capital letters.
Response: Thank you for your comment. We have changed cg as CG.

10. When the author uses phrases like "analyzed in the DNMIVD (a database)", it is not clear how/what kind of analysis is done in the database. Either explicitly mention the procedure of analysis (if any kind of analysis is done). Otherwise simply say, data is collected from a database and then XYZ tests are performed using the data.
Response: Thank you for your comment. We have explicitly pointed the procedure of analysis in the method.

11. What criteria are used by authors to identify twenty-four immune cell gene signatures, please add the details?
Response: Thank you for your comment. We have provided the detailed reference for twenty-four immune cell gene signatures.

12. Figure 1A: When authors say 'Total Unique Analyses' or 'Significant Unique Analyses', some information on these analyses/datasets must be supplied in the form of supplementary documents.
Figure 1B/C: X-axis is labelled as 'LIHC' while on the plot, the author gives data for both normal and tumour cases.
Figure 1C: Legends on the right upper corner are not readable.
Figure 1D: a proper citation is required for this image as the author did not perform any protein expression experiment in this study. Caption: (* p < 0.05, NS, not significant) looks redundant. And also check for the correct representation for symbol whether it is small 'p' or capital 'P' for P-value, according to that change it throughout the manuscript. Figure 6A/C/E: Texts in these figures are not easy to read on zoom. Figure 7: Legends in these figures are not readable. Also, the caption should be rephrased to give a sound idea about what figures highlights. Figure S2: Legends in these figures are not readable.
Response: Thank you for your comment. We have changed figure legends according to your suggestions.

14. The article ends rather abruptly and would benefit from a section on the limitations of current methods used in this study. Impact of the research outcomes and clinical significance in chronic diseases prediction?

Response: Thank you for your comment. We have included the limitations of our study and the impact of current research for further studies.

16. The discussion and Conclusion section needs more effort in terms of publishable work.

Response: Thank you for your comment. We have revised the discussion and conclusion section.