**Response to reviewers’ comments**

I am very much thankful to the editor sand reviewers for their deep and thorough review Thank you for your efforts

The required changes were done and highlighted in revised manuscript.

**Response to reviewer 1**

Comment 1: tiny sample size

Response 1: Thank you for pointing this out. We agree with this comment. But the sample size was calculated according to IRB committee recommendations.

Comment 2: the control group should equal the case in a number.

Response 2: Thank you for your comment This paper examines the hypothesis that, in some cases, the use of a large control group may provide a study with a greater power than equal sample This way forward is supported by Guo and Luh (2013) in the following statement: “Equal allocation design is popular because of convenience and efficiency, but it is not practical”.

Comment 3: inclusion criteria and exclusion criteria must be clarified.

Response 3: thanks again but we had demonstrated the inclusion and exclusion criteria in fig 1 flowchart to avoid high similarity in plagiarism.

Comment 4: abbreviations must be mentioned in detail.

Response 4: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments as we have added **list of abbreviation** to revised manuscript.

Comment 5: prevalence of HCV in non-Hodgkin's lymphoma must be clarified in this study.

Response 5: Thank you for your silent observations, the prevalence of the current study was shown in table 2 and in section of discussion line 191 and 192 but this prevalence in the current study not in Egypt as the current study was case control study not cross sectional studies so we could not correctly calculate the prevalence in whole country .

Comment 6: comparison between your marker and other diagnostic tools to detect its role.

Response 6: as the diagnosis of NHL pathological mainly so in table 2 we have already compare the level of the studied epigenetic marker and all clinicopathological characteristics

Comment 7: the title of the paper is concise for occult hepatitis C 6 patients only.

Response 7:

7- the title of the paper is concise for occult hepatitis C 6 patients only.

Comment 7: Thank you for your silent observations, but the sample size of the whole study was recommended by IRB so the sample of occult c was small so we hope in the next publication conducted the study on large sample size

Reviewer 2:

Introduction ‎

**‎** Comment 1.‎ Evolving evidence suggests that lncRNA Myocardial Infarction Associated ‎Transcript (MIAT) dysregulation is associated with different ‎cancers. please add more data and details about Lnc RNA-MAIT and cancers ‎with more references, and previous studies have been done on this topic ‎

Response 1:The required changes were done and highlighted in revised manuscript in response to reviewer comments

‎ Comment 2.‎ Sample size is small?‎

Response 2:Thank you for pointing this out. We agree with this comment. As I have mentioned before, the sample size was calculated according to IRB committee recommendations.

‎ Comment 3.‎ Primary mediastinal large B-cell lymphoma, testicular, and primary DLBCL ‎of the central nervous system were excluded; causes of exclusion?‎p

Response 3: Thank you for pointing this out. We agree with this comment DLBCL is the most common pathological type of NHL and HCV and we in the current study compared the influence of chemotherapy on levels of Lnc RNA-MAIT so we had to select one pathological type to be easy in the evaluation in this small size study in further study we will expanded the size of the study and we will add our pathological types to the study

‎‎ Comment 4.‎ Blood samples were drawn from all subjects enrolled; what about BM ‎‎, methods, and site of bone marrow aspirate in the control group?‎

Response 4 No these tests were done for clinical and laboratory suggested NHL as we select healthy control to evaluate the epigenetic changes between healthy control and NHL- OCI patients

‎ Comment 5.‎ Criterial of the control group? Is bone marrow aspirated for this study or ‎another hematological cause?‎

Response 5 I have mentioned the response before

‎‎ Comment 6.‎ Methods of diagnosis of occult of HCV in all groups?‎

Response 7: thanks again but we had demonstrated the diagnostic criteria in criteria in fig 1 flowchart to avoid high similarity in plagiarism.

‎‎‎ Comment 7.‎ Please add the laboratories and clinical data. done for patients in ‎methodology (subjects).‎

Response 7: Sorry, according to the recent promotion requests we need low similarity in plagiarism when we add the details of the laboratory techniques we will reach un accepted level of similarity

‎ Comment 8.‎ It is logical to find significant differences between ‎ NHL and the control group, ‎but what about the difference between patients with NHL with or without occult ‎HCV infection?

‎Response 8: according to the current study results we did not classified our NHL patients in two groups with occult ‎HCV and without except in table 2 when we compared the level of the studied epigenetic markers Lnc RNA-MAIT between patients regards HCV infection

‎‎‎ Comment 9.‎ In patients with overt HCV ab, received DAAS?‎

‎ Response 9: No, we selected naive patients as we mentioned in fig. flowchart of the study to avoid the influence of DAAS on the studied epigenetic markers Lnc RNA-MAIT

‎‎‎‎‎ Comment 10.‎ we aimed in the current research to investigate LncRNA-MIAT in patients ‎with NHL and to assess its correlation with clinicopathological features and ‎progression of NHLs among Egyptian patients with OCI- HCV, in the title you ‎investigate as a non-invasive diagnostic marker of non-Hodgkin's lymphoma ‎associated with occult hepatitis C virus infection, but you investigate it in ‎already diagnosed and confirmed cases ‎

Response 10: Thank you for pointing this out. we aimed to evaluate circulatory LncRNA-MIAT as noninvasive marker but fist in the research we should be sure of the diagnosis of NHL to compare between control and case later on after metanalysis it could be used as evidence base noninvasive marker of diagnosis of NHL.

Reviewer 3:

Many thanks for nominating me to review this manuscript demonstrating the Clinical significance of LncRNA-MIAT as a non-invasive diagnostic marker of non-Hodgkin's lymphoma associated with occult hepatitis C virus infection.

I observe minor revisions from a pathologic point of view, and I recommend paper acceptance after revision.

Comment1 Small sample size is one of the significant limitations of this study; the study was conducted on a common disease. However, only 20 cases were included: why?

Response 1: Thank you for pointing this out. We agree with this comment. As I have mentioned before, the sample size was calculated according to IRB committee recommendations.

Comment 2- This research was the first study that explores the relative expression level of lncRNA MIAT in Egyptian patients with NHL to find an early and non-invasive biomarker of NHL, in particular, NHL associated with OCI. This paragraph was written in results, although it showed no results, so it is better to mention them in the discussion than in the result section.

Response 2: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 3- We in the current research designed; please delete 'We' and avoid its repetition.

Response 3: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 4- Circulatory lncRNA-MIAT may serve as a promising non-invasive diagnostic, prognostic, and predictive biomarker. How can you conclude that although there is no follow-up in this study?

Response 4: in the current study we follow the treated patients for we treated with 6–8 cycles of CHOP, but we agreed with you we need longer period for better evaluation in the future research we will Do this

Comment 5- Correct some grammar & writing mistakes.

Response 5: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Reviewer 4:

Thanks for your thorough work and the effort that has been done into this research.

Comment 1: A file has been uploaded with notes. Please read carefully and correct the notes you asked for.

Response 1: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 2- The introduction should add a more detailed paragraph about (INC -RNA/IMIAT) pathophysiology.

Response 2: The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 3-BMA is optional for all cases as BMB is already enough, so could you tell me your reason for BMA and BMB together?

Response3: The diagnostic validity of BMB is higher than that of BMA. However, BMA serves as a good positive test in screening lymphomas for marrow disease. A negative BMA does not exclude involvement. Thus, smears should be taken as a complimentary procedure.

Comment 5-Hepatitis B examination should be done for all your patients, and also, you have some patients who have already received rituximab. So, it is a weak point in your study to ignore it.

Response 5: we exclude hepatitis B and other hepatitis as we had mention in flowchart in fig 1

Comment 6-why did you not include the child-Pugh score in your patient evaluation and selection data?

Response 6: Thank you for pointing this out we selected compensated patients to avoid any error related gene detection and we added this sentence to flowchart in fig 1

Comment 7-Did you use PET-CT for any of your patients at primary diagnosis?

Response 7: As we mention in section of patients and methods “**The NHL diagnosis was established in all patients by pathology in conjunction with immunophenotype studies** and subclassified according to the World Health Organization classification and the investigations, anticancer treatments, and follow-up examinations were completed.”

Comment 8-References should be written in one style, e.g., APA style

Response 8: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 9-English editing should be done as there are too many grammatical mistakes.

Response 9: Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

Comment 10- check the uploaded file.

Response 10:Thank you for your silent observations. The required changes were done and highlighted in revised manuscript in response to reviewer comments.

**Editor Comments to Author:**

1. Please check the author names and affiliations included on your Title Page, mainly that the spelling of all authors' names is correct. This is because they are cited in the order you would like them to appear in the final article. In addition, each author's affiliation details are correct.

2. Please include a 'Structured Abstract': not more than 250 words, broken down into, i.e., Aims, Patients & Methods/Materials & Methods, Results, and Conclusions. For authors presenting the results of clinical trials, the guidelines recommended by CONSORT should be followed when writing the abstract (http://www.consort-statement.org/), and the clinical trial registration number should be included at the end of the abstract, where available.

3. Please include up to 10 keywords in your revised manuscript (including the four keywords you selected as part of the submission process).

4. Please amend the references as per the author's guidelines:

a. References should be numerically listed in the reference section in the order in which they occur in the text.

b. References should appear as a number, i.e., [1, 2] in the text.

c. References should cite three authors et al.: it is our house style to list a maximum of six authors, and if there is more than this, three authors et al.

5. Please ensure that all tables and boxes are titled and cited in the text.

I've included a link to the African Journal of gastroenterology and hepatology Author Guidelines which explains these sections in more detail: https://ajgh.journals.ekb.eg/journal/authors.note.

6. please check the PDF file of your manuscript regarding plagiarism checking.

7. Please add the scale bar, annotations, magnifications, and program that generated these figures. Also, it is better to submit figures with high resolution and brightness.

I am very much thankful to the editor sand reviewers for their deep and thorough review Thank you for your efforts. The required changes were done and highlighted in revised manuscript We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Sincerely,