



SDI Review Form 1.6

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2013_IJTDH_8017
Title of the Manuscript:	Co- Infection of HIV and HepatotropicViruses: Impact on the Biochemical and HaematologicalMarkers of Patients in Northeastern Nigeria
Type of the Article	

General guideline for Peer Review process:

This journal's peer review policy states that **NO** manuscript should be rejected only on the basis of '**lack of Novelty**', provided the manuscript is scientifically robust and technically sound.

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PART 1: Review Comments

	Reviewer's comment	Author's comment (if agreed with reviewer, correct the manuscript and highlight that part in the manuscript. It is mandatory that authors should write his/her feedback here)
Compulsory REVISION comments	The study design should be thoroughly described Study subjects should be sufficiently discussed The method for sample size calculation and selection of study units should be revised Clinical parameters especially ART history of patients should be presented Normal reference values for haematological and biochemical biomarkers should be described The conclusion needs to be revised especially with respect to the main findings Identified gaps and way forward should be clearly presented Title Since your focus is on those only with shared route of transmission with HIV, your title is good if it reflects this Impact is measured in long time- the appropriate method being longitudinal studies, prospective cohort. Since your study is a onetime assessment, it's better suited with comparative cross-sectional that assess associations between co infection and biomarkers Study area- northeast Nigeria- your study was conducted in two states but generalized for 6 states found in Northeastern Nigeria. What's the basis for generalization? Do you think the result in two states could be representative for the whole region? Abstract The background and the objectives should be written separately. Methodology- the purpose of employing western blot method should be described Introduction Adequate scientific base for the possible association between HIV or co infections with various hematological and biochemical biomarkers is not established. Please revise your introduction as such Material and methods	The study design has been revised to reflect issues raised by the reviewer such as sufficient discussion of study subjects which include clinical history of the patients in respect to ART, use of normal reference values of haematological and biochemical parameters. The conclusion has been revised to reflect main findings and gaps have been identified and way forward suggested. The issue of sample size and selection of study units have been revised. Title The title has been modified to read "The effect----- . The study does not just show association but actually measures the effect of either mono or co-infections on the parameters studied. Study Area: Although the study was conducted in two states in northeastern Nigeria, the generalization to the six states bothers on one of the study units – University of Maiduguri Teaching Hospital (UMTH). This hospital serves as a referral centre to the six states in the region. Every state in the region has Federal Medical Centre (FMC) which



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	The study design is not defined and sufficiently described. Please discuss the type of design for your study, case control, cohort, and cross sectional... your study subjects should be clearly described. Are they on ART? If so, how long do they are followed on ART? What is their regimen? Please revise your descriptions of the automations, its manufacturers and model. Usually the automacine and model number is written together and the manufacturer described in bracket. The procedure for ELISA is not sufficiently described. Please describe quality control measures you employed Statistical analysis needs rewriting. The confidence level you employed, the type of test for association or significance needs to be clearly described. Line 68- Separate study population from study period. Usually, study period is written either with study design or study area. Line 71- it's necessary to describe where and how you obtain socio demographic and clinical data, which could be from hospital or patient record review or lab. Register. Result In your methodology you mentioned the use of ANOVA but I couldn't find any analysis with ANOVA in your result In your result you use a P-value based on chi-square results for depicting association between parameters. It's known that a P-value based on chi-square is crude and it doesn't portray the specific association between the dependent and independent variable. As a result true association or effect of each factor on HIV morbidity should be measured by adjusting for other socio demographic and clinical factors. Do you perform any so such procedures? If so please describe Line 100-103- the number of subjects included as comparison groups is not similar. Since I am clear with your study design, I couldn't comment on the proportion between the controls and cases. Please explain your design and then the number of study subjects needed to be included under each group Line 110- (P=05) what is it? Pages 7- please describe the absence of significant association between co infection and sex with a P value. Table 2- since HIV status of your controls is predetermined; it's better to describe their sex distribution in text.	represents the tertiary health care delivery in Nigeria. So all the FMC in each state still refer patients to UMTH. Abstract The background and the objectives have been separated. Methodology: The purpose of using Western blot is briefly described. Introduction: It has been revised to provide adequate scientific bases for the possible effect of HIV mono and co-infections on haematological and biochemical biomarkers. Materials and Methods: Study design has been described to reflect the type of design, information about the subjects in respect to ART. Description of the automations have been revised accordingly. The procedure of ELISA and the quality control measures used have been sufficiently described . The statistical analysis has been re-written as advised. Study population has been separated from the study period The source of socio demographic and clinical data has been indicated. Results:
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	Table IV- while numbering tables, it's advised to use similar numbering system, either the roman number or Arabic numbering. So please revise table numbering Table 4- please use standard abbreviation for liver function test enzymes. And describe it at the end of the table for clarity Discussion During discussion I couldn't find any theoretical basis for HIV or co infection and biomarkers with respect to why and how HIV or Hepatotropic viruses affect biomarker values of a patient Line 137-145- It's better to be included in the introduction section Line 146- you have mentioned that all of your subjects acquire HIV through sexual intercourse but you didn't mention it in your result. Line 156-.....in agreement with [145].(2008) please mention either the study or the author before the reference. Line 161-164- you tried to compare three groups, control, monoinfected and co infected. In the result part on page 7 presents crude associations between controls and infected individuals without discriminating between monoinfected and co infected ones. So please describe crude associations between individual groups and then adjust the association. Line 164- "It would appear as evidenced by CD4 count in our study that the degree of immune suppression may increase with hepatotropic virus's co-infections such as HBV and HCV" this statement is not supported by statistical associations with P-value. So indicate the P-value for the association Line 167- you claim that your result is different from other researches done in other parts of Nigeria. But you didn't clarify why it is different. Please discuss why your result is different from other studies you mentioned Line 181-184- "Liver enzymes AST, ALT ALKP levels are higher in HIV/HBV/HCV co-infection as evidence by the mean value of these biomarkers when compared with the values in HIV mono-infection. The high values of these biomarkers depict degenerative liver diseases in contrast to a report [12] that, liver enzymes are stable in HIV mono and co-infections"	The analysis data using ANOVA will be sent as 'Supplementary ' to the main submission. Association of HIV morbidity with socio-demographic and clinical factors was beyond the scope of this study. The number of patients was 109 while control was 100. We were constrained by funds and logistics to use equal number in both cases please. No statistical analysis was carried out for sex and the infections. Only the prevalence rate has been used to draw inference. The sex distribution on table 2 has been described in text. The numbering system on the tables is now consistent. Standard abbreviation for liver enzymes have been used as advised and has been described below the table. Discussion: It has been modified to reflect theoretical basis for HIV or co infection and biomarkers with respect to why and how HIV or Hepatotropic viruses affect biomarker values of a patient Line 137-145- has been corrected as advised. Line 146 and 156, have been corrected as advised.
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	We know that to evaluate the function of liver, the most important enzymatic test is ALT. In your study the mean level of ALT in all groups is within the normal reference range (0-50U/L) so how do you justify your claim that co infection is responsible for deregulation of biomarkers produced by liver. If you are implying that co infection cause liver damage and result in deregulation, your ALT result doesn't support your claim. So please clarify the point. Conclusion Line 192-193- what are practical measures that can be taken for co infected patients with such findings? Please describe practical management options for such cases. Line 194- what strategies should be forwarded? Explain in detail.	Line 161-164- The use of ANOVA has given proper comparison between the control, mono and co-infection on each of the parameters studied. Line 167: It has been appropriately corrected Line 181-184: It has been appropriately corrected. Conclusion Practical measures for co-infected patients have been suggested. Practical management measures have been suggested to the best of our abilities since we are not physicians The necessary strategies to avoid to avoid the transmission to contact have been heightened.
<u>Minor</u> REVISION comments	Language especially spacing and use of prepositions Numbering of tables Use of standard abbreviations	
<u>Optional/General</u> comments	The laboratory methods employed are up to date and appropriate	