



SDI Review Form 1.6

Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	Ms_IJTDH_26619
Title of the Manuscript:	EFFECTS OF CHILDHOOD MALARIA ON THE BIOCHEMICAL AND HAEMATOLOGICAL PROFILES OF INFECTED CHILDREN IN ANAMBRA STATE, NIGERIA
Type of the Article	Original Research Article

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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	Line 17. Please confirm mean PCV of 31.73 ± 458 ? (maybe?) Line 32. "(malaria) affects half the world's population" – erroneous statement as it is not clear if the authors mean infected patients, infected non-symptomatic, people at risk, or all of these. Also needs a reference. I suggest the most recent WHO malaria report. Line 38: the 5 species of Plasmodium parasites the authors mention are NOT the most common; they are ALL the species that are able to infect humans. Line 39. "Haematological alterations that are thought to characterize..." – which alterations? Please rewrite for clarity. Line 43. The references used are inadequate. The authors cannot use references that are over 10 years old to comment on the <u>current</u> state of malaria epidemiology in a given region. Lines 50/51. "... diagnosis of malaria parasite in the blood film could be made with certainty on identification in blood films along with signs and symptoms associated with the disease" – unclear statement. I believe the authors are trying to say that a clear diagnosis of malaria can be done based on identification of the parasite in blood film along with typical signs and symptoms associated with the disease. If so, please rewrite. Lines 63 and 64. The malaria parasites are neither symptomatic nor asymptomatic as your sentence suggests; please rewrite for clarity, as this is an incorrect statement as it is. Line 75. "... selected General Hospitals". What were the	Line 17: PCV is 31.7 ± 4.58 Line 32: Correction done. Line 38: are all the species that infect humans. Line 39: Haematological alterations such as anaemia, thrombocytopenia, and disseminated intravascular coagulation. Line 43: 2011 and 2015 now cited. Line 50 – 51: Correction done. Line 63 – 64: The words symptomatic and asymptomatic have being deleted to make the statement correct. Line 75: The criteria for purposive selection these hospitals are; existence with facilities on the ground as most of them were existing only on paper, number of patients that attends the hospitals and availability of health workers who will attend to the patients. Line 86 and 87: Correction done in the revised

[illegible]



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	anaemia if on line 157 it was mentioned that there were no significant differences in the PCV and Hb concentration of both sexes in community and hospitals? Line 265. Since prevalence of <i>P. falciparum</i> in Nigeria is 100% and <i>P. vivax</i> 0% (WHO malaria report 2015), authors should be referencing sources for <i>P. falciparum</i> only. There is no relevance in justifying results obtained for <i>P. falciparum</i> with findings by others based on <i>P. vivax</i>. Line 279. Percentage parasitaemia was related to blood Hb? I expect it to be negatively correlated, but this is not clear from the text. Line 282. "The drop in Hb may be due to selective removal of parasites from infected RBCs by macrophages (pitting)". True, but much more likely to be derived from normal parasite biology. Plasmodium consumes Hb within the erythrocytes and the haeme subproduct may in turn be responsible for some of the alterations reported as significant in this study, including liver enzyme alterations. Lines 271 to 303. Results for liver enzymes, Hb alterations and PCV are all mixed and jump from one observation to another, and back again, without a conducive line. Each results should be discussed individually first, then associated with relevant others, in an organized manner. Results section: it would benefit the clarity of the results if instead of all text and tables, pie charts or other form of graphical illustration for each parameter (or group of parameters eg: biochemical findings and haematological findings) could be included to enhance clarity of results. Authors should mention if they were expecting each of the results obtained, based on the literature, and the facts behind each decision to interpret the results (eg: why gender-based segregation? Why 3 age classes and why those ages? Were the authors expecting different parasite densities in different age groups? Why?)... Furthermore, how do results correlate within themselves?	Line 279: Actually malaria parasite impacted negatively on Hb being able to explain 14.7% variations in Hb concentration of infected children, with a moderate correlation (r) of 0.384 but this was explained more in another publication. Line 282: I agreed with the reviewer and the information has been added to work. Line 271-303: The results have been rewritten. Results section have been rearranged and graphical illustrations added. 1) <i>Plasmodium falciparim</i> was identified in all the infected blood samples and this has been included in the text. 2) Correction taken and has been effected in the text. 3) All the children (either clinically well or not) were sampled and tested for malaria parasite. Those samples not
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	For example, does parasite density correlate with PCV (since females had higher parasite density and also higher PCV averages?). There is no need to say “significant ($p<0.05$)” and “not significant ($p<0.05$)” in EVERY instance. The authors should just define significance in the beginning of results section and use the terms “significant” or “not significant” henceforth. <u>Important issues:</u> 1) Nowhere in the text is explained what species of Plasmodium was identified in infected children or what is the prevalence of the species in the Anambra state (100% <i>P. falciparum</i> according to WHO malaria report 2015). This is important information and should be included for reference. 2) The first statement in the results section mention sampling from “Children (asymptomatic and symptomatic) between the ages of 0 -14.9 (4.12 ± 0.27)”, with 82 samples obtained from the community and 166 samples obtained from the hospital. This brings total sample number to 248. If the mean age of 248 children sampled is (4.12 ± 0.27) and there is such a small standard deviation, then this means that this study was effectively carried out mostly in <u>children under 5 years of age</u>, and not a statically significant number of children will be representing the older ages. This should be at least discussed since it is known that children under five years of age are one of most vulnerable groups affected by malaria. 3) <u>Why haven't uninfected controls been included in sample collection?</u> How can the values found be significant within a malaria study if there is no way to compare those values with uninfected sample values? In some of the tables standard/normal range values are indeed included but where/when/how were these numbers obtained as they are never mentioned in the text?	infected with malaria parasite served as cotroll. Results from the study were compared to Sood (2006) normal ranges for biochemical and haematologica parameters and has been mentioned in the text.
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Minor REVISION comments	Throughout the text, the word “state” is incorrectly capitalized. Please correct. Also, there are a lot of extra spaces and lack of full stops throughout the text. Furthermore, a great number of words are incorrectly spaced (eg: counter parts should be counterparts, out patient should be outpatient, extra cellular should be extracellular, etc). Please correct. Line 16. correct to “malaria parasites”; Line 60. correct to “variables have BEEN”; Lines 69-81. Format and punctuation errors throughout the text should be revised. Line 195. “children of 0.4.9 years”. Please correct. Line 257. Couldn’t it be the opposite? That insignificant changes observed in cation concentration between uninfected and asymptomatic children could explain why they are asymptomatic? Line 263. Does that mean that children above 10 years of age, who had 1-10 gametocytes (per microliter of blood?) and were asymptomatic (therefore remained in the community and did not go to hospital) had healthier biochemical ranges and less liver commitment? General questions: 1) Why was Ethical Clearance obtained in a different state than the state targeted in this study? 2) Initially, 1mL of venous blood from all study cases was collected into EDTA-coated vacutainer tubes; it is not mentioned what these samples were used for. The authors then proceed to explain preparation of thick blood smears using a drop of blood, and immediately after refer to collection of 4 more mL of blood to be used for biochemical analysis. It is not clear how much blood was collected at each time point. Was the 1mL blood initially collected used only for preparation of thick smears? Were the remainder 4mL collected at the same time?	Line 16: Corrected. Line 60: Corrected. Lines 69 – 81: Text revised. Line 195: Corrected Line 257: Correction done in the text. Line 263: Gametocytes count was not determined in relation to age but from literature pathology of malaria infection may be determined by many factors such as age, genetic factors e.g immune system e.t.c. Therefore, they may be healthier than children in the lower age group. 1) Ethical Clearance was obtained from Enugu where the University of Nigeria has its Teaching Hospital that supervised the research. 2) 5ml venous blood was collected from which 1ml was used for the malaria parasite test and 4ml was used for biochemical and haematological test. This has been corrected in the text.
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<u>Optional/General</u> comments	Overall, this is an interesting study that contributes to our understanding of the aetiology and pathology of malaria. It seems to be part of a larger body of work, reduced to fit a paper format, and could potentially benefit from expansion towards a more comprehensive sample database and further analysis. Importantly, the text needs revision in terms of punctuation, style, grammar and clarity. The results section is in special need of major revision as it is extremely hard to read and extract relevant information from it. The authors' findings are interesting but the manner in which they are described is not clear enough. It takes several passages through the text to identify valuable information among the numeric descriptions which really hold no relevant interest unless digested into more readable data.	
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