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Journal Name:	International Journal of TROPICAL DISEASE & Health
Manuscript Number:	2014_IJTDH_10912
Title of the Manuscript:	RELATIONSHIP BETWEEN SERUM C-REACTIVE PROTEIN LEVELS AND SEVERITY OF <i>PLASMODIUM FALCIPARUM</i> MALARIA IN CHILDREN SEEN IN SOUTH-SOUTH NIGERIA.
Type of the Article	Original Article

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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	Materials and Methods: The description of the data collected in each of the participants is inadequate. Exactly what blood samples were collected from each child? Were full blood counts, random blood glucose and urea and electrolytes and creatinine performed in all study children or only those with severe malaria? The researcher does indicate that blood samples for CRP levels were taken from patients and controls. Was this (CRP) the only test conducted in the controls? The statistical test used in the data analysis should be described. Currently it is not clear what tests were performed; was it analysis of variance or t-test for instance? Results: The only results reported for the control group are general characteristics and temperature. The CRP which was stated as having been done in children in the control group is not reported. It becomes unclear why the authors even bothered getting a control group for this study.	For every child (Patients and controls), blood samples were collected for malaria parasite test and the C-reactive protein (CRP) assay. Please refer Materials and Methods section. For every patient with malaria studied, including the above tests blood cultures were also done. Furthermore, a full blood count and random blood glucose was done for every child with severe malaria. Urea/electrolyte and creatinine was only done in any child with signs of renal impairment. Refer Materials and Methods. The statistical tests conducted have been included in the 'data analysis' section. C-reactive protein test done in the control group gave a mean value of 2.21 ± 2.30 (range, 0.2 to 10.0mg/l) significantly less than that in the patient group. The overall of serum CRP for the patients was 11.97 ± 13.97 (range 0.2 – 70.0mg/l), (Refer results section) The authors got a control group for this study because of the recognized influence of genetic variations on the normal levels of circulating CRP. This is estimated to be between 40 – 60%. The genetic variation is associated with higher 'normal' levels of circulating CRP in the African-American population than in the Caucasians. This difference in serum CRP levels found in various population groups reflects the need for local reference ranges. This is widely advocated, thus the use of the healthy controls in this study.



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<u>Minor</u> REVISION comments	Discussion: The authors correctly state that mean serum CRP concentrations were higher in patients with severe manifestations of malaria than in those with uncomplicated malaria. However, parasitaemia also correlated well with severe malaria. Indeed a correlation was shown between parasitaemia and CRP concentrations. In the introduction, the authors assert that the intensity of parasitaemia does not always correlate with disease severity. In this study however, the authors' findings seem to suggest that in this age group parasitaemia is useful for assessing severity. Is it possible that the CRP concentrations are more a reflection of the parasitaemia?	It has been noted from this study that CRP concentrations were higher in children with greater levels of parasitaemia. It is therefore likely, that the CRP concentrations are a reflection of the parasitaemia, as well as other variables. Hyper-parasitaemia in itself does not necessarily have major prognostic significance in older children and adults, who are semi-immune individuals. (Individuals living in an endemic area and exposed to malaria several times). Such individuals with malarial immunity often tolerate high parasitaemia without severe clinical effects. The greatest burden of malaria parasitaemia and clinical disease is therefore seen mostly in children five years of age and below, which constituted this study population. These children are so affected because they are yet to acquire the natural immunity to malaria which develops and increases with age, cumulative number of malaria episodes, and time spent in an endemic area.
<u>Optional/General</u> comments		