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| **Peer**J |
| Thank you for your submission to PeerJ. I am writing to inform you that your manuscript, "Epidemiological evaluation of rubella virus infection among pregnant women in Ibadan, Nigeria" (#2014:11:3107:0:2:REVIEW), has been rejected for publication.  The comments supplied by the reviewers on this revision are pasted below. My comments are as follows:  Editor's comments  The manuscript has been reviewed by three reviewers and serious concerns were raised by them regarding the study design and execution that preclude it acceptance in its current form. The authors are invited to resubmit the manuscript after they have made the necessary changes  Offer Erez  Academic Editor for PeerJ  Reviewer Comments  Reviewer 1 (Salvatore Andrea Mastrolia)  Basic reporting  Summary: Olubusuyi et al performed a cross-sectional study in order to establish the immunologic conditions for rubella in two Institutions, considered representative of the entire population in Nigeria.  They give recommendations aiming an effective control of the infection in Nigeria in comparison with global rubella control programs for the prevention of congenital rubella infection and associated birth defects often collectively referred to as congenital rubella syndrome (CRS). In this study immunization for rubella is evaluated in 272 pregnant patients and results in terms of positivity for IgM and/or IgG antibodies, are analyzed following maternal age, educational status and belonging Institution. No significant differences are found in the study groups.  Experimental design  Title: the title is appropriate.  Abstract: the abstract is well written. I would suggest the authors to avoid abbreviations like CRS in the abstract. CRS now reads ‘congenital rubella syndrome’ in the abstract   Introduction  1. Line 26: I would express death of the foetus as fetal demise. Corrected (paragraph 2, line 7) 2. Lines 42-49: the first part of this paragraph should me moved to the discussion since it should be the fundamental part of authors’ purpose if they want to demonstrate that an improvement in prevention programs is needed in Nigeria. Modified and moved to the discussion section (paragraph 3)  The last sentence at line 47-49 should be modified in order to close the introduction, being the connection with material and methods section. Corrected (Last sentence modified to close the introduction-paragraph 5)  Materials and methods 1. Lines 63-64: may the author explain why the selected Institutions were considered as offering a true representation of the study population? One of the selected Institutions is a tertiary hospital while the other is a secondary hospital. The Institutions attend to pregnant women of diverse academic and socio-economic status, therefore a study in such hospitals afford us the opportunity of enrolling women of different backgrounds representative of the community.- explained in the text (Study location in the materials and methods section).  2. Section: enrollment of subjects. Please read my comment in the section of general comments, regarding patient enrollment.  Validity of the findings  Results naivety  1. Lines 114-117: the authors state that patients’ enrollment was based on exposure and presentation of symptoms. In the material and methods section they were dealing only with symptoms presentation. Corrected - patients were enrolled based on consent to participate, and presence of any of the clinical presentations like observable rubella-like rash, fever, lymphadenopathy and arthralgia (Materials and methods section - enrolment of pregnant women). In case exposure to symptomatic patients with rubella, they should specify the interval between exposure and clinical evaluation and if this was occurring anyway after developing of symptoms. Addressed I would ask the authors to clarify this section according to material and methods because at the moment the approach to study design and results is confusing. Addressed  Discussion 1. Lines 119-120: here the authors state that a high prevalence of anti-RV IgG suggests previous exposure to the infection. Since they are enrolling patients based on the presence of symptoms of acute infection, can they explain the correlation between their statement and their enrollment strategy? Because the studied pregnant women were rubella vaccine naïve, presence of anti-rubella IgG is indicative of previous infection with the virus 2. Lines 125-130: the authors report other studies showing similar data compared to their study. I suggest the author to add data included in other reports to the discussion. Included – Discussion section (paragraph 2) 3. Lines 137-139: please see my comments regarding patients’ enrollment Corrected  Conclusion definite 1. Lines 165-167: what do the authors mean when they deal with “burder rates” ? Burden rates deleted (conclusions section) 2. Lines 170-172: the authors introduce in this paragraph a new concept that is not mentioned in the paper (“to ascertain potency of vaccines prior to recommendation for vaccination and review of antibody response in randomly selected individuals post vaccination to achieve elimination of rubella”). I would suggest the authors to discuss this issue in the appropriate session if they want then to mention it in the conclusion. Deleted – It was not part of the objectives of the study.  Comments for the author  General comments: I read with interest the study performed by Olubusuyi et al and I have some major concerns: procedure 1) As the authors state on line 124 (I would suggest the author to add page numbers), there other existing reports (references 14-18) dealing with the problem of immunization and prevention programs for rubella in Nigeria. After reading the manuscript, it does not seem clear what is the clinical importance of the present report and what differentiates it from previous ones. The objectives of the current study has been clearly defined to differentiate it from previous studies e.g. the current study appraised rubella infection among symptomatic pregnant women in the population (Introduction section - last paragraph).  2) The patients’ enrollment as it is described on line 68-71 and reads “Subjects were enrolled between September 2012 and June, 2013. Consenting antenatal clinic attendees were examined for presence of observable rubella-like rash, fever, lymphadenopathy and arthralgia. Subjects presenting with any of the listed clinical presentations were enrolled for the study. Subjects without any of the clinical presentations were excluded from the study”. It does not match with the purpose of the study. If I understood, the study was aiming to evaluate the immunization of Nigerian population to rubella infection, in order to establish the appropriateness of national prevention programs. Looking for patients with symptoms implies the risk of overestimating cases of acute infection, having a wrong perception of the immunization within the population. The aim of the study was to appraised rubella infection among symptomatic pregnant women in the population (Introduction section - last paragraph). 3) How could the authors exclude that the symptoms were related to other pathological conditions (flu?, other rush inducing diseases?) Possibility of other pathological conditions admitted and included in the manuscript (Discussion section – paragraph 1) 4) Rather than subjects I would use terms like pregnant patients, patients, women, throughout the paper. ‘Subjects’ now read ‘pregnant women’ 5) I would suggest the authors to refer the paper to an English editing service in order to improve written English (there are many spelling mistakes and sentences are often not clear in their structure). Addressed in the text. I think the editor can reconsider this manuscript for publication after major revision.  Reviewer 2 (Michela Quaranta)  Basic reporting  The present manuscript entitled Epidemiological evaluation of rubella virus infection among pregnant women in Ibadan, Nigeria is a simple epidemiological study aimed at appraising immunity to rubella in the pregnant population in the region. The article is well written and structured. The subject is well introduced and relevant literature has been appropriately referenced.  Experimental design  The scope of this study was to evaluate anti-RV IgM and IgG in pregnant women in the region. The authors tested by Enzyme Immunoassay for IgM and IgG in 272 serum samples. the testing was carried out in accordance with WHO guidelines. Materials and methods: 1)Considering the objective of the study, "line 57: to appraise immunity to rubella in the population", I would like to ask the authors to expound on their decision to exclude all asymptomatic patients form the study stating as strict inclusion criteria the presence of observable rubella-like rash, fever, lymphadenopathy and arthralgia. The WHO and CDC clearly state that up to 50% of rubella infections may be overt and clinically asymptomatic. In consideration of the aim of the study perhaps laboratory testing also on asymptomatic pregnant women may have been appropriate. unless the aim of the study is to determine the rate of rubella infection in symptomatic pregnant women. In a previous study [13] conducted in one of the study sites, the lead author had appraised immunity to rubella in the population. This study was designed to specifically appraise rubella infection among symptomatic pregnant women (Introduction section – last paragraph). 2) In the attached questionnaire, the following is stated "If a patient has clinical features 1 and 2 + 3, then proceed to section B for enrolment and collection of relevant information" whereas in line 83 of the manuscript we find the following: "Subjects presenting with any of the listed clinical presentations were enrolled for the study". Please clarify Corrected. It was an oversight. The questionnaire later used for the study read ‘If a patient has any of clinical features 1, 2, 3 or 4, then proceed to section B for enrolment and collection of relevant information’  3)While it seems intuitive, please clarify if serum sampling was performed in the 4-28 days interval from onset of rash (WHO recommendations) and not later than 2 months after which IgM would wane and only IgG would persist For patients with observable rash sampling was performed within 2-3 weeks. 4) I would appreciate if you might construct a clearer table regarding serological testing report distinct from the demographic variables collected as it is of difficult interpretation at the moment. Table 2 has been created for serological testing report.  Validity of the findings  No comment  Comments for the author  The study is of interest. The manuscript must be approved after clarifications specifically regarding the aim of your study in view of your selection criteria.  Reviewer 3 (Anonymous)  Basic reporting  "No Comments".  Experimental design  • The clinical symptoms should be considering gestational age Agreed. • Missing data about vaccination information, like age? Rubella vaccination is not free in Nigeria, and is usually administered to children or adults on request at a cost. None of the pregnant women enrolled reported to have previously taken rubella vaccine.  Validity of the findings  • Please add some Fetal outcome for extra finding Limitation of the study – We could not track the women for fetal outcome because the ethical approvals for the study did not cover tracking of the women post enrolment.  Comments for the author  It is very important issue more information about fetal outcome is needed Addressed |