Author's response to reviews

Title: Prevalence and type of Monoclonal Gammopathy of Undetermined Significance in an apparently healthy Nigerian population: A Cross Sectional Study

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Author's response to reviews: see over
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Re: Manuscript reference No. MS: 8278302986613008

Please find attached a revised version of our manuscript “Prevalence and type of Monoclonal Gammopathy of Undetermined Significance in an apparently healthy Nigerian population: A Cross Sectional Study”, which we would like to resubmit for publication as an original article in BMC Blood Disorder.

The comments of the reviewers were highly insightful and enabled us to improve the quality of our manuscript. In the following pages are our point-by-point responses to each of the comments of the reviewers as well as your own comments.

Revisions in the text are shown using yellow highlight for additions, and strikethrough font for deletions. In accordance with the editorial request, we have included the name of the body which gave ethical approval with a reference number, stated clearly that a written informed consent was obtained and a section on limitation of the study have been added to the discussion.

The manuscript and figures have been formatted to conform to the journal style. We hope that the revisions in the manuscript and our accompanying responses will be sufficient to make our manuscript suitable for publication in BMC Blood Disorders. For reasons of financial constraint, we are willing to use the services of Edanz for copyediting with the assurances of acceptance for publication.

We shall look forward to hearing from you at your earliest convenience.

Yours sincerely,

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Responses to the comments of Reviewer #1

1. The authors do not describe this group of selected people very well, it is never stated if the entire 414 persons were Africans only or how they were included in the study and therefore it is hard to say if they represent Nigerian population in general.

Response:
It is stated on page 5; “Four hundred and fourteen apparently healthy Nigerian adult volunteers without a known liver disease, lymphoproliferative disease, HIV/AIDS, on any immunosuppressant, or organ transplantation were enrolled into the study. Subjects were selected using stratified sampling, with strata defined as the constituent counties or other geographic subdivisions of Lagos; a metropolis. Prospective participants were approached face to face by a trained recruitment coordinator and enrolled once they consent and meet the study enrollment criteria. The median age of the population studied is 19.3 years, life expectancy is 47.56 years and only about 3% of the Nigerian population is above 65 years. The Nigerian population is a very young population with close to half of its population below 15 years. It is therefore not surprising that participants enrolled into the study had a median of 45.00 years, though range of 20 to 84 years and that 44.4% of the sample population were in the age range 40-49 years while only 34% were above 50 years and 1.22% above 70 years. We think the study population represents the age distribution of adult Nigerians and the general Nigerian adult population.

The age-specific incidence rate of multiple myeloma varies by race. The median age at diagnosis is younger in blacks than in whites. Since recent data shows that MM is consistently preceded by monoclonal gammopathy of undetermined significance (MGUS), it is pertinent that we look for MGUS in the younger population of blacks. This informs the decision to look at all adult in our study rather than just people above 50 years as was done in the study by Landgren et al in Ghana.

Responses to the comments of Reviewer #2

1. Although this is correct, what is more interesting is whether the age-adjusted prevalence differs from that in e.g. US and Ghana. It would also have been interesting to see if the relation to age that is evident in the Caucasian population but not in the population of Ghana is observed. Unfortunately there a limitations of the study that makes it very difficult to decide on that.

Response:
The limitations of the study have been stated.

2. First the population size is too small. The observed prevalence of 0.24% has confidence limits (95%) of 0.01-1.38. Second there are too few patients in higher age groups to make it possible to compare with other studies. Only 34% are 50 years or older compared to 100% of patients in the Ghana study by Landgren et al. The authors should be still more clear about these limitations and stress that the data can only be used to generate a hypothesis regarding whether prevalence in Nigeria differs from Ghana or Western Countries.
Response:
Sample size as a limitation of the study has been stated. We aimed for a population based study of eligible adult to report prevalence data across age group and not specific for age above 50 years. The sampling method we used was stratified random sampling by household to avoid bias or oversampling for sex, and age, occupation etc.

3. It is not clear how the study population was recruited. Considering the known age-related incidence of MGUS, at least in western countries- the authors might have made efforts to include more patients in the higher age groups. The authors should better describe how the recruitment was planned and performed.

Response:
Salawu L et al,(WAJM, 2005), reported the median age of presentation of multiple myeloma in Nigerians as 60 years, in that report, 18.5% of the patient were 40 years or younger. Unpublished data from our hospital in Lagos also shows that it is not uncommon to see patients with multiple myeloma aged 40 years or younger. As stated earlier, recent data shows that MM is consistently preceded by monoclonal gammopathy of undetermined significance (MGUS) by 5-8 years. it is pertinent that we look for MGUS in the younger population of blacks. Several epidemiological studies (Aguzzi et al, 1992; Axelsson et al 1966; Carrel et al, 1977; Landgren et al, 2006; Ogmundsdottir et al, 2002) have also looked at MGUS in the general population including young adults. Recruitment has been described better in the manuscript.

4. The discussion is rather extensive and could be shortened.

Response: this was reviewed.

5. The authors use a reference (14) by Aguzzi et al to mention the 3% prevalence of MGUS in a Swedish population rather than quoting the original publication by Axelsson et al – the very first study of the prevalence of MGUS ever performed!

Response:
This has been corrected. The original study by Axelsson et al has been cited.