Author’s response to reviews

Title: Elevation of small, dense low density lipoprotein cholesterol—a possible antecedent of atherogenic lipoprotein phenotype in type 2 diabetes patients in Jos, North-Central Nigeria.

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Version: 1 Date: 11 Sep 2017

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Editor Comments:

1) After the Conclusions in the main body of the paper, please include a List of abbreviations.

Reviewer reports:

Klaus Parhofer (Reviewer 1): This is a study which evaluates lipid metabolism in a group of 176 diabetic patients and 154 controls in Central Nigeria. Fasting lipid parameters and LDL-subtype distribution was measured. It is shown that diabetic patients in Nigeria also have a typical dyslipidemia. In addition, the authors show that more diabetic patients fulfill criteria for diabetic dyslipidemia if the predominance of small-dense LDL is used to define this condition than if the classical lipid parameters are used. The authors draw the conclusion that LDL-subtype distribution should be included into routine assessment.
This study is interesting because it provides data from a part of the world were information on diabetes is sparse. However, the manuscript raises several aspects that need to be addressed.

1. The recommendation to measure small-dense LDL is far-fetched. There is no data showing that using small-dense LDL as a criterion to start lipid lowering therapy translates into better risk reduction than using LDL-cholesterol concentration. Therefore, most (if not all) guidelines do not recommend to measure small-dense LDL outside clinical studies and recommend using either non-HDL-cholesterol or LDL-cholesterol to guide treatment. In addition, the cutoff value used for small-dense LDL is derived from a Japanese study which may or may not make sense in the population under study.

2. It would be more important to describe the diabetic cohort in more detail. How many patients have metabolic syndrome? How are they treated? What is the HbA1c? etc.

3. The result section should be restructured. Currently there is no clear flow. First there is a comparison between diabetic and non-diabetic, then, comparisons between male and female and then again comparison between diabetic and non-diabetic and so on. It makes more sense to first describe the diabetic patients as whole group and compare them to controls. In a second step subgroups (according to gender, age, etc.) can be evaluated. If there are differences between males and females in both groups (diabetic patients and controls) then this should be taken into account during analyses (either include gender into the model or at least compare diabetic males to control males and diabetic females to control females).

MY RESPONSE TO EDITOR AND REVIEWER'S COMMENTS

Cecelia Devoto
Editorial Office
BMC Clinical Pathology

Dear Editor,

Resubmission of corrected manuscript to BMC Clinical Pathology – CPAT-D-17-00013
I hereby write to inform you that we have carried out the corrections in line with the recommendations of the reviewers to the best extent possible. The modifications are indicated below. All new additions to the manuscript have been highlighted in red in the body.

1. The title has been modified to reflect the aim of the study and conclusions that are supported by available data. The new title is: ‘Elevation of small, dense low density lipoprotein cholesterol—a possible antecedent of atherogenic lipoprotein phenotype in type 2 diabetes patients in Jos, North-Central Nigeria’. (Title page 1)

2. The Abstract has been modified to reflect the new aim of the study. (Pages 2 and 3)

3. In point 1, the reviewer expressed reservations about our application of the cut-off for small dense lipoprotein cholesterol from a Japanese population on our subjects using it to diagnose dyslipidaemia. We agree with this suggestion and have modified the discussion to reflect our agreement (Page 16). In this regard the former Table 5 which showed a validity test of different lipid parameters to determine their accuracy using recommended cut-off points for dyslipidaemia in patients with type 2 diabetes and non-diabetes has been removed from the result section.

4. A more detailed description of the diabetic cohort has been added to the result section in line with the 2nd recommendation. The duration of diabetes among our subjects was classified further into 10 years and under, and above 10 years. The duration of hypertension among diabetics with hypertension was also added. Drugs used to treat the diabetes population were mentioned and the percentages of diabetics with past histories of adverse cardiovascular events were indicated (page 9). We were unable to classify patients according to presence or absence of metabolic syndrome. This is because parameters such as waist circumference, fasting plasma glucose and HbA1c were not recorded during the study even though they were done routinely by the attending physician and used as criteria for patient selection into the study. However, reporting these parameters would have strengthened the conclusions reached in this study. We accept our failure to record these as part of the limitations of our study.

5. The result section has been restructured in line with the recommendations of the reviewer.

I. Table 1 is retained in the same position as in first manuscript.

II. The new Table 2 was formerly Table 4 with the same caption ‘Serum lipid concentrations in diabetic patients and controls’.

III. New Table 3 showing ‘serum lipid concentration in diabetic men and women was formerly Table 2.’
IV. New table 4 showing ‘serum lipid concentrations in men and women controls was formerly Table 3.

V. As noted earlier, former Table 5 which showed a validity test of different lipid parameters to determine their accuracy using recommended cut-off point for dyslipidaemia was deleted since we have not established the cut off for increased small, dense low density lipoprotein cholesterol in our population.

VI. The present Table 5 showing serum lipid concentrations in men with diabetes compared with men without diabetes is a new table.

VII. Table 6 shows serum lipid concentrations in women with diabetes compared with women without diabetes. Both tables 5 and 6 were created to add additional information to the research work in line with the recommendations of the reviewers.

VIII. Table shows a comparison of all lipid parameters compared across 3 subgroups of diabetes patients. Subgroup 1 <46 years old, subgroup 2: 46-60 years old and subgroup 3: >60 years old. This table was created in line with recommendation of the reviewer to check the effect of age on the different lipid parameters measured.

6. Finally, a list of abbreviations has been added after the conclusion in the main body of the paper.

It is obvious that the corrections requested have improved the content of the work and our new conclusions are in line with available data. We hope that the modifications done will be accepted.

We look forward to your comments on our efforts.

With regards,

Kenneth O Inaku

Corresponding author, for all the authors.