

PEER REVIEW HISTORY

BMJ Open publishes all reviews undertaken for accepted manuscripts. Reviewers are asked to complete a checklist review form (<http://bmjopen.bmj.com/site/about/resources/checklist.pdf>) and are provided with free text boxes to elaborate on their assessment. These free text comments are reproduced below.

ARTICLE DETAILS

TITLE (PROVISIONAL)	Dyslipidemias in women using hormonal contraceptives: a cross sectional study in Mulago Hospital Family Planning Clinic, Kampala, Uganda
AUTHORS	Bakesiima, Ritah; Byakika-Kibwika, Pauline; Tumwine, James; Kalyango, Joan; Nabaasa, Gloria; Najjingo, Irene; Nabaggala, Grace; Olweny, Francis; Karamagi, Charles

VERSION 1 – REVIEW

REVIEWER	Randy Bogan University of Arizona, USA
REVIEW RETURNED	07-Mar-2018

GENERAL COMMENTS	<p>Comments:</p> <ol style="list-style-type: none">1. The authors state in the abstract and Methods sections that dyslipidemias are “defined as derangements in the lipid profile levels”. This is vague terminology and unnecessary since the criteria the authors used for defining dyslipidemia is very specific: LDL > 160 mg/dl, or HDL < 40 mg/dl, or TC > 200 mg/dl, or Triglycerides > 150 mg/dl.2. It is stated that informed consent was obtained, was it written or oral?3. In the results, the authors mention that women with high fasting blood sugar had a higher prevalence of dyslipidemias than those with normal blood sugar. Since there were only 12 participants who had high fasting blood sugar, this is too small of a sample size to draw any conclusions on differences in dyslipidemia prevalence between low and high blood sugar.4. Many studies have evaluated the effect of hormonal contraceptives on lipids. The discussion and references cited do not adequately describe previous research related to this study.5. In the discussion, the authors state “Unfortunately, this is one of the first studies to report on dyslipidemias in ART users”. This indicates that the data on ART and dyslipidemia presented in the current study is a novel finding, which is an advantage rather than being “unfortunate”.6. The authors talk some about the type of hormones in contraceptives and how they are believed to affect lipids. I feel there are interesting subgroup analyses that could provide more information on the type of hormone in the contraceptive and the specific type of dyslipidemia. For example, among participants taking progestin-only injectable or implant, what specific type of dyslipidemia was most common? Is there a difference between progestin-only contraceptives and combination contraceptives in the prevalence of specific dyslipidemias?
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	7. It is not clear to me why the STROBE statement is included. There is no mention of where each item in the checklist is addressed in the manuscript.
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REVIEWER	Mohammed Zerf Physical Education Institute Laboratory OPAPS, University of Mostaganem, Mostaganem, Algeria
REVIEW RETURNED	08-Mar-2018

GENERAL COMMENTS	no comments
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REVIEWER	Anthony Agbata Federal Teaching Hospital, Abakaliki, Nigeria
REVIEW RETURNED	24-Mar-2018

GENERAL COMMENTS	<p>Abstract: Add a subheading for statistical analysis. Strengths and limitation of the study should be removed from the abstract section and placed appropriately.</p> <p>Introduction: Study design, settings and population: Explain how you arrived at your sample size for this study. Provide more background information on the study area, the characteristics of your study population. Describe the survey instrument used. See other comments and observations on the main manuscript.</p> <p>- The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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VERSION 1 – AUTHOR RESPONSE

Responses to comments by Reviewer 1 (Randy Bogan):

1. The definition for dyslipidemias has been corrected as indicated in the abstract on Page 2 and in the methods section on Page 6.
2. Written informed consent is what was obtained and this has been incorporated on Page 5.
3. It is true that the number of participants with high fasting blood sugar levels was small, so I did not make any conclusions on the finding of higher dyslipidemias amongst these participants; I only mentioned it in the bivariate analysis as a finding but it was later dropped in the multivariate analysis.
4. It is true that many studies have evaluated the effect of hormonal contraceptives on lipids, however not all were addressing the factors I addressed, and I also considered the most recent studies and those with high quality evidence for my literature.
5. The word "unfortunate" has been eliminated from the write up on Page 11.
6. Contraceptive type and its association with specific types of dyslipidemias was assessed although it was not found to be significant, and that it why it was not included in the manuscript because of the limited space.
7. STROBE statement has been included with the page numbers where each item can be found.

Responses to comments by Reviewer 3 (Anthony Agbata):

- According to the author instructions, the abstract should not have a section on statistical analysis, while the strengths and limitations are supposed to be included after the abstract.
- The survey instruments used were questionnaires and were described on Page 5 of the manuscript.

- The other comments and observations in the attached file have been worked on accordingly as indicated in the manuscript.

VERSION 2 – REVIEW

REVIEWER	Randy Bogan University of Arizona, United States of America
REVIEW RETURNED	16-May-2018

GENERAL COMMENTS	For the most part the authors addressed my previous concerns.
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REVIEWER	Anthony Agbata Federal Teaching Hospital, Abakaliki, Ebonyi State, Nigeria
REVIEW RETURNED	10-May-2018

GENERAL COMMENTS	<p>Observations:</p> <p>Some queries raised in the previous review were not addressed.</p> <ol style="list-style-type: none"> 1. How was the sample size calculated 2. The inclusion and exclusion criteria were not specific enough (see manuscript review) 3. Were there any missing variables, and how did you address the problem? <p>- The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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VERSION 2 – AUTHOR RESPONSE

Thank you Prof. Anthony Agbata for the observations. I have corrected them as indicated below:

1. The sample size was calculated using the Kish Leslie formula and Cumming formula for proportions in two groups as indicated on Page 5 in the manuscript.
2. The inclusion and exclusion criteria have been clearly spelled out in the manuscript on Page 5.
3. There were no missing variables in this data because of the strictness followed during data collection, but in case it had happened, we had accounted for 10% missing data during our sample size collection as indicated on Page.

All other queries indicated in the manuscript have been addressed as required.

VERSION 3 – REVIEW

REVIEWER	Anthony Agbata Federal Teaching Hospital, Abakaliki, Nigeria
REVIEW RETURNED	28-Jun-2018

GENERAL COMMENTS	This is an improved version of the manuscript. However, some of my earlier observations were not properly addressed. I have noted
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	<p>these points in this re-revised version. The authors should endeavor to address these concerns.</p> <p>- The reviewer provided a marked copy with additional comments. Please contact the publisher for full details.</p>
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VERSION 3 – AUTHOR RESPONSE

Reviewer’s Comments (Reviewer 3 – Dr. Anthony Agbata):

Comment: This is an improved version of the manuscript. However, some of my earlier observations were not properly addressed. I have noted these points in this re-revised version. The authors should endeavour to address these concerns.

Response: Thank you very much for your comments. We apologise for this. Inadvertently, we had not addressed some of your earlier observations. These concerns have now been addressed as follows:

- i) **Comment:** (Pg 5, lines 20 – 22): What study procedures are you referring to? These study procedures should be stated clearly for reproducibility.

Response: Women who were unable to comprehend either English or *Luganda* (the local language used in Central Uganda) or those physically or mentally unable to adhere to study procedures, such as giving of consent and the interview process were excluded.

- ii) **Comment:** (Pg 6, line 35): Use appropriate citation for this software.

Response: Data were analysed using Stata version 13.0 (StataCorp. 2013. *Stata Statistical Software: Release 13*. College Station, TX: StataCorp LP).

- iii) **Comment:** (Pg 7, line 25): State what you mean by 'long term use of hormonal contraceptive'.

Response: Due to patients’ experiences ..., we felt the need to determine whether “long term use” of HCs has an effect on lipid profiles. We have modified this sentence to reflect long term use as being “more than three months of use” of hormonal contraceptives.

- iv) **Comment:** (Pg 7, line 32): Explain further, how the patients informed the design of the study.

Response: Patients were involved in the design of the study through their contribution to the refining of the data collection tool. This was through pre-testing and piloting of the data collection tool.

- v) **Comment:** (Pg 11, line 15): ART is associated with dyslipidemias, reference needed

Response: A reference has been added (see Bekolo, 2014).

- vi) **Comment:** (Pg 13, lines 14 – 16): This reason may not be valid. Consider deleting this highlighted section.

Response: Thank you very much for this query. The contradiction is noted and the statement regarding Wei's study has been deleted from the discussion.

- vii) **Comment:** (Pg 11, lines 52 – 54, in R2): How is this possible? Explain? Does study design determine outcome? OR are you implying that your design is not appropriate to answer the research question?

Response: Thank you very much for this query. The contradiction is noted and the statement regarding Wei's study has been deleted from the discussion.

- viii) **Comment:** (Pg 12, line 33): Do you mean 'large' numbers.... You had earlier noted that this high prevalence could have been as a result of the high percentage of participants on ART.

Response: This statement has been deleted since it was not making sense.

- ix) **Comment:** (Pg 13, line 24): If you had incomplete information, that means that some data were missing. If not, delete this word.

Response: Since there was no missing data in this study, the data was complete. We therefore realise that the word "incomplete" is irrelevant. It has been deleted as advised.

- x) **Comment:** (Pg 15, line 38): Old references, update.

Response: Several references have been updated.