PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Association of Risk Factors and Breast Cancer Among Women Treated at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: Case-control study
AUTHORS	Hassen, Fatuma; Enqueselassie, Fikre; Ali, Ahmed; Addissie, Adamu; Taye, Girma; Tsegaye, Aster; Assefa, Mathewos

VERSION 1 – REVIEW

REVIEWER	Degu, Amsalu United States International University-Africa, Department of Pharmaceutics and Pharmacy Practice
REVIEW RETURNED	18-Feb-2022

GENERAL COMMENTS	Abstract please correct the study design as case control Introduction The background of the study didnot not come out clearly with flow Methods Eligibility criteria: it is not clear about te source of the control groups in the study. Did you take the one from the oncology department or what was the conditions of the controls? Sampling and sample size determination How do u came of a total of 460 study participants? The methods of sample size determination was not clear or adequately described in the write up Data collection analysis and management i think the classication of menopuase is not accurate as I think the classification of menopause is not accurate as described in the manuscript, and it should be 12 months cessation of the monthly period. What about the delay for a longer time due to hormonal contraceptives or lactation? Was it factored in during the postmenopausal the classification? Results Can you remove all the raw lines in all tables Please justify why the odds of breast cancer was 2.82 times higher among unemployed women as compared with employed in the discussion part. Discussion Can you add justification about the similarities and differences of the findings in the discussion part. References I have noticed some inconsistencies in the reference list. Please kindly correct it accordingly

REVIEWER	Atalar, Fatmahan
	Muhimbili University of Health and Allied Sciences
REVIEW RETURNED	27-Feb-2022

GENERAL COMMENTS	General observations
	1. English language used in this manuscript is understandable, however, there are several language and grammatical mistakes that need your attention. You can consult an English language expert on a native speaker. For example, it should be "compared to" not "compared with"..
	2. This is a case-control study. Should be written as a single word not "case control"
	3. There are several sentences connected without a space in between. Kindly revise it throughout.
	Title
	The title can be changed to "Association of risk factors and breast cancer among women…….." or "Relationship of risk factors with breast cancer among women…….."
	Keywords
	No need of having both "risk factors" and "reproductive risk factors" as keywords, one should be deleted.
	Abstract
	The abstract can be significantly improved. For example, the design subheading can be omitted because what is communicated there is a repetition of the first sentence of the methods subheading.
	Background
	1. The background section is too wordy. Kindly consider combining some sentences into fewer ones to make a smooth flow of facts. This is specifically for pages 2-3.
	2. In your literature build-up it will be helpful if you consider adding recently published related findings from the East Africa region. There are several articles to consult e.g Sayed et al 2021: https://doi.org/10.21203/rs.3.rs-266260/v1, Rweyemamu et al 2021: https://doi.org/10.1186/s12905-021-01536-6, etc.
	Materials and methods
	1. The study participants were recruited within a period of almost one year (may 2018-June 2019). Why didn't you extend this period to capture more samples?
	2. Eligibility criteria subsection: Restructure the second sentence, it seems uncomplete.
	3. Data collection, analysis and management: The main variables (risk factors) analyzed in this manuscript need to be defined in detail. For example, how were menarche and menopausal status defined?
	Data analysis
	Please rearrange the data analysis section considering the following comments.
	1- The tests were used to analyze the study group should be defined in detail.
	2- What were the confounding variables? What was the criterion used to evaluate confounding variables? Which test was used to determine the confounding variables?

3- Additionally, multinomial logistic regression was performed in the study, and some of the groups were admitted as reference groups. But the details of the analyses were not given. Moreover, the reason for admitted reference groups should also be indicated.

4- Please clearly specify in footnotes which tests were used to analyze and which variables were adjusted in the analysis.

Results

1- The results section needs to be organized better and needs to be summarized.

2- The information summarized in tables does not need to be repeated in the results section

3- The BMI can be categorized as follows <25 normal, 25-29.9 overweight, and >30 obese.

4- The age can be categorized according to mean age of the case group (<42 age, >42 age)

5- P-value is missing (page7 line 14)

6- Table 3 and Table 5 can be combined

7- Use the SI units throughout. For example, Kg ? KG?, m? mt?.

8- The table legends need to be revised. No need to mention "at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2020" throughout the tables. Also

9- Table 2-5 can be re-written as "Association of ………"

4. "Multivariable" not "mult variable". Kindly check it throughout.

Discussion

1. "Buying capacity" can to be replaced by "purchasing power"

2. The discussion has not incorporated recent data published from the region. There are several similar articles from East Africa that can be a good stepping stone when discussing your findings. Kindly consider adding them, some recent articles have been shared here, see my comments on the Background section.

Conclusion and recommendation

The conclusion section is drawn hastily and it can be further improved by highlighting major findings of this article and their implication to breast cancer in Ethiopian population.

Abbreviations

You have indicated BC as an abbreviation of Brest cancer. However, throughout the manuscript, BC has not appeared anywhere. Either delete it of replace "breast cancer" with "BC" throughout the manuscript.

VERSION 1 – AUTHOR RESPONSE

Comment	Action taken
Reviewer: 1	
Abstract	
please correct the study design as case control	Thank you for the comment and the correction is made accordingly.
Introduction	
The background of the study did not come out clearly with flow	Thank you for your comment. We have tried to correct the flow and un necessary details was

	removed..
Methods	
Eligibility criteria: it is not clear about the source of the control groups in the study. Did you take the one from the oncology department or what was the conditions of the controls?	Thank you for the comment and explanation is given for the eligibility criteria. Yes, we used controls from Oncology Departments and controls were women accompanying selected cases or care givers.
Sampling and sample size determination	
How did you come with a total of 460 study participants? The methods of sample size determination was not clear or adequately described in the write up	The comment is well taken and sampling and sample size calculation is adequately described. up (under and Sampling and sample size determination) Page 5, second paragraph.
Data collection analysis and management	
I think the classication of menopuase is not accurate as I think the classification of menopause is not accurate as described in the manuscript, and it should be 12 months cessation of the monthly period. What about the delay for a longer time due to hormonal contraceptives or lactation? Was it factored in during the postmenopausal the classification?	Thank you for your comment, it is well taken and correction is made in the methodology section. In addition, since the definition has been changed, minor correction was also made regarding the frequency of menopausal status and age at menopause in table 3, page 13. Regarding hormonal contraceptive use, majority of study participants responded that the reason of menses stop was their old age.
Results	
Can you remove all the raw lines in all tables	Thank you for your comment, and all the raw lines are removed from all tables (Table 1-4).
Please justify why the odds of breast cancer was 2.82 times higher among unemployed women as compared with employed in the discussion part.	Thank you for your comment. Justification is made why the odds of breast cancer was 4.28 times higher among un employed women under discussion section, page `16, last paragraph.
Discussion	
Can you add justification about the similarities and differences of the findings in the discussion part.	Thank you for your comment and justification is added in the discussion section.
References	
I have noticed some inconsistencies in the reference list. Please kindly correct it accordingly	Thank you for your comment, it is well taken and correction is made in the reference section.
Reviewer: 2	
General observations	
1. English language used in this manuscript is understandable; however, there are several language and grammatical mistakes that need your attention. You can consult an English language expert on a native speaker. For example, it should be "compared to" not "compared with"..	Thank you for your comment, it is well taken and attention was given to correct language and grammatical mistakes throughout the document. Especially in result and discussion section (page ,8 before table 1, page 14 , before table

	4, page, and page 18).
2. This is a case-control study. Should be written as a single word not "case control"	Thank you for your comment, it is well taken and correction was made throughout the document.
3.There are several sentences connected without a space in between. Kindly revise it throughout.	Thank you for your comment, and correction is wade throughout the document.
Title	
The title can be changed to "Association of risk factors and breast cancer among women……." or "Relationship of risk factors with breast cancer among women……."	Thank you for your comment, it is well taken and the title is modified as "***Association of Risk Factors and Breast Cancer among women Treated at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia: Case -control study,"*** on the tittle page.
Keywords No need of having both "risk factors" and "reproductive risk factors" as keywords, one should be deleted.	Thank you for your comment and correction is made in the abstract section. "Reproductive risk factors" is deleted from the key word list.
Abstract	
The abstract can be significantly improved. For example, the design subheading can be omitted because what is communicated there is a repetition of the first sentence of the methods subheading.	Thank you for your comment; We have tried to improve, especially the result of abstract section. Regarding putting **design** before method section is the requirement of the BMJopen journal. (it is the format of the abstract based on the journal)
Background	
1.The background section is too wordy. Kindly consider combining some sentences into fewer ones to make a smooth flow of facts. This is specifically for pages 2-3.	Thank you for your comment and the necessary correction is made. To make smooth flow, unnecessary detail is removed from background section.
2. In your literature build-up it will be helpful if you consider adding recently published related findings from the East Africa region. There are several articles to consult e.gSayed et al 2021: https://doi.org/10.21203/rs.3.rs-266260/v1, Rweyemamu et al 2021: https://doi.org/10.1186/s12905-021-01536-6, etc.	Thank you for your comment and sharing such recent literatures. Modification was made by including recent literature from East Africa in background section.
Materials and methods	
1. The study participants were recruited within a period of almost one year (may 2018-June 2019). Why didn't you extend this period to capture more samples?	Thank you for your comment, but since this study is part of PhD work which is conducted in resource limited setup; there was time and budget constraint to extend the study period.
2. Eligibility criteria subsection: Restructure the second sentence, it seems incomplete.	Thank you for your comment. The sentence is re structured and completed.
3. Data collection, analysis and management: The main variables (risk factors) analyzed in this manuscript need to be defined in detail. For example, how were menarche and menopausal	Thank you for your comment. Most of the risk factors are defined under the data collection, analysis and management section, page 7.

status defined?	
Data analysis	
Please rearrange the data analysis section considering the following comments.	
1- The tests were used to analyze the study group should be defined in detail.	Thank you for your comment, it is well taken and correction is made and tests used to analyze the study group were defined under data collection, analysis and management section, page 6, last paragraph.
2- What were the confounding variables? What was the criterion used to evaluate confounding variables? Which test was used to determine the confounding variables?	Thank you for your questions:. Confounding variables are variables whose presences affect the variable s being studied that the results do not reflect actual relationship. In this study the potential confounding variables were education, income, strenuous physical exercise, family history of breast cancer. The criteria used to evaluate confounding variables was using significance criteria with cutoff levels of p-values fixed at ≤0.05 for multiple logistic regression. The test used to determine the confounding variable is multiple logistic regression analysis. In our study we used step wise multiple logistic regression model.
3- Additionally, multinomial logistic regression was performed in the study, and some of the groups were admitted as reference groups. But the details of the analyses were not given. Moreover, the reason for admitted reference groups should also be indicated.	Thank you for your comment, the reference or the comparison group is indicated in each table as odds ratio of 1:00. Moreover, the reason for admitted reference group is based on previous similar studies.
4-Please clearly specify in footnotes which tests were used to analyze and which variables were adjusted in the analysis.	Thank you for your comment, it is well taken and types of testes and variables adjusted during analysis were specify for each tables (Table 1-4)
Results	
1-The results section needs to 1 be organized better and needs to be summarized.	Thank you for your comment, it is well taken and we have tried to organize the result section by removing unnecessary repetition. (in order to summarize the result part, redundancies are removed, eg. P values, odds ratios, confidence intervals).
2- The information summarized in tables does not need to be repeated in the results section	Thank you for your comment, it is well taken and correction is made throughout the result section. Especially, odds ratio and p Values are removed from each descriptions, before each table.
3- The BMI can be categorized as follows <25	Thank you for your comment, it is well taken

normal, 25-29.9 overweight, and >30 obese.	and correction is made in methodology section under statistical analysis. And correction is also made in table 1 page 8.
4- The age can be categorized according to mean age of the case group (<42 age, >42 age)	Thank you for your comment, but since age is one of the risk factors for breast cancer. Categorizing age according to mean age may not show the risk of breast cancer as age increases. In this study, age at diagnosis was categorized based on American Cancer Society fact and figure for breast cancer.
5- P-value is missing (page7 line 14)	Thank you for your comment, but on page 7, the total lie is only 13 and all P values were indicated.
6- Table 3 and Table 5 can be combined	Thank you for your comment, it is well taken, table 3 and table 5 are combined.
7-Use the SI units throughout. For example, Kg ?KG?, m? mt?.	Thank you for your comment, it is well taken and correction is made on page 7, paragraph 1 and table 1 page 8
8-The table legends need to be revised. No need to mention "at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2020" throughout the tables. Also	Thank you for your comment, it is well taken and table legends are revised by removing…"**at Tikur Anbessa Specialized Hospital, Addis Ababa, Ethiopia, 2020"** throughout the tables .
9-Table 2-5 can be re-written as "Association of ………"	Thank you for your comment, it is well taken and correction is made table 2-4, since table 5 is merged with table 3.
Discussion	
1."Buying capacity" can to be replaced by "purchasing power"	Thank you for your comment, it is well taken and correction is made in discussion section, page 17, first paragraph (line 7)
2.The discussion has not incorporated recent data published from the region. There are several similar articles from East Africa that can be a good stepping stone when discussing your findings. Kindly consider adding them, some recent articles have been shared here, see my comments on the Background section.	Thank you for your comment, it is well taken and comparison was made with similar studies done in East and other African countries including, Sudan, Uganda, and Cameroon).
Conclusion and recommendation	
The conclusion section is drawn hastily and it can be further improved by highlighting major findings of this article and their implication to breast cancer in Ethiopian population.	Thank you for your comment, it is well taken and we have tried to improve the conclusion section.
Abbreviations	
You have indicated BC as an abbreviation of Brest cancer. However, throughout the manuscript, BC has not appeared anywhere. Either delete it of replace "breast cancer" with "BC" throughout the manuscript.	Thank you for your comment and it is well taken; BC is deleted from the abbreviation list. Page 21, line No 1..