Author’s response to reviews

Title: Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30-49 years in Gulele sub-city of Addis Ababa, Ethiopia

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Author’s response to reviews:

Point-by-point response to reviewers’ comments on the manuscript entitled “Prevalence and severity of menopause symptoms among perimenopausal and postmenopausal women aged 30-49 years in Gulele sub-city of Addis Ababa, Ethiopia” (MS: BMWH-D-16-00086).

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We are very grateful for the very constructive and valuable comments that all reviewers have furnished us. We have taken due consideration of the comments provided and made all necessary revisions to the manuscript. We have provided a point-by-point response to the comments hereunder.

Response to Reviewer #1

Major compulsory revisions

Comment: Overall the manuscript is well written. I have several suggestions that may assist the authors with further revisions.
Authors’ response: Thank you.

Background

Comment: P4, line 13-14 - Definitions of perimenopause and premenopause in the background are not consistent with current definitions (ie premenopause is defined as prior the change in menstrual cycle, not the "one or two years preceding menopause", perimenopause refers to the time where irregularities in menstrual cycle are seen with symptoms). Suggest following the STRAW definitions for consistency. Harlow et al. Menopause 2012; 19(4):119.

Authors’ response: We have grossly revised the definitions of prememopause and perimenopause as per the reference suggested.

Methods

Comment: Study selection and subjects: More details on subject recruitment would be helpful. For example, how was the information about the study population obtained (ie how were ages available, how were the women identified)? How were the women contacted?

Authors’ response: We have provided detailed information on subject recruitment under study design and subjects in the revised manuscript.

Comment: Was there any other exclusion criteria? For example did you exclude women with certain medical conditions (for example breast cancer, chronic diseases such as renal/hepatic failure etc)? If not, was this information collected from the women (should be presented as part of the demographics).

Authors’ response: We did not collect data regarding breast cancer or chronic diseases such as renal/hepatic failure, and etc. We address this limitation and further potential for expanding our initial study in the future.

Comment: Data collection instruments: Was use of hormone therapy or CHC asked as well? Was different medical conditions captured - especially ones that may add to symptoms (for example thyroid)? Was BMI/weight collected? Smoking status? This background data is important in interpreting the prevalence/severity of menopausal symptoms.

Authors’ response: The data collection instrument did not include information on hormone therapy and other medical conditions. As this article is part of a study conducted to assess
‘Knowledge and Attitudes of Women aged 30-49 towards menopause in Gulele sub-city of Addis Ababa, Ethiopia’, such information were not available for analysis to answer our current new research question (objective). We believed that our analysis based on the available data in this article will provide a very useful piece of information/evidence regarding the prevalence and severity of menopause symptoms among women for concerned bodies. We have provided clear description of how data for this article is obtained under methods section in the manuscript.

We would like to thank you for the comments. We have used your comments in the discussion to help clarify important variables such as smoking status, obesity, hormone therapy even though we did not collect information about such background data in our study. We do believe that this is important in interpreting the prevalence and severity of menopause symptoms among women and will provide some insight for future research on menopause.

Results

Comment: P9, Lines 7 - 15, Table 1: The following information would be helpful in this section: number of women with hysterectomy, breakdown of the iatrogenic causes as mentioned in methods (BSO, chemotherapy/radiation induced), smoking status, BMI if available, medical conditions that may have overlapping symptoms with menopause. All of this information is important in interpreting the presence and severity of menopausal symptoms.

Authors’ response: We have included the number of women (n=9) who had hysterectomy. As we indicated above, we have addressed the important variable such as smoking status and other medical conditions in the discussion and we did elaborate on the limitation of our study since we did not collect this data from women.

Comment: Other information needed for postmenopausal women - age at menopause (ie LMP) and duration in menopause (for example number of years since LMP).

Authors’ response: Age at Last Menstrual Period (LMP) was collected for only postmenopausal women and the mean age at LMP for postmenopausal women was 42.6 (SD ±4.2 years) and the average duration of menopause (number of years since LMP) for these women was 2.6 (SD ± 1.8 years). We have included this in the revised manuscript.

Comment: How was monthly income (wealth quintiles) decided? Should include how this was classified in methods.

Authors’ response: Due to lack of an appropriate scale to rank the monthly income of participants in the study area, we decided to rank participants’ monthly income based on three
tertile percentile groups, with each group containing approximately the same number of cases. Using rank type ‘Tertiles’ or ‘3 Ntiles’ command in the Rank Cases function in SPSS, a rank of 1 to cases below the 33.33th percentile (labeled as lowest); 2 to cases between the 33.33th and 66.67th percentile (labeled as medium); and 3 to cases above 66.67th percentile (labelled as highest) were assigned. Thus, the participants’ monthly incomes were classified as lowest, medium, and highest. We have included this description in methods.

Discussion

Comment: P12, lines 15 -16: Where was the "age of 49 years" obtained - reference? Does the age of 49 years refer to both peri and postmenopausal women? Does it refer to the start of menopausal symptoms? It is difficult to compare the mean age in your study with this reference range without some idea of timeline since last LMP for postmenopausal women. The age of 40 years - is the mean age in your sample but may not represent the same thing as the reference range of "49 years".

Authors’ response: Thank you so much for pointing this. We removed the description of “age of 49 years” and alternatively we revised the stated paragraph grossly to reflect our revised analysis finding of mean age at LMP for postmenopausal women which was 42.6 years and the average duration of menopause (number of years since LMP) for these women at study time was 2.6 years. Our revision can be found in the revised manuscript under the discussion.

Comment: P12 - 13 - It may be helpful to have information on HT use or other treatment options for menopausal symptoms. This will provide some context when interpreting the symptoms and severity reported. As well it would be helpful to have demographic information such as smoking status and other medical conditions to be able to interpret the findings.

Authors’ response: We have included detailed information on hormone and other treatment options in discussion. Our revision can be found in track changes in the revised manuscript.

Conclusion

Comment: P14, Line 1 - "age of menopause was 40.1 years". Be cautious in indicating this as the age of menopause. This is the age of your sample, not the age of menopause.

Authors’ response: We have carefully revised the conclusion and other sections of the manuscript. We now believe that the information being conveyed will be clear to the readers.
Comment: Table 2: Much of the information in Table 2 is already in Table 3. Not sure if Table 2 is also needed. It could be removed.

Authors’ response: We have removed Table 2 and emphasized data in Table 3 (now Table 2).

Comment: Table 5 - why did you choose to present the data in this format versus the mean scores on the MRS scale?

Authors’ response: We chose to present frequency of severe MRS score for each subscale and an overall MRS score to obtain a more categorized view of our participants’ experiences. We were also interested in understanding the range of self-reported severity for each symptom and category (sub-scales) of symptoms. Since no previously published study exists, we wanted to ensure that Western-dominated definitions and symptoms did not bias our results. Thus, we presented our findings slightly differently.

Response to Reviewer #2

Major concern:

Comment: It appears that this report is a substudy of a larger national (?)study with the restrictive age range of 30-49. This is a significant methodologic problem if the goal as noted in the intro (page 4, line 12) is to examine menopause symptoms across the perimenopause and postmenopause age range, which commonly extends through the mid-50s. Why this particular "slice" of the data were analyzed for this purpose, given such a shortcoming, requires stronger rationale. Related to this problem, no recruitment methods are provided, no inclusion/exclusion criteria are given. Also, the % of women who did not meet the peri or post definitions is not given.

Authors’ response: As shown in the methods section of the manuscript, this specific article is a part of a broader study conducted to answer multiple research objectives, (that required a total sample 599 women), entitled “Knowledge and attitude of women aged 30-49 years towards menopause in Gulele sub-city of Addis Ababa, Ethiopia.” The larger study intended to recruit women actively undergoing menopause or the period immediately before and after. Therefore, the target age is less than the global average age at menopause. Additionally, no standard on average age at menopause has been established for Ethiopia.

We understand that our current study is not a representation of Ethiopian women since the study is conducted in only one area of Addis Ababa. From the larger study, which interviewed 588 women, our current sub-study included only 226 women while 362 women did not meet our
definition of active menopausal experience (peri- or postmenopause) and therefore would not have completed the MRS.

To clarify the message being conveyed further, we have thoroughly revised the text of the manuscript and we have also included details description about the recruitment of study subjects and inclusion/exclusion criterion.

Comment: There are a number of important inconsistencies that make it difficult to evaluate the key findings and their interpretations. For example, the definitions of menopause (line 3, page 2), and premenopause (page 4, line 13) overlap with those used to define perimenopause (page 4, line 12). Please explain these discrepancies

Authors’ response: Thank you so much for pointing this. We have completely revised the definitions of terms related to menopause and we now feel that there are no more contradictions.

Comment: The data in Table 3 suggest that all symptoms were higher in the Postmenopause group, yet, the discussion reports that psychologic symptoms were higher in the peri group (line 3, page 12). Please clarify and refer to specific tables when reporting these findings.

Authors’ response: Thank you so much for pointing this. We have re-run our analyses to check that symptoms were higher among postmenopausal women in our study. Accordingly we have carefully included our revision in the revised manuscript.

Comment: Typically before comparing two groups on the outcome variables of interest, an analysis is performed of demographic characteristics in each group in order to determine their potential as confounding variables. For eg, were the two peri/post groups similar in age? education? ethnicity? all of these demographics are known to influence menopause symptoms in other populations. Alternatively, why wasn't a multiple regression performed to provide some insights on your findings?

Authors’ response: We have reanalyzed the demographic characteristics of the study participants and revised the text of the manuscript accordingly. We had performed logistic regressions in the larger study but did not feel this analytic model would provide insight as our sample is limited and want to proceed with caution in our reporting. Our re-analysis output and revision to the manuscript can be found in the revised manuscript.
Comment: Also, the authors report that the average age of the sample was 40 yrs, and that the average age of "menopause" was also age 40 (see Conclusion) - a surprising finding well-short of the worldwide average of age 51. In addition, a third of the group was classified as postmenopausal (n=75), yet just 9 were reported to have experienced induced menopause, so how to explain this somewhat high rate in such a young sample? Please clarify.

Authors’ response: We apologize for the confusion in reporting the average age of the menopause reported as 40 in the conclusion. We clarify that the mean age of our study participants is 40 years, which was restrictive based on the 30-49 year age range. We collected data regarding age at Last Menstrual Period (LMP) for only postmenopausal women and the average age at LMP for postmenopausal women in our study was 42.6 years and the average duration of menopause (number of years since LMP) for these women at study time was 2.6 years. As our objective is to assess prevalence and severity of menopause symptoms among our small sample size, we refrained from concluding that age at menopause to be 42.6 years. We rather emphasized on reporting the prevalence and severity of menopause symptoms among women. Accordingly, we have carefully revised and included our editions in the revised manuscript. We now feel that the message being conveyed is more clear.

Comment: All findings and data tables should be rounded up to just one decimal point or use whatever is the journal's conventional standards.

Authors’ response: We have rounded up all figures in the manuscript to one decimal point as per the comment.

Comment: Descriptive data categories for education status should be subdivided using more conventional groupings. The group “grade 1-University” provides no insight about the median level…or % across the range. A more typical grouping would be: less than high school, high school only, university, The category "able to read and write vs not able" is confusing: does this apply to those below grade 1?

Authors’ response: We have revised data categories for education again as none (to mean no formal education), primary education (to mean below high school), secondary education (high school) and college/university in order to reflect the education status of women in our study. We have recoded those women who are able to read and write through informal education and those who are unable to read and write as ‘no formal education’ category. We have included our revision in the revised manuscript.
Comment: Please explain the ethnic groups presented in Table 1 - without a clear explanation in the legend or text, this information is not helpful for non-African readers. Also how is "orthodox" different from Protestant?..

Authors’ response: We have provided explanation of the ethnic groups presented in table 1 immediately under table 1 in the form of legend. In Ethiopia, the majority of people practice Orthodox Christianity, followed by Islam while Protestant comprises a minority of the total populations in religion. Even though Orthodox and Protestant fall under category of Christianity religion, there are several distinguishing differences in religious teachings understood culturally. The two religions have separate church and administrative systems. In our study, information regarding religion of the respondents was collected as it appears in data collection as Orthodox, Muslim, Catholic and Protestant.

Comment: Why was "loss of interest in sex" used as the menopause symptom to estimate sample size for this study.. Is this a particularly culture-specific experience in this region? Ie more so than hot flashes, for eg??

Authors’ response: Due to lack of a previous study that assessed the prevalence and severity of menopause symptoms in our country and population, we are forced to estimate the sample size based on a study conducted in another country. To estimate our sample size, we used an expected proportion (P) from a study with similar study design and multi-ethnic population that would give larger sample size. The specific symptom of “loss of interest in sex” was one of the most highly reported symptom in this alternate study, which we also based our estimate. We additionally used the standardized Menopause Rating Scale (MRS), which has been used in different international populations and validated in clinical and epidemiologic studies on menopause symptoms.

Comment: I cannot comment on the appropriateness of the sampling method - an epidemiologist should review this section.

Authors’ response: We have consulted an epidemiologist regarding the appropriateness of the sampling method and confirmed the use of our methodology. We have also made additional clarification in the revised manuscript.

Comment: The methodologic limitations described above (especially the upper age limit) should be presented in the discussion. Also, the statement "since only menopausal women were selected for participation, no comparable group exists" is confusing, as other studies have used age-
matched cohorts of premenopausal and even male cohorts (as controls) for symptom comparisons.

Authors’ response: We have revised the entire manuscript. We have also made all necessary modifications to the manuscript and have clarified the message being conveyed. Moreover, we have also discussed limitations of the current study in discussion and we believe that the revised manuscript will provide useful information about the prevalence and severity of menopause symptoms among women in the study.

Comment: In its present form there are errors in English grammar and syntax; although understandable, these errors serve to detract from the quality of the work. The authors should seek assistance from an experienced editor.

Authors’ response: We have significantly revised the English grammar and syntax of the manuscript with the help of an experienced and native speaker.

Response to Reviewer #3

Comment: Item 12 - the statement is crucial for improving the quality health of women in perimenopausal and postmenopausal. It will be nice to elaborate on the implication regarding public health application. Just to explain how significant is that?

Authors’ response: We have carefully revised and included the comment in the revised manuscript.

Methods

Comment: It is important to describe the study design used and its rationale to justify its relevance to the objective of the study however sampling and sample is well articulated.

Authors’ response: We have described the study design as per the comment under the Methods section.

Comment: Include briefly the data collectors’ background and knowledge on health issues. The word ‘community health extension workers’ might have a different meaning and scope in other countries. Explain the duration of the training and its outcome regarding their competence.
Authors’ response: In Ethiopia, health extension workers are salaried female community health workers with secondary school education and receive a 1-year training in basic health service delivery. They are selected from the local community that they serve and begin working in the community at 75% of their time and spend the remaining 25% of their time working at the regional health post level. We have briefly included this in the revised manuscript to provide country-specific context.

Comment: The ethical considerations need to be thoroughly explained and considering all the risk and cultural factors, handling of completed questionnaires etc.

Authors’ response: We have revised ethical considerations again as per the comment provided. We have included more details under the Methods section and a further explanation under the broader title ‘Declaration’ in the revised manuscript as per the journal requirement.

References

Comment: Adding of more recent publications, 2015-2016 will add value in the manuscript. A lot of old references have been used. Menopause and its health problems has been adequately researched in many developed, developing and underdeveloped countries. It would also increase the understanding of the phenomenon among women of different racial groups.

Authors’ response: We have revised references again and used some more recent references. We note that there is a paucity of research conducted on menopause experiences of women in low- and middle-income countries and have had to rely on existing literature, which is sometimes outdated.