PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Impact of meibomian gland dysfunction on quality of life and mental health in a clinical sample in Ghana: A cross-sectional study
AUTHORS	Asiedu, Kofi; Dzasimatu, Selassie; Kyei, Samuel

VERSION 1 – REVIEW

REVIEWER	Zhao, Yun-E Wenzhou Medical University
REVIEW RETURNED	24-Mar-2022

GENERAL COMMENTS	The manuscript “Impact of meibomian gland dysfunction on quality of life and mental health in a youthful clinical sample” aimed to determine the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions. Though it’s interesting, there are some concerns need be raised. 1.Over what period of time was the data collected? 2.It’s because of eye symptoms that cause anxiety and other psychological symptoms. Asymptomatic MGD patients account for a large proportion in MGD group, it may result in the no-significant-results between MGD and non-MGD group. If the patients of symptomatic MGD and non-MGD are compared, may it become significant? 3.Are the numbers in Table3 r and p? please clarify it. 4.Lid margin hyperemia and inflammation, if visible for their own, can cause anxiety. As the authors wrote, sometimes blepharitis or meibomitis is treated as dry eye or superficial punctate keratitis, which may result in ineffective treatment. However, dry eye or superficial punctate keratitis caused by blepharitis or meibomitis may play a more important role in psychosomatic symptoms, the authors did not evaluate it, which is a major limitation.

REVIEWER	Hida, Richard Universidade de Sao Paulo Hospital das Clinicas
REVIEW RETURNED	27-May-2022

GENERAL COMMENTS	GENERAL CONSIDERATIONS - The authors have determined the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions.. - Please detail if “youthful clinical sample” includes patients between 17 to 40 years old as mentioned in line 22, page 7.

	ABSTRACT - The authors have mentioned as purpose: “This study aimed to determine the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions.” - The authors have mentioned as conclusion: “In conclusion, the study revealed a trend of worsening quality of life with MGD even though the mean difference between MGD and non-MGD groups was insignificant.” Please be very careful in statistical analysis. If statistics shows no difference, THERE IS NO TRENDING, it is not worsening. Please re-write the conclusion. Please do not conclude sentences that cannot be supported by data shown. METHOD - The authors have mentioned “Subjects were included in the study if they did not have any of the following…” inclusion criteria is not enough, since the authors have mentioned that “All patients who met the inclusion criteria were recruited.” I would suggest mentioning: “Patients with MGD, posterior blepharitis, BUT less than 5 seconds, signs and symptoms of evaporative dry eye, above x age, etc etc were included in this study.” Please reconsider describing the INCLUSION CRITERIA with caution and detailed. - The authors have mentioned: “All participants completed the ocular surface disease index, short version of the depression, anxiety, and stress scale (DASS-21) and dry eye quality of life score (DEQS) questionnaire before the clinical examination.” Please be very careful with details on how MGD was diagnosed. All included patients in the study group MUST have diagnosed MGD based on some measurement. So please detail how MGD patients included in this study and how MGD was diagnosed. Please see comments above. Please be careful regarding the sample. The studied sample was 54 individuals AND NOT 215 individuals. 158 individuals are control group. - It is very important to include, if possible, BUT or any other test that evaluates tear stability to characterize evaporative dry eye or MGD. It is a very important outcome measurement. - How do the authors classify as MGD with no symptoms? RESULT - The authors have mentioned: “At the end of study, 215 met the inclusion criteria and gave informed consent to participate” please understand that study group is 54 individuals with MGD. So the one that met the criteria is 54 and not 215. - Table 1 may not be necessary. DISCUSSION - The authors have mentioned as purpose: “Therefore, this study aims to ascertain the association and impact of MGD on quality of life and psychosomatic symptoms.” - The authors have mentioned as conclusion: “In conclusion, the study revealed a trend of worsening quality of life with MGD even though the mean difference between MGD and non-MGD groups was not significant. However, symptomatic MGD counterparts had worse quality of life and psychosomatic symptoms than their asymptomatic MGD. Therefore, clinicians managing MGD and lid margin disease should recognize the impact of symptoms of MGD on patients' quality of life and target their therapeutic management to ameliorate the symptoms, not rely on only improvements in objective measures as proof of therapeutic success.”

	- Please do not mention anything that cannot be supported by data shown. - Statistics does not show trends. If statistics showed no difference, the authors cannot conclude any worsening. This is very important when statistical analysis is applied. Please conclude something related to data shown. - If clinicians should recognize the impact of symptoms of MGD or not is not part of the purpose of this study and no data is shown. Please show data or delete this sentence. - Please conclude something based on data shown. Do not mislead the information or conclusion.

VERSION 1 – AUTHOR RESPONSE

Reviewer #1:
Dr. Yun-E Zhao, Wenzhou Medical University

Comments to the Author:
The manuscript “Impact of meibomian gland dysfunction on quality of life and mental health in a youthful clinical sample” aimed to determine the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions. Though it’s interesting, there are some concerns need be raised.
1.Over what period of time was the data collected?
Authors response
“The data was collected in period of one month. The data collection was done during the routine university of cape coast medical screening mandated for all first year students.” see highlight on page 6

2.It’s because of eye symptoms that cause anxiety and other psychological symptoms. Asymptomatic MGD patients account for a large proportion in MGD group, it may result in the no-significant-results between MGD and non-MGD group. If the patients of symptomatic MGD and non-MGD are compared, may it become significant?
Authors response
Thank you very much for this comment. We have separated the groups into three namely symptomatic MGD, asymptomatic MGD and Non-MGD controls and our results indicate as suggested that the Symptomatic MGD has worse quality of life compared to asymptomatic MGD and non-MGD controls. Kindly see table 1 (page 11)

3. Are the numbers in Table3 r and p? please clarify it.
Authors response
Thank you for this comment. They are indeed r and p. We have included some footnotes below table. (see page 12)

4. Lid margin hyperemia and inflammation, if visible for their own, can cause anxiety. As the authors wrote, sometimes blepharitis or meibomitis is treated as dry eye or superficial punctate keratitis, which may result in ineffective treatment. However, dry eye or superficial punctate keratitis caused by blepharitis or meibomitis may play a more important role in psychosomatic symptoms, the authors did not evaluate it, which is a major limitation.
Authors response
We collected data on fluorescein tear break up time and ocular surface staining. Together with the OSDI score we have used the DEWS II criteria to classify patients into dry eye and non-dry eye. We have conducted the analysis among the three groups namely symptomatic MGD , asymptomatic

MGD and non-MGD adjusting for the presence of dry eye to determine any potential difference in quality of life scores.(see table 1). Description for data collection process for fluorescein tear break up time and ocular surface staining have been included in the methods section. (See page 9)

Reviewer: 2
Dr. Richard Hida, Universidade de Sao Paulo Hospital das Clinicas, Universidade Federal de Sao Paulo Escola Paulista de Medicina

Comments to the Author:
Dear authors,
BMJ Open
Manuscript Number ID: bmjopen-2022-061758
Title: Impact of meibomian gland dysfunction on quality of life and mental health in a youthful clinical sample.

GENERAL CONSIDERATIONS
- The authors have determined the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions.

Authors Response
Yes please, that is what we sought to do.
- Please detail if “youthful clinical sample” includes patients between 17 to 40 years old as mentioned in line 22, page 7.
Authors response
Thank you very much for drawing attention to this. We have modified the title to read “Impact of meibomian gland dysfunction on quality of life and mental health in a clinical sample in Ghana: A cross-sectional study” base on your comment and that of the editor’s. We initially considered the sample youthful given the mean age was 21.9 (±3.8) years as those with upper age limit were few.

ABSTRACT
- The authors have mentioned as purpose: “This study aimed to determine the impact of Meibomian gland dysfunction (MGD) on quality of life and psychosomatic conditions.”
- The authors have mentioned as conclusion: “In conclusion, the study revealed a trend of worsening quality of life with MGD even though the mean difference between MGD and non-MGD groups was insignificant.” Please be very careful in statistical analysis. If statistics shows no difference, THERE IS NO TRENDING, it is not worsening. Please re-write the conclusion. Please do not conclude sentences that cannot be supported by data shown.
Authors response
Thank you very much for this comment. We have revised the conclusion to reflect our data. The conclusion now reads “In conclusion, the study revealed no difference in quality of life scores between MGD and non-MGD groups. However, the symptomatic MGD group had worse quality of life and psychosomatic symptoms than the asymptomatic MGD group and non-MGD group.” (Please see page 15).

METHOD
- The authors have mentioned “Subjects were included in the study if they did not have any of the following…” inclusion criteria is not enough, since the authors have mentioned that “All patients who met the inclusion criteria were recruited.” I would suggest mentioning: “Patients with MGD, posterior blepharitis, BUT less than 5 seconds, signs and symptoms of evaporative dry eye, above x age, etc etc were included in this study.” Please reconsider describing the INCLUSION CRITERIA with caution and detailed.

Authors response
We have revised the inclusion criteria with caution and detail. Kindly see revision in highlighted in the manuscript. (Please see red highlight is paragraphs 1&2 of the method section on page 6).

- The authors have mentioned: “All participants completed the ocular surface disease index, short version of the depression, anxiety, and stress scale (DASS-21) and dry eye quality of life score (DEQS) questionnaire before the clinical examination.” Please be very careful with details on how MGD was diagnosed. All included patients in the study group MUST have diagnosed MGD based on some measurement. So please detail how MGD patients included in this study and how MGD was diagnosed. Please see comments above. Please be careful regarding the sample. The studied sample was 54 individuals AND NOT 215 individuals. 158 individuals are control group.
Authors response
Thank you very much. We have included how MGD was diagnosed as requested. Kindly see page 6. “MGD diagnosis was made based on both gland expressibility and quality of secretion score of 1 or greater in either eye with or without lid margin abnormalities as previously reported [5]. Among those with meibomian Gland Dysfunction, a subject was considered asymptomatic if the Ocular Surface Disease Index score was less than 13 and symptomatic if the Ocular Surface Disease Index score was 13 or greater.”

- It is very important to include, if possible, BUT or any other test that evaluates tear stability to characterize evaporative dry eye or MGD. It is a very important outcome measurement.
Authors response
We have detailed how MGD was diagnosed. We use the MGD 2011 workshop criteria. (Please see highlight on page 6).
- How do the authors classify as MGD with no symptoms?
Authors response
We followed the MGD workshop 2011 criteria that used the OSDI. (Please see highlight on page 6).

RESULT
- The authors have mentioned: “At the end of study, 215 met the inclusion criteria and gave informed consent to participate” please understand that study group is 54 individuals with MGD. So the one that met the criteria is 54 and not 215.

Authors response
We have amended that 54 participants met the inclusion criteria. Thank you Kindly see “Fifty-four patients with MGD, based on the MGD workshop criteria with or without posterior blepharitis between the ages of 17-40, were included in the study group. Another group, 158 non-MGD group serve as controls. The data was collected in one month.” on page 6.
- Table 1 may not be necessary.
Authors response
“The content of Table 1 has been replaced. We collected data on fluorescein tear break up time and ocular surface staining. Together with OSDI score we have used the DEWS II criteria to classify patients into dry eye and non-dry eye. We have conducted the analysis among the three groups namely symptomatic MGD , asymptomatic MGD and non-MGD adjusting for the presence of dry eye to determine any potential difference in quality of life scores.(see table 1).

DISCUSSION
- The authors have mentioned as purpose: “Therefore, this study aims to ascertain the association and impact of MGD on quality of life and psychosomatic symptoms.”
- The authors have mentioned as conclusion: “In conclusion, the study revealed a trend of worsening quality of life with MGD even though the mean difference between MGD and non-MGD groups was

not significant. However, symptomatic MGD counterparts had worse quality of life and psychosomatic symptoms than their asymptomatic MGD. Therefore, clinicians managing MGD and lid margin disease should recognize the impact of symptoms of MGD on patients' quality of life and target their therapeutic management to ameliorate the symptoms, not rely on only improvements in objective measures as proof of therapeutic success."
Authors response
We have removed statement not supported by the data. Our conclusion now reads "In conclusion, the study revealed no difference in quality of life scores between MGD and non-MGD groups. However, the symptomatic MGD group had worse quality of life and psychosomatic symptoms than the asymptomatic MGD group and non-MGD group. However, symptomatic MGD counterparts had worse quality of life and psychosomatic symptoms than their asymptomatic MGD." (please see highlight on page 15).

- Please do not mention anything that cannot be supported by data shown.
Authors response
Thank you. We have removed all such statements.
- Statistics does not show trends. If statistics showed no difference, the authors cannot conclude any worsening. This is very important when statistical analysis is applied. Please conclude something related to data shown.
Authors' response
We have deleted those statements not supported by data.
- If clinicians should recognize the impact of symptoms of MGD or not is not part of the purpose of this study and no data is shown. Please show data or delete this sentence.
Authors' response
We have deleted those statements not supported by data.
- Please conclude something based on data shown. Do not mislead the information or conclusion.
Authors' response
We have deleted those statements not supported by data.

VERSION 2 – REVIEW

REVIEWER	Zhao, Yun-E Wenzhou Medical University
REVIEW RETURNED	26-Jul-2022

GENERAL COMMENTS	All my comments are adequately revised.

VERSION 2 – AUTHOR RESPONSE

Please note that reviewer #2 comments have been evaluated in house. While doing so, we noted that some comments require further attention:

*Please further clarify the inclusion criteria, as stated by reviewer #2 . "Subjects were included in the study if they did not have any of the following:.." is not sufficient.

RESPONSE

Please the inclusion criteria have been expanded to read “Subjects were included in the study if they were aged 17-40 years, were not undergoing any surgical or cosmetic ophthalmic procedures, not taking medications known to affect meibomian glands such as isotretinoin, hormone replacement therapy or bio-identical hormone therapy, no known psychiatric disorder such as schizophrenia, not using any systemic medications known to improve meibomian gland function such as azithromycin and doxycycline, not having Sjogren syndrome, connective tissue disease (such as rheumatoid arthritis), not undergone haematopoietic stem cell transplantation, not using any prebiotics or probiotics, omega-3 fatty acids supplements and multi-vitamins.

Subjects were excluded from the study if they had any of following: contact lens wear, diabetes, pterygium, pregnancy, history of ocular trauma, pinguecula, history of eye surgery, active infection, or inflammation of the eye at the time of the study. An optometrist conducted all clinical assessments of subjects.” Please see page 5 under “Methods” section

*In addition, as previously requested, please work to improve the statistical reporting of your manuscript.

RESPONSE

Thank you. Please the statistical reporting of the manuscript has been improved to read “The mean age of the entire sample was 21.9 (±3.8) years, with a range of 17 to 40 years. The number of males and females in the sample was 105 and 107, respectively. Fifty-four participants had MGD and 158 did not have MGD served as controls. Among the MGD group 33 had symptomatic MGD and 21 had asymptomatic MGD.

There was no statistically significant difference in the quality of life scores (DEQS) between MGD and non-MGD groups. There was no statistically significant difference in the mean quality of life scores between subjects with MGD and subjects without MGD ($t = 1.57$, $P = 0.12$). The quality of life scores (DEQS) ($p = 0.022$) were significantly higher in the symptomatic MGD group compared to the asymptomatic MGD group. There was no significant difference in quality of life scores (DEQS) ($p = 0.037$) in the asymptomatic MGD group compared to healthy controls. This is shown in table 1.

Using Pillai’s trace in the MANOVA, there was a significant effect of MGD on depression, anxiety, and stress ($V=0.05$, $F(3,208)=3.76$, $P = 0.012$). Separate T-tests were done for each of the subsections of the DASS-21. The depression ($p = 0.031$) and anxiety ($p=0.003$) subscales showed a significant difference between the MGD group and the non-MGD group; however, there was no difference in the stress ($p=0.33$) subscale between the groups. Again, using Pillai's trace in the MANOVA, there was a significant effect of the type of MGD (symptomatic or asymptomatic) on depression, anxiety, and stress ($V=0.24$, $F(3, 51)=5.24$, $P=0.003$). The depression ($p=0.001$) and anxiety ($p=0.02$) subscales showed a significant difference between the symptomatic MGD and non-MGD groups. However, there was no difference in the stress subscale between the groups. This is shown in Tables 2 .

Of importance, depression and anxiety subsection scores of the DASS-21 and DEQS scores showed relatively low correlations between themselves and the clinical parameters of MGD with significant correlations co-efficient for following: DEQS and meibomian gland expressibility scores ($r = 0.14$ $p=0.048$); Anxiety score and meibomian gland expressibility scores ($r = 0.17$, $p = 0.012$), DEQS and Telangiectasia ($r=0.16$ $p= 0.021$); and DEQS and Anxiety ($r = 0.15$, $p = 0.012$). The correlation analysis is shown table 3.” Please see the abstract (page 2) and pages 8-9 of the manuscript under the “results” section

* Please complete a thorough proofread of the text and correct any spelling and grammar errors that you identify.

RESPONSE

Thank you. Please the manuscript has been edited using Grammarly software.