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) | Factors Associated with Intimacy in Female Taiwanese Patients with Systemic Lupus Erythematosus: A Cross-sectional Study |
|---------------------|-------------------------------------------------------------------------------------------------------------------|
| AUTHORS             | Hsu, Chia-Wen; Hsu, Bao-Bao; Koo, Malcolm; Lu, Ming-Chi                                                              |

VERSION 1 – REVIEW

| REVIEWER             | Tsai, Chang-Youh                                                                                                    |
|----------------------|----------------------------------------------------------------------------------------------------------------------|
|                      | Taipei Veterans General Hospital, Division of Allergy, Immunology & Rheumatology                                  |
| REVIEW RETURNED      | 06-Oct-2021                                                            |

GENERAL COMMENTS

This is a well-designed study and well-written manuscript. I have only few concerns:
1. Marital status is the most important factor that affect the intimacy of people in Asian countries such as Taiwan, especially in females. Although the authors have listed the marital status of the studied subjects, they did not correlate this variable to the intimacy status in patients.
2. The detailed questionnaires regarding the intimacy status were not described. This might lead to ambiguity in the statistical analysis. For example, sexual desire may be influenced by either psychological status such as depression or physiological status such as fatigue which may only totally originated from high disease activity.
3. Inter-current infections should also be recorded as contributing factor.
4. If possible, SF-36 seems to be a better evaluating tool for this kind of issue.

REVIEWER

Phuti, Angel
Charité Universitätsmedizin Berlin

REVIEW RETURNED

14-Oct-2021

GENERAL COMMENTS

The study is of great importance in the field of neglected disease. The authors conducted a study that highlights a need for awareness on sexuality and SLE. However, while the study design is appropriate, it is inadequate, needs some a modification before it could be considered for any publication.
* All domains of the LupusQoL could have been measured and a test of associations done to avoid this major limitation. The authors pointed out only two domains which are SLE manifestations (limitations). Other factors like emotional health and pain (under-measured physical and psycho-social aspects of SLE) were omitted in the study and not considered as a limitation altogether. In general, pain, emotions and sexual wellbeing are strongly
connected and this was omitted. It would be important to determine its extent in SLE patients if an author studies intimacy.

1. The authors stated the limitations of the study: the domains-fatigue and body images.
Since the data collection cannot be reversed or modified, the authors need to find publications that compare and contrast this finding and strongly discuss it in the discussion. Then under the limitations, while they acknowledge theirs, they could modify it by using a conclusion of their discussion. This won't make the limitations too strong.
The reviewer would like to give an example of a study that captured factors affecting intimacy/sexuality in SLE - and they are a few more in other contexts.

A Phuti, B Hodkinson, M Tikly & M Schneider (2020) ‘The feeling of not being entitled to something’: fertility, pregnancy, and sexuality among women with systemic lupus erythematosus in South Africa, Scandinavian Journal of Rheumatology, 49:3, 214-220, DOI: 10.1080/03009742.2019.1657492

2. Abstract and Conclusions: Reads like a results section (repetition). This could be made shorter and a recommendation would make the message stronger.

3. Language editing issues- for example
   line 74: ...of SLE would affect vs. would affected
   line 83: ...Patients who were aged 20... vs Patient who were aged 20...
   line 176: ...Physicians might need to.... vs Physicians might needed to...

4. Patient involvement and Public...
The first sentence can be a bit misleading. Rather start a sentence: Suggestion:
To avoid biases, patients were not involved in the study design, analysis and manuscript write up.
The four lines are filled with filler words/sentences. The extra word count could be used to write more important information.

5. Table 2: Showing the questions of the LupusQoL-domain Intimacy would give a better view and understanding.

VERSION 1 – AUTHOR RESPONSE

Reviewer 1, Comment 1:
This is a well-designed study and well-written manuscript. I have only few concerns:
1. Marital status is the most important factor that affect the intimacy of people in Asian countries such as Taiwan, especially in females. Although the authors have listed the marital status of the studied subjects, they did not correlate this variable to the intimacy status in patients.
Response to Reviewer 1, Comment 1:
We appreciate the reviewer’s positive comments. We agree that marital status is the most important factor that affects the intimacy of women in Asian countries. We have changed the grouping of marital status to “Married vs. single, widowed, divorced” from the original “single vs. married, widowed, divorced” to better reflect the effect of marital status on intimacy. The variable marital status was included in the simple linear regression model (Table 2). We found married women had a
significantly lower score in the intimate relationships domain of the LupusQoL. However, the variable was not retain in the multiple linear regression model, using a stepwise variable selection procedure, indicating that it is not an independent factor associated with the outcome. We have also use “enter” procedure to evaluate the effect of marital status in the multiple regression model. The results showed that the variable marital status did not reach statistically significance with little change in the regression coefficients of the other significant variables in the model.

Reviewer 1, Comment 2:
The detailed questionnaires regarding the intimacy status were not described. This might lead to ambiguity in the statistical analysis. For example, sexual desire may be influenced by either psychological status such as depression or physiological status such as fatigue which may only totally originated from high disease activity.
Response to Reviewer 1, Comment 2:
We thank the reviewer for the suggestion. We have added the two questions on the intimate relationships domain of the LupusQoL in the Methods section. The two questions are (1) Because of the pain I experience due to Lupus I am less interested in a sexual relationship and (2) Because of my Lupus I am not interested in sex. (line 99–101)
Regarding the possibility that sexual desire may be influenced by either psychological status such as depression or physiological status such as fatigue, we have added new regression analyses in the revised manuscript. We evaluated the association between intimate relationships domain of the LupusQoL and other seven domains of the LupusQoL, including physical health, emotional health, body image, pain, planning, fatigue, and burden to others. Results from the multiple linear regression analysis showed that only physical health (std β = 0.13, p = 0.001), fatigue (std β = 0.18, p = 0.006), and burden to others (std β = 0.20, p = 0.002) were significantly and independently associated with the intimate relationships domain of the LupusQoL among female patients with SLE. We have revised the manuscript with the above findings and a new Table 3. (line 139–146)

Reviewer 1, Comment 3:
Inter-current infections should also be recorded as contributing factor.
Response to Reviewer 1, Comment 3:
The patients with SLE in our study were recruited from the rheumatology outpatient department of our study hospital. Those with active infection were excluded from this study. We have added this statement in the Methods section. (line 92)

Reviewer 1, Comment 4:
If possible, SF-36 seems to be a better evaluating tool for this kind of issue.
Response to Reviewer 1, Comment 4:
SF-36 could be a useful evaluating tool for this kind of issue. However, the SF-36 is typically used for the general population, and its items do not cover specific SLE impairment, such as sexual dysfunction. Therefore, we chose a disease-specific quality of life measurement – the Lupus Quality of Life questionnaire (LupusQoL) in this study. LupusQoL has been shown to be a valid and reliable tool to evaluate the health-related quality of life in patients with SLE in the United Kingdom (McElhone et al., 2007), the United States of America (Jolly et al., 2010), and China (Wang et al. 2013).

References:
Wang SL, Wu B, Leng L, Bucala R, Lu LJ. Validity of LupusQoL-China for the assessment of health related quality of life in Chinese patients with systemic lupus erythematosus. PLoS One. 2013;8(5):e63795.
McElhone K, Abbott J, Shelmerdine J, Bruce IN, Ahmad Y, et al. Development and validation of a disease-specific health-related quality of life measure, the LupusQol, for adults with systemic lupus erythematosus. Arthritis Rheum 2007;57: 972–979 PubMed.
Reviewer 2, Comment 1:
The study is of great importance in the field of neglected disease. The authors conducted a study that highlights a need for awareness on sexuality and SLE. However, while the study design is appropriate, it is inadequate, needs some a modification before it could be considered for any publication.
* All domains of the LupusQoL could have been measured and a test of associations done to avoid this major limitation. The authors pointed out only two domains which are SLE manifestations (limitations). Other factors like emotional health and pain (under-measured physical and psycho-social aspects of SLE) were omitted in the study and not considered as a limitation altogether. In general, pain, emotions and sexual wellbeing are strongly connected and this was omitted. It would be important to determine its extent in SLE patients if an author studies intimacy.
1. The authors stated the limitations of the study: the domains- fatigue and body images. Since the data collection cannot be reversed or modified, the authors need to find publications that compare and contrast this finding and strongly discuss it in the discussion. Then under the limitations, while they acknowledge theirs, they could modify it by using a conclusion of their discussion. This wont make the limitations too strong.
The reviewer would like to give an example of a study that captured factors affecting intimacy/sexuality in SLE - and they are a few more in other contexts
A Phuti, B Hodkinson, M Tikly & M Schneider (2020) ‘The feeling of not being entitled to something’: fertility, pregnancy, and sexuality among women with systemic lupus erythematosus in South Africa, Scandinavian Journal of Rheumatology, 49:3, 214-220, DOI: 10.1080/03009742.2019.1657492

Response to Reviewer 2, Comment 1:
We did not clearly express our study in the limitations section in the original manuscript. In fact, we did ask our study patients to respond to the complete version of the LupusQoL, which consists of 34 items grouped in eight domains of health-related quality of life, including physical health (8 items), emotional health (6 items), body image (5 items), pain (3 items), planning (3 items), fatigue (4 items), intimate relationships (2 items), and burden to others (3 items). Our research team has published another paper [A comparison of the correlation of Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) and Systemic Lupus Erythematosus Disease Activity Score (SLE-DAS) with health-related quality of life. J Clin Med 2021;10:2137.], which analyzed all eight domains of the LupusQoL.
We agree with the reviewer that there are many factors, including pain, fatigue, and body image, could affect the intimate relationships in patients with SLE. We follow the suggestion of the reviewer and the recommended manuscript by Phuti et al., we analyzed the association of other seven domains, including physical health, emotional health, body image, pain, planning, fatigue, burden to others, with the intimate relationships domain of the LupusQoL using both simple and multiple linear regression analyses. Results from the simple linear regression analysis showed that all seven domains, including physical health, emotional health, body image, pain, planning, fatigue, and burden to others, were significantly associated with the intimate relationships domain of the LupusQoL. However, results from the multiple linear regression analysis indicated that only physical health (standardized [std] β = 0.13, p = 0.001), fatigue (std β = 0.18, p = 0.006), and burden to others (std β = 0.20, p = 0.002), were significantly and independently associated with the intimate relationships domain of the LupusQoL in our patients. (line 139–146)
A limitation of our study is the evaluation of physical health, emotional health, body image, pain, planning, fatigue, and burden to others were obtained from the LupusQoL. Questionnaires specifically
designed to measure pain, emotions, and sexual wellbeing will be needed in future studies to verify our results. (line 189–191)
We have mentioned the above in the Results, Discussion, and limitation. A new Table 3 was also added to the revised manuscript.

Reviewer 2, Comment 2:
Abstract and Conclusions: Reads like a results section (repetition). This could be made shorter and a recommendation would make the message stronger.
Response to Reviewer 2, Comment 2:
We have revised the conclusion of the abstract and the main text with a recommendation. (line 48–51 and 192–196)

Reviewer 2, Comment 3:
Language editing issues - for example line 74: ...of SLE would affect vs. would affected line 83:
...Patients who were aged 20... vs Patient who were aged 20...
line 176: ...Physicians might need to... vs Physicians might needed to...
Response to Reviewer 2, Comment 3:
We have corrected these mistakes. (line 76 and 86)

Reviewer 2, Comment 4:
Patient involvement and Public...
The first sentence can be a bit misleading. Rather start a sentence: Suggestion:
To avoid biases, patients were not involved in the study design, analysis and manuscript write up. The four lines are filled with filler words/sentences. The extra word count could be used to write more important information.
Response to Reviewer 2, Comment 4:
We appreciate the reviewer’s comment and have revised the sentences as follows: To avoid biases, patients were not involved in the study design, conduct, analysis, reporting, or dissemination plans of this research. (line 98–101)

Reviewer 2, Comment 5:
Table 2: Showing the questions of the LupusQoL-domain Intimacy would give a better view and understanding.
Response to Reviewer 2, Comment 5:
We thank the reviewer’s comment and have added the two questions on the intimate relationships domain of the LupusQoL in the Methods section. The two questions are (1) Because of the pain I experience due to Lupus I am less interested in a sexual relationship and (2) Because of my Lupus I am not interested in sex. (line 99–101)