Author’s response to reviews

Title: Clinical and histological characterization of oral pemphigus lesions in patients with skin diseases: a cross sectional study from Sudan

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Authors' responses to reviews: see over
Dear BioMed Central Editorial Team,

Thank you for the review of our manuscript, *(Clinical and histological characterization of oral pemphigus lesions in patients with skin diseases: a cross sectional study from Sudan)*, and for the valuables and favourable comments from the reviewers. The manuscript has been revised and edited according to the suggestions from reviewers. Please find attached:

- Authors' responses to reviews
- Version (3) manuscript.

Sincerely yours,

On behalf of the authors,

Nada M Suliman
Reviewer: Thorakkal Shamim

Thank you very much for your review of our manuscript

Reviewer: “In the present scenario, we Dentists will relay on immunofluorescence either direct and indirect and ELISA.”

Authors’ response: we stated that neither direct nor indirect immunofluorescence tests were used in the public health sectors in Sudan to confirm PV diagnosis (page 21). Diagnosis of pemphigus was totally dependent on history, clinical characteristic and it is confirmed by histological picture using H & E staining (the histopathology is done by private laboratories and paid for by the patients). This leads to lack of fresh biopsies and blood samples, however, paraffin embedded biopsy specimens are available. Taking into consideration the above mentioned conditions, we formulate our aim to raise the accuracy of PV diagnosis according to the available material. Thus, our aim was to evaluate the significance of the routine histology along with immunohistochemical examination on formalin-fixed paraffin-embedded biopsy specimens in patients with pemphigus vulgaris. Our results confirmed that the test is reliable to confirm the diagnosis of PV. We believe this study would encourage health workers to verify their diagnosis using the same technique if they do have similar situation.

Reviewer: “Already known information about oral pemphigus vulgaris is listed”.

Authors’ response: Since 1942, the information regarding clinical and histological features of PV is very stable and not many changes had been added to [1, 2]. New information regarding pathogenesis, therapeutic modalities and disease distribution is booming every now and then. While global literature shows specific pattern of geographical distribution of PV world widely, nothing is known about oral PV in Sudan. Investigation across countries are essential to determine differences in prevalence, etiology and other aspects of diseases due to cultural, geographic, and other factors. Our study is the first to explore the existence of the disease in Sudan. This study adds new information to the global literature about different aspects of oral
PV in Sudanese patients. In addition, the study showed the value of formalin-fixed paraffin embedded biopsy in situations where fresh biopsies and blood samples are not available.

**Reviewer:** “The study will be interesting if the authors have considered genetic studies (genomic aspect of pemphigus vulgaris).”

**Authors’ response:** It would be very interesting to have genomic aspects of pemphigus vulgaris in the Sudanese people. Unfortunately this is beyond the scope of the present study.

**Reviewer:** “In the histopathological aspect authors can add cytological study using Papanicolaou (Pap) stain and methylene blue stain to detect acantholytic cells in oral pemphigus vulgaris”

**Authors’ response:** We do agree with your suggestion to have inexpensive, non-invasive and rapid test to detect acantholytic cells. Tzanck smear to detect acantholytic cells was routinely used in the dermatology hospital in Sudan. However, cytomorphologic examination helps in screening questioned cases of PV rather than giving a definitive diagnosis, while cytoimmunology is crucial for definite diagnosis. Therefore, in our study the acantholytic cells were ensured by the hospital and the diagnosis was confirmed by the histopathology. Our study took further steps to ensure the definitive diagnosis for PV. The challenge was to make use of available material in order to improve the diagnostic quality and give definitive diagnosis since proper treatment depends on which disease is involved. Therefore, we did the immunohistochemical examination on formalin-fixed paraffin embedded biopsy for definitive diagnosis because fresh biopsies and blood samples were hard to attain. Our results support previous studies that showed the possibility of using formalin-fixed paraffin embedded biopsy to confirm the diagnosis of PV [3, 4]. In addition, we aimed to encourage histopathologists who receive patients’ biopsies in formalin media to confirm diagnosis of PV by applying the immunohistochemical examination in formalin-fixed paraffin embedded biopsies.

**Reviewer:** “The authors can follow simple scoring system for oral pemphigus vulgaris”
**Authors’ response:**
The scoring system in pemphigus aims to assess disease activity and monitor disease progression over time in order to provide adjustable and precise dose of therapy that is parallel to the disease activity. According to the literature a number of scoring systems have been proposed but the gold standard scoring system has not been developed yet. The first step in selecting appropriate scoring systems is to determine the specific objectives of the study, whether they are descriptive, predictive, discriminative or evaluative and the exact purpose of using such a measure. In our study we use OLAS scoring system (page 8) to see if the disease activity discriminates between patients according to their Socio-demographic distribution (page 13). Our modified scoring system consists of objective and subjective parameters based on an established protocol (page 8). We believed this scoring system is comprehensive and sensitive to discriminate patients according to their Socio-behavioural distribution. The scoring system that you suggested we apply, was used for descriptive purposes [5], as used in your mentioned study. However, our study is discriminative as well as descriptive.

**Reviewer:** “In the immunohistochemical study the authors should elaborate class of IgG and complement (for eg; IgG3, IgG4, C3, C4) useful for diagnosing pemphigus vulgaris. Authors have just given IgG and C3 in the immunohistochemical and study is incomplete”.

**Authors’ response:**
It is a good idea to search for IgG subclasses; however, this is beyond the scope of the current study (page 6). After all, since 1964 the total IgG and C3 have been used routinely for diagnosis of PV.


Reviewer: DIMITRIOS IOANNIDES

Thank you very much for your review of our manuscript

Reviewer: “What would be interesting to know a dermatologist who is dealing with pemphigus patients is the treatment modalities chosen and their efficacy and Safety”.

Authors’ response: treatment modalities are beyond the scope of the current study, however, treatment modalities will be considered in our future study.

Thank you for the suggestion
Reviewer: Hiroyasu Endo

Thank you very much for your review of our manuscript