

Dear F6 Publishing,

Thank you for giving me the opportunity to submit a revised draft of our manuscript titled **DIABETIC FOOT ULCER: A COMPREHENSIVE REVIEW OF PATHOPHYSIOLOGY AND MANAGEMENT MODALITIES** to World Journal of Clinical Cases. We appreciate the time and effort that you and the reviewers have dedicated to providing your valuable feedback on my manuscript. We are grateful to the reviewers for their insightful comments on our paper. We have been able to incorporate changes to reflect most of the suggestions provided by the reviewers. In addition to comments, all spelling and grammatical errors pointed out by the reviewers have been corrected. We look forward to hearing from you in due time regarding our submission and to respond to any further questions and comments you may have.

Reviewer one comment: 03372482

Scientific Quality: Grade A (Excellent)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

Diabetic foot ulcers (DFU) are a debilitating and severe manifestation of uncontrolled and prolonged diabetes that presents as ulceration, usually located to the plantar aspect of the foot. Approximately 15% of individuals with diabetes will eventually develop one of these ulcers, and out of these individuals, 14-24% of them will require amputation of the ulcerated foot due to bone infection or other ulcer-related complications. The pathologic mechanisms of DFU are described in terms of a triad: neuropathy, vascular insufficiency, and secondary infection due to trauma of the foot. Standard local and invasive care along with novel approaches like stem cell therapy paves the way to reduce morbidity, decrease amputations, and prevent mortality from DFU. In this manuscript, we review the literature for the current pathophysiology, preventive options, and definitive management of diabetic foot ulcers. In General: it's a good paper and the subject of the manuscript is applicable and useful. Title: the title properly explains the purpose and objective of the article Abstract: abstract contains an appropriate summary for the article, the language used in the abstract is easy to read and understand, and there are no suggestions for improvement. Introduction: authors do provide adequate background on the topic and reason for this article and describe what the authors hoped to achieve. Results: the results are presented clearly, the authors provide accurate research results, and there is sufficient evidence for each result. Conclusion: in general: Good and the research provides sample data for the authors to make their conclusion. Grammar: Need Some revision. (Check The Paper Comments). Please provide and edit the following information in the Paper 1. Conflict of Interest. 2. Source of Funding. 3. Some references without DOI. 4. Writing references according to the terms of the journal. 7. The result and discussion must be in one paragraph. Finally, this was an attractive article. In its current state, it adds much new insightful information to the field.

Response:

Thank you for the insightful comments. Suggested changes including inclusion of documents addressing Conflict of interest, source of funding have been provided. DOI and PMID has been added to all the references with the exception of references obtained from official websites like CDC.

Reviewer two comment: 04213605

Scientific Quality: Grade E (Do not publish)

Language Quality: Grade C (A great deal of language polishing)

Conclusion: Rejection

This manuscript lacks depth and is poorly written as advancements in this area are only summarized by the authors but not discussed. More detailed information should be included and discussed.

Response:

Thank you for the comments. The paper has been overhauled now. Hope the new manuscript will meet your standards.

Reviewer three comment: 05667559

Scientific Quality: Grade D (Fair)

Language Quality: Grade A (Priority publishing)

Conclusion: Major revision

Title. Does the title reflect the main subject/hypothesis of the manuscript? Yes Abstract. Does the abstract summarize and reflect the work described in the manuscript? Yes Key Words. Do the key words reflect the focus of the manuscript? Yes Background. Does the manuscript adequately describe the background, present status and significance of the study? No. Should be improved- comment in the text Methods. Does the manuscript describe methods (e.g., experiments, data analysis, surveys, and clinical trials, etc.) in adequate detail? No, I have not found any information about the key used by the authors when reviewing the literature, e.g. - the last 10 years? what database did they look at? Results. Are the research objectives achieved by the experiments used in this study? What are the contributions that the study has made for research progress in this field? Not applicable Discussion. Does the manuscript interpret the findings adequately and appropriately, highlighting the key points concisely, clearly and logically? Are the findings and their applicability/relevance to the literature stated in a clear and definite manner? Is the discussion accurate and does it discuss the paper's scientific significance and/or relevance to clinical practice sufficiently? All my comments are within the text. References. Does the manuscript appropriately cite the latest, important and authoritative references in the Introduction and Discussion sections? Does the author self-cite, omit, incorrectly cite and/or over-cite references? Over 50% of the references are more than 10 years old...to prove that the authors' article is needed on the publishing market they should update the literature. Quality of manuscript organization and presentation. Is the manuscript well,

concisely and coherently organized and presented? Is the style, language and grammar accurate and appropriate? Yes 13 Research methods and reporting. Authors should have prepared their manuscripts according to BPG's standards for manuscript type and the appropriate topically-relevant category, as follows (3) PRISMA 2009 Checklist - Evidence-Based Medicine, Systematic review,. Letters to the Editor will be critically evaluated and only letters with new important original or complementary information should be considered for publication. A Letter to the Editor that only recapitulates information published in the article(s) and states that more studies are needed is not acceptable? This is not a systematic review. Ethics statements. Not applicable

Response: Thank you for the insightful comments. The paper has been updated with better references. Background and discussion sections have been overhauled to better meet standards. PRISMA 2009 checklist for systematic review has been reviewed and changes made to the manuscript.

Reviewer four comment: 06140863

Scientific Quality: Grade C (Good)

Language Quality: Grade B (Minor language polishing)

Conclusion: Minor revision

The authors have carried out a coherent and descriptive review of the literature on the pathophysiology and management modalities of diabetic foot ulcers. In order to improve the quality of the work, I suggest that the authors add a table that includes the level of recommendation for each of the practices used in ulcer management and the degree of evidence in the academic literature. An interesting example can be found in the update on the management of diabetic foot ulcers written by Estelle Everett and Nestoras Mathioudakis (doi:10.1111/nyas.13569).

Response:

Thank you for the insightful comments. We have added an extra table with levels of recommendation as you suggested.

Sincerely,

Our Team

Joel Raja , Amir Khouzam, Miguel Maturana, Sharif Kayali, Nephertiti Efeovbokhan