



**ESPS PEER-REVIEW REPORT**

**Name of journal:** World Journal of Diabetes

**ESPS manuscript NO:** 25012

**Title:** Preliminary study on overproduction of reactive oxygen species by neutrophils in diabetes mellitus

**Reviewer’s code:** 02446204

**Reviewer’s country:** Japan

**Science editor:** Fang-Fang Ji

**Date sent for review:** 2016-03-01 10:55

**Date reviewed:** 2016-03-01 14:20

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input type="checkbox"/> Grade A: Priority publishing	Google Search:	<input type="checkbox"/> Accept
<input type="checkbox"/> Grade B: Very good	<input type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Duplicate publication	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade D: Rejected	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Minor revision
<input type="checkbox"/> Grade E: Poor		[Y] No	<input type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		[Y] No	

**COMMENTS TO AUTHORS**

This research article is very well rewritten, clearly presenting for the first time augmented ROS productions in type 2 DM patients’ neutrophils. The data were solid and trustworthy; however, the molecular mechanism for augmented ROS productions was not accessed. Nonetheless, to perform further detailed examinations using patients’ neutrophils is not an easy task, and above all, the presented finding per se is worth reporting to settle the controversy over the involvement of ROS in type 2 DM pathology. Thus, I believe that this manuscript is a strong candidate for the publication in WJD. Major concerns 1) In page 12, lines11-12, the phrase “ ..., who also demonstrated increased ROS production in DM (Houstis et al., 2006)” should be replaced by “..., who demonstrated the involvement of increased ROS production in insulin resistance in type 2 DM using a cell culture model and murine models (Houstis et al., 2006)”. The work by Houstis et al. was not a clinical study and the work presented in the current manuscript may be the first report to show clinical relevance of the involvement of ROS in pathological progression of type 2 DM. I would like to encourage authors to make this point clearer in Discussion. Minor concerns 1) In page 3, line 3,



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the word "follow" should be corrected as "follows". 2) It would be better if authors could add scale bars in Figure 1.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
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Title: Preliminary study on overproduction of reactive oxygen species by neutrophils in diabetes mellitus
Reviewer's code: 02445758
Reviewer's country: Taiwan
Science editor: Fang-Fang Ji
Date sent for review: 2016-03-01 10:55
Date reviewed: 2016-03-03 13:56

Table with 4 columns: CLASSIFICATION, LANGUAGE EVALUATION, SCIENTIFIC MISCONDUCT, CONCLUSION. It contains checkboxes for various review criteria like 'Grade A: Excellent', 'Priority publishing', 'Google Search', etc.

COMMENTS TO AUTHORS

The goal of the present study is to explore the ROS level in neutrophils isolated from diabetic patents and non-diabetic volunteers. The authors found the level of ROS in the diabetic patients' neutrophils was higher than that in healthy volunteers' neutrophils, and suggested that ROS level is associated with the pathology of diabetes. Although some interesting results are presented, the data are too preliminary to publish in the present form. Major points: 1. The authors should address the possible mechanism responsible for higher ROS levels in diabetic patients' neutrophils. The authors might analyze the expression of NADPH oxidase in diabetic and non-diabetic neutrophils. 2. The authors could conduct the experiments by measuring ROS level in cell lines such as HL-60 cells after incubation with high glucose concentration. Minor points 1. part of data in Fig 2 is repeatedly presented in Fig.3. 2. The authors should carefully discuss that ROS causes diabetes or diabetes leads to increase ROS generation.



ESPS PEER-REVIEW REPORT

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Reviewer's country: Greece
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COMMENTS TO AUTHORS

Dear author, This is an interesting paper but major revision is needed before it can be accepted for publication. I will refer to some of the major problems detected. Page 4, beginning of the second paragraph: Repetition. See end of the first paragraph of the paper. Page 5: Regarding the study. Why did you not choose patients with the same basic characteristics? i.s. same medical treatment, duration of DM and family history? Did someone of the healthy volunteers receive any medical treatment, e.g statins? Please refer in detail. Regarding the table, some medications are mentioned with the brand name. Please correct. The title of the table should change to demographics and characteristics of the patients, instead of basic details. Page 6, first paragraph last line: immediately OR within 2 hours? Page 7: Regarding statistical analysis. How was the study statistically designed? Why patients were 6 and controls only 3? Why did you use such a limited sample of patients and controls? Page 8: figure 1. This is an image not a figure. Last paragraph refers to "resting condition". The last nine lines however do not belong to the resting condition. Page 12: You refer to a study by Alba-Loureiro et al which needs more discussion. Regarding the outcomes of the study: What about statins received by



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your patients? Could statins influence the results of your study? Please discuss in detail. What about herbals received by one patient? Please discuss in detail Many comments in the paper lack references, report presence or absence of relevant references. Please, update your paper with recent references. Needs minor grammar polishing.



ESPS PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
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Title: Preliminary study on overproduction of reactive oxygen species by neutrophils in diabetes mellitus
Reviewer's code: 00742314
Reviewer's country: Brazil
Science editor: Fang-Fang Ji
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COMMENTS TO AUTHORS

Reviewer comments This paper analysed the production of ROS in neutrophils derived from diabetes patients. The authors reported an increased ROS production in diabetes-derived neutrophils both at resting and after PMA stimulation. The main concerns regarding the paper relies on the small sample size (6 diabetics and 3 controls), which limits their capability to generalize the findings, and lack of novelty in the results. Thus, my recommendation is against the publication. Specific comments are provided below in order to help the authors to improve their paper: ? Regarding the abstract section, it could be better written. The methods is poorly described, since it lacks important information to understand how the study was performed. Also, the results could be improved; ? The introduction section did not approach properly the neutrophil respiratory burst in diabetes patients. It is not possible to know what the evidence is in the field with the introduction. Several studies could be explored throughout the introduction (PMID: 16959366; PMID: 18390927; PMID: 19519161; PMID: 12196480); ? Most references are too old. An update is necessary; ? In the methods section: o According to the authors, one of the inclusion criteria was age range of 60-80 years. However, one



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patient aged 82 years old (patient 3, table 1) was included; o Age from the control group was quite different (30-50 years old) from that of the diabetes group. I guess it raises concern about the validity of the comparison, since neutrophil functions are altered with aging; o What about the Ethics Committee approval? Was there written consent? In the paper, only verbal consent was described; o The assessment of neutrophil oxidative burst needs a better description. The experiments were performed in duplicate or triplicate? For how long neutrophils were stimulated with PMA?; o Leishman staining needs to be described in the methods; ? Regarding the results: o Why that time scale was chosen, with measurements until 50 seconds? o Also, a 'radical escalation index' was cited in last sub-section of the results. Please, describe it better; o In the figure 3, mean and SEM are presented, whereas mean and SD are presented in figures 1 and 2. Please, standardize that; ? Most of the discussion is not discussion; it is rather a literature review. Please, focus on discussing the study findings; ? Please, keep the conclusion answering only the study aim. It is not a place to discuss methodology or give direction to future research.