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## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 36189

**Title:** Oxidative stress in adults with extraintestinal manifestations of celiac disease

**Reviewer's code:** 01555264

**Reviewer's country:** Iran

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-10-11

**Date reviewed:** 2017-10-11

**Review time:** 4 Hours

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 checked="" type="checkbox"/> Grade B: Very good	<input checked="" type="checkbox"/> Grade B: Minor language polishing	<input type="checkbox"/> The same title	<input checked="" type="checkbox"/> High priority for publication
<input type="checkbox"/> Grade C: Good		<input type="checkbox"/> Duplicate publication	
<input type="checkbox"/> Grade D: Fair	<input type="checkbox"/> Grade C: A great deal of language polishing	<input type="checkbox"/> Plagiarism	<input type="checkbox"/> Rejection
<input type="checkbox"/> Grade E: Poor	<input type="checkbox"/> Grade D: Rejected	<input checked="" type="checkbox"/> No	<input type="checkbox"/> Minor revision
		BPG Search:	<input type="checkbox"/> Major revision
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

paper well prepared my only issue is the title that not follow the rest of paper.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 36189

**Title:** Oxidative stress in adults with extraintestinal manifestations of celiac disease

**Reviewer's code:** 00069819

**Reviewer's country:** Jordan

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-10-11

**Date reviewed:** 2017-10-13

**Review time:** 2 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" 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		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

In this study the Authors present their results of the magnitude of the effect of oxidative stress in adult patients with celiac disease. The manuscript is complete and well written. The topic is of major interest to a large readership, although it is not novel. However, the paper has the following flaws: 1. The title is not reflected in the abstract nor in the core tip; that's, the studied subjects are celiac patients with extraintestinal manifestations. This should be specified both in the "aim" and the "methods" sections of the abstract, as well as in the core tip. 2. The sample size may be too small to draw valid conclusions. A type 2 statistical error could undermine the results. 3. The introduction section is too long. A couple of paragraphs should be deleted. 4. The clinical characteristics of study subjects (with emphasis on their specific extraintestinal manifestations) should be added to the demographic data (table 1) or described in a separate table. 5. The Authors state that the study is prospective; actually this is a case-control study, and not a prospective study. 6.

The discussion section should start by stating the main results and their significance, rather than with a repetition of what was already stated in the introduction section. Also, the Authors state "We explored, for the first time, the role of serum uric acid as a non-enzymatic plasma antioxidant in adult patients with CD"; this statement is inaccurate, as the topic has been previously tackled and published by several authors. 7. The study limitations (e.g. sample size, self-reported adherence to GFD,...) should be stated clearly before the conclusions. 8. The conclusions are somehow weak. The Authors should expand on the potential that several nutrients exert antioxidant effects and influence gene expression, therefore representing a useful approach for nutritional intervention in CD subjects. Additionally, the Authors should discuss the usefulness of nutritional genomics as a tool for targeted medical nutrition therapy, and possibly suggest further basic research, extensive epidemiological studies and controlled intervention trials.

## PEER-REVIEW REPORT

**Name of journal:** World Journal of Gastroenterology

**Manuscript NO:** 36189

**Title:** Oxidative stress in adults with extraintestinal manifestations of celiac disease

**Reviewer's code:** 03260089

**Reviewer's country:** Italy

**Science editor:** Ya-Juan Ma

**Date sent for review:** 2017-10-11

**Date reviewed:** 2017-10-14

**Review time:** 3 Days

CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
<input type="checkbox"/> Grade A: Excellent	<input checked="" 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 checked="" 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		<input checked="" type="checkbox"/> No	<input checked="" type="checkbox"/> Major revision
		BPG Search:	
		<input type="checkbox"/> The same title	
		<input type="checkbox"/> Duplicate publication	
		<input type="checkbox"/> Plagiarism	
		<input checked="" type="checkbox"/> No	

## COMMENTS TO AUTHORS

Considerations when preparing a peer-review report (1) is the overall structure of the manuscript complete? A complete manuscript will contain title, abstract, key words, introduction, materials, methods, experimental procedure, results, discussion, conclusion, acknowledgements, and references. Yes (2) what is the scientific question proposed in the manuscript? This should be clearly presented in the introduction section, along with the pertinent background, rationale, aim, major findings and potential significance of the study. Collectively, this information should inform whether the manuscript would be interesting enough to warrant readers' attention? The aim of our study was to determine the involvement of oxidative stress in the mechanism of mucosal injury of the small intestine and to assess the effect of oxidative stress on the course of cd in adult patients with non-classic symptoms and extraintestinal manifestations. (3) which special (unique, innovative and/or timely, appropriate) methods and techniques

are adopted in the manuscript? This should be clearly presented in the methods section. In addition, does the manuscript provide adequate details of methods (including experimental design, subjects or materials, data collection methods, and statistical methods) to allow a reader to repeat the research? The expression of il-1 $\beta$ , tnf- $\alpha$ , il-10, hsp-70, hif-1 $\alpha$ , sod, and bax transcripts in human samples was determined by rt-pcr. (4) is the source of the data that is presented reliable? This will be indicated by the information presented in the results section. The information in the results section will also indicate the academic significance of the main findings (including figure and tables). Yes (5) what are the results obtained from the data that is presented in the manuscript? This information will make up the discussion section. It will also answer the questions of whether the results answered the proposed scientific question, achieved the aim of the study, or confirmed or rejected the hypothesis proposed in the manuscript. The results of biochemical tests are presented in table 3. what about t-tg / ema status of cd patients in gfd? Why a lot of cd patients were not on gfd? A too big percentage of cd patients on grd have a great duodenal damage (40% have a marsh 3 damage -> their results can't be considered with the group of cd patients responsive to gfd) (6) what are the conclusions of the manuscript? These should be clearly presented in the conclusion section. In addition, the section should present the contributions of the conclusions to the field and the weaknesses of the study, and provide future research directions. In conclusion, by its association with intestinal damage, the course of the disease, and perhaps extraintestinal disorders, oxidative imbalance appears to be one of the major factors implicated in the pathogenesis of cd. (7) does the manuscript cite all important, relevant and timely references? No (8) is there any indication of academic misconduct in the manuscript? No (9) does the manuscript conform to the academic rules and norms and include a human and animal rights statement, institutional review board statement, informed consent statement, clinical trial registration statement, institutional animal care and use committee statement, animal care and use statement, biostatistics statement, and conflict-of-interest statement? Yes (10) does the manuscript describe any important new methods, problems in or directions of research? Yes (11) does this manuscript contribute to understanding the pathogenesis of disease, disease diagnosis, and treatment or prevention? Yes (12) does the title of the manuscript contain key words, and is the title interesting enough to attract readers' attention? Yes (13) does the topic of the manuscript fall within the scope of world journal of gastroenterology? Yes (14) does the language of the manuscript reach the standard of publishing? Yes peer-reviewers' conclusions (1) what are the new visions that the manuscript offers to readers? A deepening of the role of oxidation products on the cd (2) are there any weaknesses or deficiencies in the manuscript? What about t-tg / ema status of cd patients in gfd? Why a lot of cd patients were not on gfd? A too



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big percentage of cd patients on grd have a great duodenal damage (40% have a marsh 3 damage -> their results can't be considered with the group of cd patients responsive to gfd) a) "the immune disturbances play a critical role in the pathogenesis of cd[15], but there have been no studies on the role of heat-shock proteins (hsps) in the development of this disorder." This seems not true protein-protein interaction network of celiac disease. Gastroenterol hepatol bed bench. 2016 fall;9(4):268-277. autoimmunity to heat shock proteins and vitamin d status in patients with celiac disease without associated dermatitis herpetiformis. J steroid biochem mol biol. 2017 oct;173:23-27. distinct and synergistic contributions of epithelial stress and adaptive immunity to functions of intraepithelial killer cells and active celiac disease. Gastroenterology. 2015 sep;149(3):681-91.e10. increased heat shock protein 72 expression in celiac disease. J pediatr gastroenterol nutr. 2010 nov;51(5):573-8. heat-shock protein 70-1 and hla class ii gene polymorphisms associated with celiac disease susceptibility in navarra (spain). Hum immunol. 2001 aug;62(8):821-5. expression of hsp-65 in jejunal epithelial cells in patients clinically suspected of coeliac disease. Autoimmunity. 1999 oct;31(2):125-32. (3) can the experiences and lessons presented in the manuscript improve the readers' practice? Little (4) does the content of the manuscript have value for publication? If not, rejection should be recommended yes, but after the distinction between cd patients on gfd with histological damage of marsh 3 from those with histological marsh 0 or 1 (5) is the manuscript concise, clear, comprehensive, and convincing? Yes, apart from the criticism i discussed above