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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
Manuscript NO: 31311
Title: Obesity, metabolic syndrome and diabetic retinopathy: Beyond hyperglycemia
Reviewer's code: 02640461
Reviewer's country: Brazil
Science editor: Jin-Xin Kong
Date sent for review: 2016-11-10
Date reviewed: 2016-11-24

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

COMMENTS TO AUTHORS

The review is relevant once the prevalence of metabolic syndrome has increased in recent years. The mechanisms of development of retinopathy in these patients with and without establish history of diabetes should be discussed. There are few corrections in manuscript: 1) In introduction section is necessary to characterize the metabolic syndrome. According, the metabolic syndrome not is a disease; this is a condition when the individual have three or more risk factors associated. 2) In introduction section, first paragraph, eleven line, to delete the parenthesis after glucagon. The second part of the sentence is confusing: "or hormones that can interfere with insulin secretion such as catecholamines", repeating the previous information, so suggest excluding this part. "These endocrine disorders are associated with sustained release of hormones that are antagonistic to insulin action including growth hormone, glucocorticoids, catecholamines or glucagon), or hormones that can interfere with insulin secretion such as catecholamines". 3) In introduction section, first paragraph, eighteen line, the word Insulin is in capital letter; twenty line, the same with Acromegaly 4) The purpose of

review not is clear at the end of the introduction section: "Therefore, the focus of this review will be on development of diabetic retinopathy lesions in patients with primary DM either type-1 or type-2 rather than secondary diabetes." Not is commented about metabolic syndrome (is the title). So, suggest rewrite similar as is in the abstract section: "This review will summarize the current literature on the prevalence and impact of the metabolic syndrome on retinopathy in subjects with and without established history of diabetes. This review will also discuss some of the mechanisms through which components of the metabolic syndrome can contribute to the development of retinopathy. 5) In the Development of Retinopathy in Subjects without a History of Diabetes section, on second paragraph, ten line, the name of study is "The Hoorn", correct for the Hoorn. 6) The sentence: In addition, Hb A1c level and waste to hip ratio (WHR) were risk factors in the nondiabetic individuals [30]. These finding suggest that retinal pathologies begin to develop prior to a clinical diagnosis of hypertension and/or that other conditions play a role and cumulatively result in retinopathy." These results in reference number 30 are sufficient to affirmation? Correct the Hb A1c for HbA1c. 7) In the Retinopathy in subjects with Metabolic Syndrome but no history of diabetes section, on second paragraph, eleven line, the sentence: "However, other studies looking at individuals older than 40 and obese, calculated using BMI, found no significant correlation between the metabolic syndrome and retinopathy independent of diabetes (reviewed in[85])." Why the reference is written between "reviewed" inside parentheses? 8) There are two sentence in different moments on manuscript that are repeated: In the Insulin resistance and the Metabolic Syndrome section, on second paragraph, eleven line: "This could be attributed to the inability of the BMI calculation to accurately estimate body composition[61, 62] while the WHR is an indicator for central obesity and is associated with insulin resistance [64]." In the Retinopathy in subjects with Metabolic Syndrome but no history of diabetes section, on second paragraph, seventeen line: "The discrepancies speak to a number of possible factors including inability of the BMI calculation to accurately estimate body composition[61, 62] while the WHR is an indicator for central obesity and is associated with insulin resistance[64]." 9)

"Given that hyperglycemia and hypertension are the strongest risk factors for the development of retinopathy lesions, and that the metabolic syndrome is strongly associated with the development of these conditions, it appears that it would be beneficial to clinically address individuals with the

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
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Reviewer's country: Italy
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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		[ ] Duplicate publication	
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COMMENTS TO AUTHORS

Authors should also emphasise the role of NAFLD, further expression of the Metabolic Syndrome, while taking into account the micro-macro circulation of Diabetes Mellitus.

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PEER-REVIEW REPORT

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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
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		[Y] No	

COMMENTS TO AUTHORS

Mbata et al., have surveyed the literature aimed at describing the relationship between diabetic retinopathy (DR) and metabolic syndrome (MeS). As the authors state, the notion that type 1 and type 2 diabetes are associated with DR, a key manifestation of hypertriglyceridemia-induced damage to the retinal microvasculature, is overwhelmingly supported by many studies. Many of these studies have been discussed in detail in the Review. However, based on the title of the review "Diabetic Retinopathy and the Metabolic Syndrome: Beyond hyperglycemia", I was expecting that the authors will be specifically dealing with the paradoxical relationship between DR and MeS, with concrete examples that conform to the conventional view as well as research showing that MeS (without hyperglycemia) may also cause DR. Therefore, the authors need to specifically discuss studies that investigated the relationship between DR and MeS without hyperglycemia (one of the 5 criteria of MeS outlined in the Table 1). A curious reader is unlikely to gain much of substance from authors' laundry-list of mechanisms involved in DR if alternative mechanisms that do not involve an active role of

hyperglycemia are not explicitly discussed. To achieve this goal, the authors need to present a more discerning view of the literature that deals with DR and its relationship to MeS, with and without hyperglycemia. This would entail re-writing the sections that deal with mechanisms of DR to elaborate processes that occur. In light of these changes the BODY of the Review, the ABSTRACT, CORE TIP and CONCLUSION sections will need to be drastically revised. In addition to the suggestions that I have made above to improve the content of the Review, this manuscript will gain enormously by a THOROUGH EDITING in order to RECTIFY the Proper Usage of English language and Grammar. There are too numerous to count errors that MUDDLE the INTENDED MEANING of IDEAS discussed in this otherwise REASONABLE Review of literature.

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PEER-REVIEW REPORT

Name of journal: World Journal of Diabetes
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CLASSIFICATION	LANGUAGE EVALUATION	SCIENTIFIC MISCONDUCT	CONCLUSION
[ ] Grade A: Excellent	[ ] Grade A: Priority publishing	Google Search:	[ ] Accept
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COMMENTS TO AUTHORS

Mbata et al. outline current data on the role of metabolic syndrome and its components on retinopathy in subjects with and without established history of diabetes. I have some concerns, which require attention. Major comments - The authors could discuss the role of eicosanoids (leukotrienes, prostacyclin, and thromboxane), hypoxia-inducible factor-1, and growth factors (vascular endothelial growth factor and platelet- derived growth factor) in diabetic and metabolic syndrome-associated retinopathy. - Current treatment recommendations for diabetic retinopathy could be mentioned. - The authors could made a figure that presents the pathways leading to the development of retinopathy in subjects with and without history of diabetes.