

Dear Editor,

We are grateful to you and the reviewers for your precious time in reviewing our manuscript. Your constructive and valuable comments are highly appreciated. We have revised the text to address your concerns and it is our belief that the manuscript has substantially improved after making the suggested edits. Below we provide the point-by-point response to the reviewers' comments and concerns.

Response to Reviewer 1:

No.	Comments	Response
1.	<p>This is a good recap of the existing knowledge on the interplay vitamin D and magnesium status in glycemic control and insulin sensitivity. It will be beneficial to include</p> <ul style="list-style-type: none">- a brief roundup of vitamin D and magnesium biochemistry- along with their implications in metabolic syndrome related parameters to emphasize their mechanistic role in insulin action.- In that regard, there are few references listed below that may useful to cite in this manuscript (1-6) <p>1. Alswailmi FK, Shah SIA, Nawaz H. Immunomodulatory role of vitamin D: Clinical implications in infections and autoimmune disorders. Gomal J Med Sci. 2020;18(3):132-8. doi: 10.46903/. 2. Iqbal S, Shah SIA, Sikandar MZ, . Relationship between serum vitamin D and insulin resistance in normal weight and overweight or obese men. Professional Med J. 2019;26(11):1810-4. doi: 10.29309/tpmj/2019.26.11.237. 3. Iqbal S, Wyne H, Shah SIA. Comparative study of serum magnesium and lipid profile in normal weight, over-weight and obese young adult males. Proceedings SZPGMI. 2019;33(2):1-5.</p>	<p>Thank you for the brilliant suggestions.</p> <p>A brief roundup on biochemistry of vitamin D and magnesium in association with insulin resistance have been summarized in Figure 1 and 2.</p> <p>Figure 1 describes the interrelation of vitamin D and magnesium in the regulation of insulin synthesis and release from the pancreatic beta cells. It highlights the role vitamin D-VDR-RXR-VDRE complex in modulating insulin secretion. Magnesium in the form of MgATP and MgADP play vital roles in regulating glucokinase activity.</p> <p>Figure 2 highlights the role of MgATP in the autophosphorylation process of B-subunits of insulin receptor tyrosine kinase; a crucial step in initiating an intracellular signaling pathway. The vitamin D-VDR-RXR-VDRE complex also play important role in regulating GLUT 4 synthesis at the target organs.</p> <p>All suggested references (reference 1, 2, 3, 4, 5, and 6) have been cited accordingly and highlighted in yellow.</p>

	<p>4. Khashim Alswailmi F, Shah SIA, Nawaz H, Al-Mazaideh GM. Molecular Mechanisms of Vitamin D-Mediated Immunomodulation. <i>Galen Med J</i>. 2021;10:e2097. doi: 10.31661/gmj.v10i0.2097. PubMed PMID: 35572849; PubMed Central PMCID: PMC9086864.</p> <p>5. Shah SIA, Iqbal S, Sikandar MZ, Qazi UY, Haq I. Serum vitamin D and cardiometabolic markers: A comparative study in adult men based on body mass index. <i>IJUM Med J Malaysia</i>. 2021;20(2):67-74.</p> <p>6. Shah SIA, Sikandar MZ, ., Qazi UY, Haq I. Comparative assessment of vitamin D and parathyroid hormone as risk factors of myocardial infarction and their correlation with lipid profile. <i>Medical Science</i>. 2021;25(107):185-91.</p>	
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Response to Reviewer 2:

No.	Comments	Response
1	The topic of this review article is very interesting and, in my opinion, manuscript could be accepted for publication if authors resolve the following issues: - the introduction is missing the references	Thank you for the highlight. Citation of references have been added to the introduction.
2	Please, refrain from using the term “diabetic”	The term diabetic throughout the manuscript has been changed to diabetes except for “diabetic kidney disease” as it is a recognized term used in the international guideline (KDIGO 2022).
3.	Please, define the terms “vitamin D deficiency” and “vitamin D insufficiency”	<p>Additional description to the term vitamin D deficiency and insufficiency has been made and highlighted in yellow.</p> <p>“Although several different cutoffs have been used to characterize the risk of deficiency, most studies defined deficiency as a serum 25 (OH)D level of</p>

		<30 nmol/L which often falls within the range of 25–30 nmol/L, while insufficiency is defined as a serum 25(OH)D level between 30 and 50 nmol/L ^[7,16] .”
4.	Please, provide more accurate definition of diabetes mellitus	<p>The definition of diabetes mellitus has been added and highlighted in yellow.</p> <p>“Diabetes mellitus (DM) is a chronic metabolic disease that results from the impairment of insulin release, resistance to peripheral insulin action, or both leading to persistent hyperglycemia. Genetic predisposition and behavioral and environmental risk factors are interrelated and contributes to the development of DM^[9,10].”</p>
5.	In my opinion, assertion that “vitamin D has been linked to everything” is not appropriate -	<p>Amendment has been made and highlighted in yellow.</p> <p>“The “sunshine vitamin,” or vitamin D, has received widespread attention in recent decades because it has been linked to not only skeletal health but also many non-skeletal diseases, such as certain types of cancer, metabolic syndrome, immune diseases, and cardiovascular disease^[12].”</p>
6.	Please, use the uniform abbreviation for glycated hemoglobin	Changes have been made as per suggestion. The standardized term used throughout the manuscript is HbA1c.
7.	In my opinion, it is not necessary to report p values from the cited studies	Changes have been made as per suggestion. All p values have been removed.
8.	What is the meaning of the terms “poor” and “good” diabetes mellitus?	<p>The term is supposed to reflect patients’ glycemic control. For clarity, we have decided to amend the term to good/poor glycemic control.</p> <p>Changes has been made as per suggestion.</p>

		<p>“This finding was supported by a study on diabetes patients which showed that those with poor glycemic control had significantly lower mean vitamin D and serum magnesium levels than those with good glycemic control^[5]. Moreover, Salwani et al. reported that a hypomagnesemia of 0.88 ± 0.10 mmol/L was commonly observed in the poor glycemic control group, while good glycemic control patients had a higher magnesium level of 0.94 ± 0.10 mmol/L^[48].”</p>
9.	The list of reference should be revised in order to make it uniform in style	Corrections and addition to references have been made. The list of references have been revised as per journal requirement.
10.	The manuscript requires thorough language and technical polishing	Certificate of editing by Enago is attached.
11.	Please, check for accuracy of units in which the values of magnesium are expressed from the cited sources	<p>The serum magnesium unit used in the original article (reference 45) is mg/dL. For standardization purpose, we decided to change all serum magnesium level to SI unit mmol/L. The initial mg/dL is converted to mmol/L.</p> <p>Change has been made and highlighted in yellow.</p> <p>“The occurrence of early diabetic kidney disease has also been observed to be more common in patients with a magnesium level of ≤ 0.741 mmol/L^[45].”</p>
12.	Adding figures illustrating the reviewed mechanisms would significantly improve the quality of the manuscript.	Figures(1 and 2) have been added.

We hope the manuscript after careful revisions meets the reviewers’ recommendations and suitable for publication in the World Journal of Diabetes. We look forward to hear from you at your earliest convenience.

Sincerely,

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