

Reply to the reviewers' comments

Reviewer Number	Original comments of the reviewer	Reply by the author(s)	Changes done on page number and line number
1	The Discussion section is modest.	<p>Thank you, dear reviewer, for the comment.</p> <p>Correction has been made as per dear reviewer.</p>	
1	Abstract: not properly written	<p>Thank you, dear reviewer, for the comment.</p> <p>Diabetes mellitus is one of the chronic metabolic noncommunicable diseases that has attained worldwide epidemics. It threatens healthy life around the globe, with mild-to-severe secondary complications and causes significant morbidity owing to specific microvascular abnormalities such as retinopathy, nephropathy and neuropathy, and macrovascular complications such as ischaemic heart disease and peripheral vasculopathy. Diabetic retinopathy (DR) research has had significant advancements over the past decades; one-third of people with diabetes have DR. In addition, it can lead</p>	

		<p>to several anterior segment complications such as glaucoma, cataract, cornea, conjunctiva, and lacrimal glands and other ocular surface diseases. Uncontrolled DM also led progressive damage to corneal nerves and epithelial cells, as a result it increases the risk of anterior segment disorders ranging from dry eye disease, persistent epithelial defects to sight-threatening complications such as corneal ulcer. Although DR and other associated ocular complications are well-known, the complexity of its aetiology and diagnosis makes therapeutic intervention challenging. Strict glycemic control, early detection and regular screening, and meticulous management is the key to halting the progression of the disease. In this review manuscript, we aim to provide an in-depth understanding of the broad spectrum of diabetic complications in the anterior segment of the ocular tissues and illustrate the progression of diabetes and its pathophysiology, epidemiology, and prospective therapeutic targets. This first such review article will highlight the role of diagnosing and treating patients with a plethora of anterior-segment diseases associated with diabetes, which are often neglected.</p>	
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1	Conclusion: The section devoted to the explanation of the results section (and conclusion) is hard to follow. Moreover, the conclusions reached are really far from the empirical results.	<p>Thank you, dear reviewer, for the comment.</p> <p>Ocular surface changes like reduced tear film stability and secretion, reduced sub-basal nerve plexus density, and reduced corneal sensitivity can occur before the clinical evidence of peripheral neuropathy in patients with diabetes mellitus. Hence these parameters have the potential to be used as non-invasive biomarkers for peripheral neuropathy for earlier prediction of complications of diabetes mellitus.⁵⁵</p> <p>Although various treatment modalities were introduced for the treatment and prevention of anterior segment disorders associated with DM, further researches are still need to be done for the development of better treatment strategies. A proper guideline for screening ocular surface pathologies resulting from uncontrolled DM should also be developed and established. A better understanding in both patients and healthcare practioners especially diabetologist, ophthalmologists, paramedical staff of the impact, of DM</p>	

		<p>on the anterior segment of the eye would be important for the optimal management of DM.</p> <p>We have added this inside the manuscript.</p>	
1	The discussion should be rather organized around arguments avoiding simply describing details without providing much meaning, Spacing, punctuation marks, grammar, and spelling errors should be reviewed thoroughly found so many typos throughout the manuscript	<p>Thank you, dear reviewer, for the comment.</p> <p>Correction has been made as per dear reviewer.</p>	
1	English is modest. Therefore, the authors need to improve their writing style. In addition, the whole manuscript needs to be checked by native English speakers.	<p>Thank you, dear reviewer, for the comment.</p> <p>Correction has been made as per dear reviewer.</p>	
2	<p>The manuscript has been peer- reviewed, and it's ready for the first decision</p> <p>Language Quality: Grade B (Minor language polishing)</p> <p>Scientific Quality: Grade C (Good)</p>	<p>Thank you, dear reviewer, for the comment.</p>	
3	<p>I recommend the manuscript to be published in the World Journal of Clinical Cases Before final acceptance when</p> <p>Scientific Quality: Grade C (Good)</p>	<p>Thank you, dear reviewer, for the comment.</p>	

	<p>Language Quality Grade B (Minor language polishing)</p> <p>Conclusion: Accept (General priority)</p>		
	<p>Specific Comments to Authors: This first such review article will highlight the role of diagnosing and treating patients with a plethora of anterior segment diseases associated with diabetes, which are often neglected.</p>	<p>Thank you, dear reviewer, for the comment.</p>	
4	<p>Scientific Quality: Grade D (Fair)</p> <p>Language Quality: Grade C (A great deal of language polishing)</p> <p>Conclusion: Major revision</p>	<p>Thank you, dear reviewer, for the comment.</p>	
	<p>Are there controversies in this field?</p> <p>What are the most recent and important achievements in the field?</p> <p>In my opinion, answers to these questions should be emphasized.</p>	<p>Thank you, dear reviewer, for the comment.</p> <p>Despite the advice for annual ocular examination in patients with DM as a cost-effective novel method to prevent blindness, screening is poorly implemented and not able to effectively deal with the raising demand with the</p>	

	<p>booming population with newly diagnosed DM.⁵⁵ The introduction of advanced digital technologies, including Artificial Intelligence, and telehealth technology have created new opportunities in screening, diagnosis, and management of DM related ocular complications. Novel hybrid telemedicine systems have been well introduced to allow a wider range for DM related eye screening. It carries diagnostic sets including a combination of mobile ultra-field mounted cameras on vehicles in vans. ⁵⁶⁻⁵⁸ Recently, the MII RetCam and the Remidio Fundus on Phone are two devices that successfully introduced in India for teleophthalmology community-based DR screening. ^{59,60}</p> <p>The Artificial Intelligence (AI), particularly deep learning (DL) algorithms has been increasing in big data management and automated image-recognition task, which is helpful for early detection of DM related ocular complications such as diabetic retinopathy.⁶¹⁻⁶³</p> <p>Remote monitoring technologies have been escalated during the pandemic COVID-19 and noticed as an effective solution for timely detection of pathologies and appropriate care for</p>	
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	<p>patients with DM related ocular diseases outside the hospital and the clinics. 64,65</p> <p>Recently, a novel effective anti-VEGF used for treatment for diabetic macular edema. Conbercept (Chengdu Kanghong Biotech, Sichuan, China) is a recombinant human VEGF receptor-Fc fusion protein with a much more potent affinity to VEGF compared to bevacizumab and ranibizumab and blocks VEGF-A/B/C isoforms and PGF, and helpful to resolve the macular edema effectively. 66</p> <p>Though there are more controversy in treating the DM related ocular complications effectively, new technologies and treatment strategies has been evolving to enhance the treatment protocol and screening concept.</p> <p>We have added this inside the manuscript.</p>	
Perhaps, in some cases, novelty of the recent achievements should be highlighted by indicating the year of publication in the text of the manuscript	<p>Thank you, dear reviewer, for the comment.</p> <p>55. Li JPO, Liu H, Ting DSJ, et al. Digital technology, tele-medicine and artificial intelligence in ophthalmology: a</p>	

	<p>global perspective. <i>Prog Retin Eye Res.</i> 2021; 82:100900.</p> <p>56. Afshar AR, Oldenburg CE, Stewart JM. A novel hybrid fixed and mobile ultra-widefield imaging program for diabetic teleretinopathy screening. <i>Ophthalmol Retina.</i> 2019;3(7):576–579.</p> <p>57. Rajalakshmi R, Prathiba V, Arulmalar S, Usha M. Review of retinal cameras for global coverage of diabetic retinopathy screening. <i>Eye.</i> 2021;35(1):162–172.</p> <p>58. Karakaya M, Hacisoftaoglu RE. Comparison of smartphone-based retinal imaging systems for diabetic retinopathy detection using deep learning. <i>BMC Bioinform.</i> 2020;21(4):1–18.</p> <p>59. Kaur R, Singh H, Samria S, et al. MII RetCam assisted smartphone-based fundus imaging (MSFI)—a boon for paediatric retinal imaging. <i>Eye.</i> 2020;34(8):1307–1309.</p> <p>60. Natarajan S, Jain A, Krishnan R, Rogye A, Sivaprasad S. Diagnostic accuracy of community-based diabetic retinopathy screening with an offline artificial intelligence system on a</p>	
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	<p>smartphone. JAMA Ophthalmol. 2019;137(10):1182–1188.</p> <p>61. Schmidt-Erfurth U, Sadeghipour A, Gerendas BS, Waldstein SM, Bogunović H. Artificial intelligence in retina. Prog Retin Eye Res. 2018;67:1–29.</p> <p>62. Abramoff MD, Lavin PT, Birch M, Shah N, Folk JC. Pivotal trial of an autonomous AI-based diagnostic system for detection of diabetic retinopathy in primary care offices. NPJ Digit Med. 2018;1:1.</p> <p>63. Ramesh PV, Ramesh SV, Subramanian T, Ray P, Devadas AK, Ansar SM, et al. Customised artificial intelligence toolbox for detecting diabetic retinopathy with confocal truecolor fundus images using object detection methods. TNOA J Ophthalmic Sci Res 2023; 61:57-66.</p> <p>64. Keenan TDL, Goldstein M, Goldenberg D, Zur D, Shulman S, Loewenstein A. Prospective, longitudinal pilot study: daily self-imaging with patient-operated home OCT in neovascular age-related macular degeneration. Ophthalmol Sci. 2021;1:2.</p>	
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	<p>65. Maloca P, Hasler PW, Barthelmes D, et al. Safety and feasibility of a novel sparse optical coherence tomography device for patient-delivered retina home monitoring. Trans Vis Sci Technol. 2018;7(4):8.</p> <p>66. White N.H., Sun W., Cleary P.A., Tamborlane W.V., Danis R.P., Hainsworth D.P., Davis M.D., DCCT-EDIC Research Group Effect of prior intensive therapy in type 1 diabetes on 10-year progression of retinopathy in the DCCT/EDIC: Comparison of adults and adolescents. Diabetes. 2010;59:1244–1253.</p> <p>We have added this inside the manuscript.</p>	
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	<p>It threatens healthy life around the globe, with mild-to-severe secondary complications and causes significant morbidity owing to specific microvascular abnormalities such as retinopathy, nephropathy and neuropathy, and macrovascular complications such as ischaemic heart disease and peripheral vasculopathy. Diabetic retinopathy (DR) research has had significant advancements over the past decades; one-third of people with diabetes have DR. In addition, it can lead to several anterior segment complications such as glaucoma, cataract, cornea, conjunctiva, and lacrimal glands and other ocular surface diseases. Uncontrolled DM also led progressive damage to corneal nerves and epithelial cells, as a result it increases the risk of anterior segment disorders ranging from dry eye disease, persistent epithelial defects to sight-threatening complications such as corneal ulcer. Although DR and other associated ocular complications are well-known, the complexity of its aetiology and diagnosis makes therapeutic intervention challenging. Strict glycemic control, early detection and regular screening, and meticulous management is the key to halting the progression of the disease. In this review manuscript, we aim to</p>	
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<p>Conclusion The section devoted to the explanation of the results</p>	<p>Thank you, dear reviewer, for the comment.</p> <p>Ocular surface changes like reduced tear film stability and secretion, reduced sub-basal nerve plexus density, and reduced corneal sensitivity can occur before the clinical evidence of peripheral neuropathy in patients with diabetes mellitus. Hence these parameters have the potential to be used as non-invasive biomarkers for peripheral neuropathy for earlier prediction of complications of diabetes mellitus.⁵⁵</p> <p>Although various treatment modalities were introduced for the treatment and prevention of anterior segment disorders</p>	

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5	<p>Cinical Cases berore na accepunce, when revising the manuscript, the author must supplement and improve the highlights of the latest cutting-edge research results, thereby further Improving the content of the manuscript.</p>	<p>Thank you, dear reviewer, for the comment.</p> <p>Innovations In screening and treatment protocols</p> <p>Despite the advice for annual ocular examination in patients with DM as a cost-effective novel method to prevent blindness, screening is poorly implemented and not able to effectively deal with the raising demand with the booming population with newly diagnosed DM.⁵⁵ The introduction of advanced digital technologies, including</p>	

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	<p>To this end, authors are advised to apply a new tool, the RCARCA is an artificial intelligence technology based open multidisciplinary citation analysis database In it upon obtaining search results from the keywords entered by the author, "Impact Index Per Article under Ranked by should be selected to find the latest highlight articles, which can then be used to further improve an article under preparation/peer-review/revision</p>	<p>Thank you, dear reviewer, for the comment.</p> <p>We have added recent related citations inside the manuscript.</p>	

