RESEARCH ARTICLE

Ocular complications associated with diabetes and the risk of sustainable blindness: A real world analysis

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Abstract

Objective: To evaluate the frequencies of ocular comorbidities among patients with type II diabetes, and the association with multiple systemic factors.

Method: The retrospective, cross-sectional study was conducted at the Al Ibrahim Eye Hospital, Karachi, and comprised diabetic eye clinic data from April 2014 to February 2022. Demographic, biochemical and ophthalmic findings of the patients were recorded. Ocular findings analysed were best-corrected visual acuity, lens status, corneal changes, optic disc assessment, intraocular pressure and signs of retinopathy and its grading. Data was analysed using SPSS 22.

Results: Of the 43,723 subjects, 22,677(51.86%) were males and 21,046(48.13%). The overall mean age was 54.14±10.68 years. There were 21,680(49.58%) patients with diabetes duration 5-10 years. Overall, 33,876(77.5%), had some ocular morbidity, while 9,847(22.5%) had no such complaints. The commonest morbidity was cataract12,607(28.8%), followed by refractive errors 8,508(19.5%), vision-threatening diabetic retinopathy 2,553(5.83%) and suspected glaucoma 1,211(2.76%). Vision-threatening diabetic retinopathy and suspected glaucoma represented sustained blindness risk 3,764(8.6%). Increasing levels of low-density lipoprotein were significantly associated with advanced diabetic eye disease and clinically significant macular oedema ($p<0.05$), while glycated haemoglobin >6.4 was associated significantly with diabetic retinopathy and suspected glaucoma ($p<0.05$).

Conclusion: Diabetes caused some or the other ocular morbidity that needed intervention. Poor control of biochemical parameters was seen to increase frequency of ocular complications.

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Introduction

Diabetes mellitus (DM) is a global problem affecting approximately 537 million adults aged 20-79 years in 2021, and is likely to reach 634 million by 2030.[1] Pakistan with a population of more than 220 million and a prevalence of diabetes at 26.3% is facing a DM epidemic.[2] DM is known for its complications, including eye–related complications. Some of these ophthalmic complications, like retinopathy, are the result of poor glycaemic control.[3] Other eye diseases, like cataract, glaucoma and ocular surface diseases, have also been found in higher frequency among diabetics at a younger age.[4] Ever increasing DM prevalence demands periodic evaluation of distribution and determinants of its complications. There has been some work done to evaluate the association of DM with multiple ocular complications internationally[5] but most of the work has been focussed around diabetic retinopathy (DR)[6-8] and sustainable blindness (SB).[9] DM prevalence and its associated complications in all ages are causing significant morbidities, but data from Pakistan is still lacking in certain areas. Association of different factors of diabetes, such as sugar level and lipid profile, have been explored with DR,[10,11] but not much work has been done with co-ocular morbidities, such as cataract and glaucoma.

Considering the overall burden of the disease and its co-morbidities, it is highly essential to evaluate not only the frequencies of the ocular co-morbidities, but the overall risk of SB associated with DR and its risk with systemic factors, such as lipid profile and glycated haemoglobin (HbA1c). The current study was planned to evaluate the frequencies of ocular comorbidities among patients with type II DM (T2DM), and the association with multiple systemic factors.

Materials and Methods

The retrospective, cross-sectional study was conducted at the Al Ibrahim Eye Hospital, Karachi, and comprised diabetic eye clinic (DEC) data from April 2014 to February 2022, under the project "Strengthening Pakistan's response to Diabetic Retinopathy". After approval from the institutional ethics review committee, data was retrieved using non-probability purposive sampling technique. Data of all individuals who attended DEC during the stipulated period was included, while incomplete data was excluded. Systemic factors had been documented by the diabetologist (general physician), while ocular assessments

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had been done and documented by the ophthalmologist having more than 5 years of experience in medical retina. All the entries had been made in real time. Fasting blood glucose (FBG), random blood glucose (RBG), HbA1c, lipid profile, serum creatinine, urine detail report (DR), blood pressure (BP), height and weight of all patients were recorded. Detailed eye examination findings were documented, including best-corrected visual acuity (BCVA), lens status, corneal changes, optic disc assessment, intraocular pressure (IOP), measurement, optic disc assessment and retina examination on slit lamp along with retinal images for the presence of DR signs. DR was graded as per the Diabetic Retinopathy Severity Scale (DRSS)[12] and presence or absence of neovascularisation were noted.

Data was analysed using SPSS 22. Mean±standard deviation were used to express continuous variables, while frequencies and percentages were used for categorical variables. Normality of data was checked through Shapiro-Wilk test, and the data was found to be normally distributed. DR severity with biochemical parameters was assessed using chi-square test or Fisher's exact test, as appropriate, and continuous data of HbA1c for each ocular comorbidity was assessed using one-sample t-test. Contingency 2x2 table between DM duration and HbA1c levels was generated to calculate odds ratio (OR). P≤0.05 was considered statistically significant.

Results

Of the 43,723 subjects, 22,677(51.86%) were males and 21,046(48.13%). The overall mean age was 54.14±10.68 years. There were 21,680(49.58%) patients with DM duration 5-10 years, followed by 14,346(32.2%) with <5 years, and 7,697(17.6%) with DM duration >10 years. Biochemical parameters of patients with ocular morbidities were noted (Table 1).

Overall, 33,876(77.5%), had some ocular morbidity, while 9,847(22.5%) had no such complaints. The commonest morbidity was cataract 12,607(28.8%), followed by refractive errors 8,508(19.5%) and DR 4325(9.9%) (Figure). Vision-threatening DR (VDTR) 2,553(5.83%) and ocular hypertension (OH) / neovascular glaucoma (NVG) / suspected glaucoma 1,211(2.76%) together represented SB risk 3,764(8.6%).

Among DR cases, non-proliferative diabetic retinopathy (NPDR) was found to be the commonest type 1,772(40.9%), followed by clinically significant macular oedema (CSME) 1.318(30.5%), proliferative DR (PDR) 622(14.5%) and advanced diabetic eye disease (ADED) 613(14.2%).

No significant association of DR was found with increasing levels of cholesterol and triglycerides (TGs). Increasing levels of LDL were directly associated with ADED and CSME (p<0.05). HbA1c >6.4 was associated significantly with higher frequency of DR and suspected glaucoma (p<0.05) (Table 2).

Table-1: Biochemical parameters of patients with ocular complications.

Biochemical Test	Cataract (Mean±S.D) (n=12607)	Refractive Error (Mean±S.D) (n=8508)	Diabetic Retinopathy (Mean±S.D) (n=4325)	Glaucoma suspect/OHT (Mean±S.D) (n=1211)	*p*-value
FBG	170.07±67.13	166.31±58.51	172.95±72.33	153.50±39.80	0.045
RBG	249.48±111.02	233.86±98.80	265.34±107.60	230.97±102.25	0.037
HbA1c	9.20±2.12	10.07±3.02	9.47±2.24	8.58±2.02	0.189
Lipid profile:					
Serum Cholesterol	197.79±69.78	193.68±60.03	203.38±87.67	187.38±51.35	0.299
Serum Triglyceride	196.39±116.96	206.97±163.73	192.12±104.93	190.13±96.65	0.152
LDL	133.87±37.27	132.68±36.01	137.30±47.77	131.06±38.83	0.341
HDL	37.40±10.34	37.12±9.38	36.82±10.11	37.29±7.36	0.857
Serum Creatinine	1.49±0.74	1.19±0.14	1.20±0.77	1.09±0.50	0.231

OHT: Ocular hypertension, FBG: Fasting blood glucose, RBG: Random blood glucose, HbA1c: Glycated haemoglobin, HDL: High-density lipoprotein, LDL: Low-density lipoprotein, SD: Standard deviation.

Table-2: Association of biochemical parameters with severity of diabetic retinopathy (DR).

Cholesterol ranges (mg/dL)	**Stages of DR** (n=654)				**Total**	**p-value**
	ADED	**CSME**	**NPDR**	**PDR**		
	n (%)	n (%)	n (%)	n (%)	n (%)	
< 200	30 (58.8)	123 (45.9)	156 (59.8)	46 (62.2)	355 (54.3)	0.006
200-239	7 (13.7)	82 (30.6)	62 (23.8)	18 (24.3)	169 (25.8)	
≥ 240	14 (27.5)	63 (23.5)	43 (16.5)	10 (13.5)	130 (19.9)	
Triglycerides ranges (mg/dL)	**Stages of DR** (n=642)					
< 150	21 (45.7)	114 (43)	100 (38.5)	33 (46.5)	268 (41.7)	0.195
150-199	14 (30.4)	54 (20.4)	74 (28.5)	13 (18.3)	155 (24.1)	
≥ 200	11 (23.9)	97 (36.6)	86 (33.1%)	25 (35.2)	219 (34.1)	
LDL ranges (mg/dL)	**Stages of DR** (n=639)					
< 100	9 (18)	41 (15.8)	50 (19.3)	20 (28.6)	120 (18.8)	0.023
100-129	13 (26)	61 (23.5)	84 (32.4)	24 (34.3)	182 (28.5)	
130-159	12 (24)	72 (27.7)	67 (25.9)	13 (18.6)	164 (25.7)	
≥ 160	16 (32)	86 (33.1)	58 (22.4)	13 (18.6)	173 (27.1)	
HDL ranges (mg/dL)	**Stages of DR** (n=638)					
≤ 40	28 (58.3)	192 (72.7)	173 (67.6)	43 (61.4)	436 (68.3)	0.033
41-59	20 (41.7)	72 (27.3)	78 (30.5%)	27 (38.6)	197 (30.9)	
≥ 60	0 (0)	0 (0)	5 (2)	0 (0)	5 (0.8)	

ADED: Advanced diabetic eye disease, CSME: Clinically significant macular oedema, NPDR: Non-proliferative diabetic retinopathy, PDR: Proliferative diabetic retinopathy, HDL: High-density lipoprotein, LDL: Low-density lipoprotein.

Table-3: HbA1c levels in cataract, glaucoma and diabetic retinopathy (DR) patients.

HbA1c in Cataract		HbA1c in Glaucoma		HbA1c in Diabetic Retinopathy	
Mean±SD	*p-value	Mean±SD	*p-value	Mean±SD	*p-value
9.20±2.12	0.001	8.58±2.02	0.001	9.47±2.24	0.001

HbA1c: Glycated haemoglobin, SD: Datbdard deviation. *One sample t-test (test value of HbA1c was 6.5).

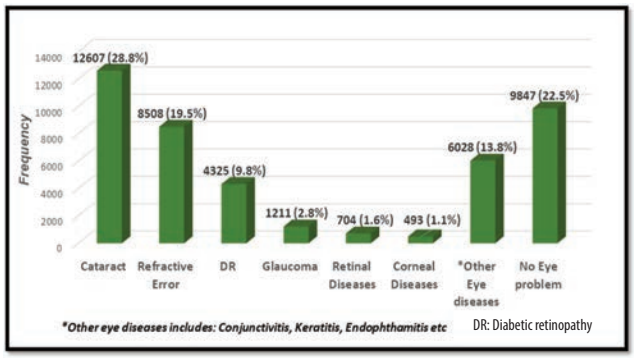

Figure: Ocular morbidities among diabetic patients (n=43,723).

Uncontrolled diabetes (HbA1c >6.5) was a significant risk factor in cataract, glaucoma and DR patients (Table 3). The odds of having uncontrolled diabetes were 3.77 times higher for patients having diabetes for >5 years compared to those having diabetes for ≤5 years.

Discussion

Diabetes and its growing prevalence is a global health risk. According to the second National Diabetes Survey of Pakistan (NDSP), overall prevalence of known diabetics is in the range of 19-26%, making Pakistan a highly prevalent area for DM globally.[2] A number of studies documented the DM impact on sight and ocular complications.[5,13,14]

Though similar studies have been done worldwide, the current study, to the best of our knowledge, is the first of its kind in Pakistan, having a large dataset representative of the wider community.

A study in Nigeria reported cataracts in 53(66.3%) of its patients, glaucoma in 44(55%), DR in 25(32.1%), and diabetic macular oedema in 25(32.1%), but its sample size was just 80 patients.[15] The same was the case with a study in Yamen which reported DR prevalence of 55% (95% CI 49.6-60.1), having only 350 patients.[16]

An important study in Japan included a very large sample size of 66,923 diabetics, and reported most frequent complication to be DR (23.6%), which was much higher than the frequency noted in the current study.[17] The study in Japan also reported NVG in 0.3% patients.[17]

Studies, including the current one, have reported significant risk of cataract development due to DM, but it is very difficult to identify DM as the only risk factor for cataract development.[18] It does, however, highlight increased risk of earlier development and disability which can be treated. This again is important for national and international policymakers as with increased DM there is increased risk of cataract development, with more patients requiring cataract surgery.[19,20] It is important to understand that cataract can also limit DR screening and subsequent increased risk of SB due to undetected progression of DR.[21]

The frequency of glaucoma in diabetics is variable, from 2.5% to 15.6%.[22,23] The main reason for such variation is difficulty in confirming the glaucoma diagnosis. The current study had 1.1% patients who were initially identified as glaucoma suspects either had suspected optic nerve head or intraocular pressure (IOP) with Goldman applanation tonometer of ≥21mmHg or the presence of Rubeosis Iridis with associated high IOP.

The current study highlighted it's the increased risk with uncontrolled systemic factors, such as increasing HbA1c, with DR progression. Much work has been done previously on HbA1c and DM duration to be associated risk factors for not only earlier DR development, but also DM progression.[24] Similar results were documented in the current study.

The possible role of uncontrolled lipid profile with DR progression has been explored earlier.[25] The current study found no direct correlation of increasing cholesterol to be associated with either presence or progression of DR, nor any relationship was found with any other ocular complications. However, LDL and HDL were directly related to progressive DR, and were also associated with cataract and suspected glaucoma cases.

The current study has limitations, like being a single-centre, retrospective study.

Conclusion

More than three-fourth diabetics had some form of ocular morbidity. Poor control of biochemical parameters was seen to increase the frequency of ocular complications. Thus, greater emphasis needs to be put on better glycaemic control.

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Conflict of Interest: None.

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References

1. International Diabetic Federation. IDF Diabetes Atlas 10th Edition 2021. [Online] [Cited 2022 June 08]. Available from: URL: https://diabetesatlas.org/atlas/tenth-edition/

2. Basit A, Fawwad A, Qureshi H, Shera AS. Prevalence of diabetes, pre-diabetes and associated risk factors: second National Diabetes Survey of Pakistan (NDSP), 2016–2017. BMJ Open. 2018; 8:e020961 doi: 10.1136/bmjopen-2017-020961.
3. Seid MA, Dagnew B. Predictors of Poor Plasma Glucose Maintenance in Type II Diabetic People with Ophthalmic Complication: The Case of Dessie Hospitals in Ethiopia. Diabetes Metab Syndr Obes. 2021; 14:2317-24. doi: 10.2147/DMSO.S291674.
4. Chiles NS, Phillips CL, Volpato S, Bandinelli S, Ferrucci L, Guralnik JM, et al. Diabetes, peripheral neuropathy, and lower-extremity function. J Diabetes Complications. 2014; 28:91-5. doi: 10.1016/j.jdiacomp. 2013.08.007.
5. Sayin N, Kara N, Pekel G. Ocular complications of diabetes mellitus. World J diabetes. 2015; 6:92-108. doi: 10.4239/wjd.v6.i1.92
6. Mumtaz SN, Fahim MF, Arslan M, Shaikh SA, Kazi U, Memon MS. Prevalence of diabetic retinopathy in Pakistan: A systematic review. Pak J Med Sci. 2018; 34:493-500. doi: 10.12669/pjms.342.13819.
7. Khalid S, Moin M, Khan MI. Screening of diabetic retinopathy in a diabetic medical center. Pak J Ophthalmol. 2015; 31:140-45.
8. Mahar PS, Awan MZ, Manzar N, Memon MS. Prevalence of type-II diabetes mellitus and diabetic retinopathy: The Gaddap study. J Coll Physicians Surg Pak. 2010; 20:528-32.
9. Wykoff CC, Khurana RN, Nguyen QD, Kelly SP, Lum F, Hall R, et al. Risk of blindness among patients with diabetes and newly diagnosed diabetic retinopathy. Diabetes Care. 2021; 44:748-56. doi: 10.2337/dc20-0413
10. Huri HZ, Huey CC, Mustafa N, Mohamad NF, Kamalden TA. Association of glycemic control with progression of diabetic retinopathy in type 2 diabetes mellitus patients in Malaysia. Braz J Pharm Sci. 2018; 54:e17484. doi:10.1590/s2175-97902018000217484
11. Chatziralli IP. The Role of Glycemic Control and Variability in Diabetic Retinopathy. Diabetes Ther. 2018; 9:431-34.
12. Moshfeghi A, Garmo V, Sheinson D, Ghanekar A, Abbass I. Five-Year Patterns of Diabetic Retinopathy Progression in US Clinical Practice. Clin Ophthalmol. 2020; 14:3651-59. doi: 10.2147/OPTH.S275968.
13. Konstantinidis L, Carron T, de Ancos E, Chinet L, Hagon-Traub I, Zuercher E, et. al. Awareness and practices regarding eye diseases among patients with diabetes: a cross sectional analysis of the CoDiab-VD cohort. BMC Endocr Disord. 2017; 17:56. doi: 10.1186/s12902-017-0206-2.
14. Nentwich MM, Ulbig MW. Diabetic retinopathy-ocular complications of diabetes mellitus. World J diabetes. 2015; 6:489. World J Diabetes. 2015; 6:489–99. doi: 10.4239/wjd.v6.i3.489
15. Asimadu IN, Kizor-Akaraiwe NN, Ezegwui IR, Okeke S. Ocular Morbidity Among Persons with Diabetes in Enugu, Nigeria. SN Compr Clin Med. 2020; 2:782-7. Doi:10.1007/s42399-020-00323-y
16. Bamashmus MA, Gunaid AA, Khandekar RB. Diabetic retinopathy, visual impairment and ocular status among patients with diabetes mellitus in Yemen: a hospital-based study. Indian J Ophthalmol. 2009; 57:293-8. doi: 10.4103/0301-4738.53055.
17. Kume A, Kashiwagi K. Recent Epidemiological Status of Ocular and Other Major Complications Related to Diabetes Mellitus in Japan. Ophthalmologica. 2020; 243:404-12. doi: 10.1159/000506747.
18. Rao GN, Khanna R, Payal A. The global burden of cataract. Curr Opin Ophthalmol. 2011; 22:4–9. doi: 10.1097/ICU.0b013e3283414fc8.
19. Dineen B, Bourne RR, Jadoon Z, Shah SP, Khan MA, Foster A, et al. Pakistan National Eye Survey Study Group. Causes of blindness and visual impairment in Pakistan. The Pakistan national blindness and visual impairment survey. Br J Ophthalmol. 2007; 91:1005-10. doi: 10.1136/bjo.2006.108035.
20. Memon AF, Mahar PS, Memon MS., Mumtaz SN, Shaikh SA, Fahim, MF. Age-related cataract and its types in patients with and without type 2 diabetes mellitus: A Hospital-based comparative study. J Pak Med Assoc. 2016; 66:1272-76.
21. Fahadullah M, Memon NA, Salim S, Ahsan S, Fahim, MF, Mumtaz, SN, et.al. Diagnostic accuracy of non-mydriatic fundus camera for screening of diabetic retinopathy: A hospital based observational study in Pakistan. J Pak Med Assoc. 2019; 69:378–82.
22. Khandekar R, Zutshi R. Glaucoma among Omani diabetic patients: A cross-sectional descriptive study. Eur J Ophthalmol. 2004; 14:19–25. doi: 10.1177/112067210401400104.
23. Ellis JD, Evans JM, Ruta DA, Baines PS, Leese G, MacDonald TM, et.al. Glaucoma incidence in an unselected cohort of diabetic patients: is diabetes mellitus a risk factor for glaucoma? DARTS/MEMO collaboration. Diabetes Audit and Research in Tayside Study. Medicines Monitoring Unit. Br J Ophthalmol. 2000; 84:1218-24. doi: 10.1136/bjo.84.11.1218.
24. Almutairi NM, Alahmadi S, Alharbi M, Gotah S, Alharbi M. The Association Between HbA1c and Other Biomarkers with the Prevalence and Severity of Diabetic Retinopathy. Cureus. 2021; 13:e12520. doi: 10.7759/cureus.12520.
25. Keech AC, Mitchell P, Summanen PA, O'Day J, Davis TM, Moffitt MS, et.al. Effect of fenofibrate on the need for laser treatment for diabetic retinopathy (FIELD study): a randomized controlled trial. Lancet. 2007; 370:1687-97. doi: 10.1016/S0140-6736(07)61607-9.