Wavefront Aberration Analysis in Diabetic Children and Adolescents with Normal Vision

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Research article

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Abstract

Background: To compare the differences in wavefront aberrations between healthy and diabetic children with normal central vision and to investigate the causes of declined visual quality in diabetic children.

Methods: This was a case-control study. Children with or without diabetes with normal central vision were selected as case and control group. The wavefront aberration parameters, including spherical aberration, coma aberration, root mean square of total wavefront aberration, root mean square of higher-order wavefront aberration, and corneal curvature, were measured by an automatic multifunctional ophthalmoscope. Statistical analysis was performed to determine the differences in average binocular wavefront aberration between groups. The correlations between wavefront aberration and age, visual acuity, corneal endothelium, intraocular pressure, axial length, corneal diameter, central corneal thickness, crystal thickness, anterior and posterior surface curvatures, and anterior chamber depth were analyzed in the diabetic group.

Results: 32 patients with diabetes and 38 age- and sex-matched individuals were enrolled. The mean total and higher-order aberrations in diabetic group were slightly higher than those in control group, with no significant difference between groups ($P > .05$). The root mean squares of the aberrations correlated with anterior and posterior surface curvatures ($P3\text{mm} = .014$, $P5\text{mm} = .021$; $P3\text{mm} = .035$, $P5\text{mm} = .038$, respectively), but not with age, visual acuity, corneal endothelium, intraocular pressure, axis, corneal diameter, central corneal thickness, crystal thickness, and anterior chamber depth.

Conclusions: For diabetic children, subtle changes in lens may lead to changes in wavefront aberrations and this may be the causes of visual impairment. These findings indicate the need to strengthen early screening and close follow-up of wavefront aberrations in diabetic children.

Trial registration: This was a case-control study based on a hospital population (NCT 03587948). Date of registration was 07/03/2018. The name of the registration is Shanghai Children and Adolescent Diabetes Eye Study.

Background

Owing to the younger age of onset of diabetes mellitus, the incidence of diabetes in children and adolescents is gradually increasing worldwide^[1-2]. Globally, by 2017, the number of children and adolescents (<20 years of age) with type 1 diabetes had reached 1,106,500. This includes about 47,000 Chinese patients, with the incidence in China ranking 4th in the world. In China, the number of patients with type 1 diabetes, type 2 diabetes, and other types of diabetes per 100,000 children and adolescents in 2010 was 96.8, 8.0, and 3.3 respectively, with approximately 286,000 people in total, showing a significant upward trend over the past 15 years^[4]. Diabetes mellitus in children and adolescents can cause ocular surface diseases (including dry eyes, corneal diseases, etc.), retinopathy, glaucoma, cataract, refractive abnormalities, and other complications, which may lead to significant visual loss or even blindness^[4].

In recent years, wavefront aberrations that can be used to evaluate the visual quality of human eyes, have been receiving increasing attention. A wavefront aberration is based on the concept of an ideal spherical or planar wavefront of a point source or a planar source when passing through an optical system. If there is a geometric aberration, the corresponding wavefront is no longer the ideal wavefront. The deviation between the actual wavefront and the ideal wavefront is called wavefront aberration^[5]. Aberrations in refractive components such as the cornea, tear film, lens, and the vitreous, and deviations in the optical axis among them will result in a decline in retinal imaging quality, thereby affecting visual quality^[6-8]. Wavefront aberrations are common in diabetic patients. Six studies at home and abroad have found that the total aberration and higher-order aberration in adult diabetic patients are higher than those in the control group^[11-16], and the difference is statistically significant. The total higher-order aberration in type I diabetes patients is slightly higher than that in patients with non-insulin-dependent diabetes^[17]. There are many reasons for the wavefront aberrations caused by diabetes mellitus: the corneal epithelial defect caused by diabetes mellitus, reduced corneal endothelial cell reserve capacity, and abnormal morphology^[9], all of which affect the maintenance of the corneal epithelial liquid barrier and the dynamic balance between corneal endothelial cells and water-sodium diffusion in the aqueous humor, thus causing changes in corneal thickness, and anterior and posterior surface curvatures, leading to wavefront aberrations^[10]. These factors also exist in children with diabetes mellitus. However, to date, there has been no relevant study on wavefront aberrations in children and adolescents with diabetes mellitus. This may be due to the relatively less attention paid to children with diabetes mellitus, and the low degree of cooperation among children during wavefront aberration examinations.

To investigate the causes of declined visual quality in diabetic children, we designed and conducted this study. We believe that with the increasing number of adolescents and children with diabetes mellitus, the results for wavefront aberration parameters in adolescents and children with diabetes can be used to select and evaluate the therapeutic methods for some eye diseases, such as concurrent cataract, and to explain why some children whose central visual impairment has not yet occurred reported that their visual quality had declined. Identifying the refractive components that have changed at this time can provide reference data for preventing or decelerating further visual impairment. Therefore, these analyses have good application value and social significance. This paper presents a case-control study of wavefront aberration changes in diabetic children and adolescents without central visual impairment in Shanghai, China.

Methods

This study conforms to the ethical principles of the Helsinki Declaration, and all subjects signed informed consent forms. This study was approved by the Ethics Committee of Children's Hospital of Fudan University. The ethics number of this study is Fuerlunshen (2018) 01.

Research subjects

This was a case-control study based on a hospital population (NCT 03587948).

From December 2018 to February 2019, children and adolescents with diabetes in the Children's Hospital of Fudan University, Shanghai, China were selected as the case group. Among the children and adolescents visiting the hospital at the same period of time, age- and sex-matched children without diabetes were selected as the control group.

The inclusion criteria for the subjects were as follows: (1) provision of informed consent from the guardian; (2) age greater than 6 years and less than 17 years; (3) diagnosis of type 1 or type 2 diabetes mellitus according to WHO-related diagnostic criteria; and (4) distant best corrected visual acuity = 1.0. The exclusion criteria as follows: (1) eyelid diseases such as entropion, ectropion, trichiasis, blepharoptosis, and facial paralysis leading to eyelid dyskinesia; (2) conjunctivitis: pterygium, conjunctivitis; (3) history of chemical injury on the surface of the eye; (4) eye surgery and total retinal laser photocoagulation within 6 months; (5) systemic diseases such as dry eye syndrome, Parkinson's disease, rheumatoid arthritis, Graves' disease, and systemic lupus erythematosus.

Sample size calculation

According to a previous study ^[18], the higher-order aberration in the diabetic group was 0.44 (+0.10 μm), while that in the control group was 0.34 (+0.14 μm). By considering $\alpha = 0.05$ and power = 0.8, we determined that a sample size of 25 participants each would be required in the case and control groups ^[19,20].

Examination method

The team consisted of three ophthalmologists, three optometrists, and 15 assistants associated with the Shanghai General Hospital Affiliated to Shanghai Jiaotong University and Children's Hospital of Fudan University. An ophthalmologist with extensive experience in ophthalmology diagnosis and epidemiology research served as the project director.

The examinations were conducted at Shanghai Eye Diseases Prevention & Treatment Center. First, basic information questionnaire assessment and subjective symptom survey were conducted. The basic information included data for age, sex, medical history, duration of diabetes mellitus, medication history, family history of diseases, height and weight, and ophthalmopathy and refraction in parents. This survey was completed by both the participants and their guardians.

Subsequently, ophthalmologic examinations were conducted as follows: (1) Slit-lamp examinations (SL130, Zeiss, Germany): the eyelid, conjunctiva, cornea, anterior chamber, iris, pupil, and lens were assessed in these examinations. (2) Intraocular lens biometer examination (IOL Master 700, Zeiss, Germany): an IOL biometer was used to measure the eye axis, lens thickness, pupil diameter, anterior chamber depth, central corneal thickness, and corneal curvature. (3) Wavefront aberration examination (VX120, VISIONIX, France): In a dark environment, children were guided to take their seats and place their mandibles on the jaw pad of the machine. They were then asked to fix their eyes on the target at the center of the laser spot grating. After the children fully cooperated, the examiner focused with the

operating rod and adjusted the aberration after focusing accurately. The optical center of the instrument was identical to the pupil center, and measurements were obtained three times. We recorded the findings when the repeatability of the higher-order aberration pattern and root mean square value was the best, the error of lower-order aberrations (myopia and astigmatism) and optometry was the smallest, the focusing of the original photograph was the best, and the analysis value of the examination result showed the least central deviation. The average value of aberrations in both eyes was obtained. (Table 1).

Table 1.
Wavefront aberration measurement parameters

Parameter	Description	Parameter	Description
K1mm	Maximum corneal curvature	C_R_5	Comet aberration (measurement range, 5 mm)
K2mm	Minimum corneal curvature	C_R_7	Comet aberration (measurement range, 7 mm)
K1_axis	Flat axis	A_R_3	Axial degree (measurement range, 3 mm)
K2_axis	Steep axis	A_R_5	Axial degree (measurement range, 5 mm)
Cyl	Cylindrical degree	A_R_7	Axial degree (measurement range, 7 mm)
KPi	Keratoconus predictive index	RMS_3	Root mean square value of aberration (measurement range, 3 mm)
S_R_3	Spherical aberration (measurement range, 3 mm)	RMS_5	Root mean square value of aberration (measurement range, 5 mm)
S_R_5	Spherical aberration (measurement range, 5 mm)	H_RMS_3	Root mean square value of higher-order aberration (measurement range, 3 mm)
S_R_7	Spherical aberration (measurement range, 7 mm)	H_RMS_5	Root mean square value of higher-order aberration (measurement range, 5 mm)
C_R_3	Comet aberration (measurement range, 3 mm)		

(4) Best corrected visual acuity and diopter examinations of both eyes were performed as follows: after dilation using cyclopentol, the best corrected visual acuity was detected by the international standard LogMAR visual acuity chart, and the diopter value was confirmed by a computerized automatic optometry machine (KR-8900; Topcon, Japan). (5) Swept Source OCT: (Topcon, Japan) An SS-OCT examination was conducted to scan scan 6 × 6 mm square area of retina to find out presence or absence of diabetic macular edema.

The diagnosis of diabetes mellitus (including type 1 and type 2) was based on the following WHO-related diagnostic criteria ^[21]: (1) Presence of typical symptoms (such as polydipsia, polyuria, and unexplained weight loss), fasting blood glucose ≥ 7.0 mmol/L or postprandial blood glucose ≥ 11.1 mmol/L. (2)

Absence of typical symptoms, with only fasting blood glucose ≥ 7.0 mmol/L or postprandial blood glucose ≥ 11.1 mmol/L. Tests were repeated, and patients who tested positive for the above indices were diagnosed as having diabetes mellitus. (3) In the absence of typical symptoms, only fasting blood glucose ≥ 7.0 mmol/L or postprandial blood glucose ≥ 11.1 mmol/L, and 2 hours glucose tolerance test ≥ 11.1 mmol/L may be diagnosed as diabetes mellitus (including type 1 and type 2).

The project leader trained the staff of the investigation team before the formal investigation. After the training, the project leader performed the preliminary test in the investigation hospital, completed the consistency assessments of the results, and checked the measuring tools. The project leader reviewed all survey data after each survey.

Statistical method

BMI = body weight (kg) / height (m^2) was calculated in this study. SPSS 24.0 was used for statistical analysis. Measurement data were expressed as average $\pm$ standard deviation, and categorical data were expressed as frequencies and percentages. Statistical methods included independent-sample t test and Pearson correlation analysis, etc. First, the Kolmogorov-Smirnov method was used to test whether the data conformed to normal distribution; then, an independent-sample t test was used for parameters showing a normal distribution, and the Mann-Whitney test was used for parameters with a non-normal distribution. Significant differences in the wavefront aberration index between the case and control groups were determined. Next, Pearson correlation analysis was used to determine the clinical factors that are significantly related to the wavefront aberration index. P values < 0.05 indicated statistically significant differences.

Results

Comparison of general information

A total of 32 children with diabetes were enrolled in the case group. Another 38 healthy subjects participated in the study as the control group. There was no significant difference in sex composition between the two groups ($P > 0.05$). There was no significant difference in age composition between the two groups either ($P > 0.05$). The lens thickness of the case group was significantly higher than that of the control group ($P < 0.05$) (Table 2). Diabetic macular edema was absent in both groups. In the case group, there were 30 patients with type 1 diabetes. Average duration of diabetes was 3.83 (± 2.54) years, and the average level of glycosylated hemoglobin was 7.18 (± 2.33) mmol/L.

Table 2.
Basic characteristics of the case and control groups

Clinical factors	Case group (n=32)	Control group (n=38)	Statistical value	P
Age (years)	10.81 ± 3.22	9.84 ± 2.46	t= 1.43	0.157
Female	18	18	$\chi^2 = 0.549$	0.459
Best corrected visual acuity	-0.03 ± 0.09	-0.02 ± 0.07	t= 0.800	0.427
Corneal endothelium cell count	3059.74 ± 238.94	3075.4 ± 256.85	t= -0.236	0.815
Non-contact tonometer	16.28 ± 2.84	15.79 ± 2.65	t= 0.723	0.472
Eye axis	23.60 ± 1.19	23.99 ± 1.04	t= -1.416	0.162
Corneal diameter	11.89 ± 0.48	12.10 ± 0.44	t= -1.860	0.068
Central corneal thickness	256.23 ± 27.22	558.82 ± 34.13	t= 0.182	0.856
Lens thickness	3.46 ± 0.16	3.36 ± 0.19	t= 2.315	0.024
Anterior surface curvature of lens	7.80 ± 0.30	7.79 ± 0.27	t= 09.173	0.863
Posterior surface curvature of lens	7.80 ± 0.32	7.78 ± 0.28	t= 0.302	0.764
Anterior chamber depth	3.05 ± 0.34	3.17 ± 0.27	t= -1.481	0.144

Wavefront aberration parameter comparison

T test and Mann-Whitney test were used to compare the wavefront aberration parameters in children and adolescents between the case and control groups. The results indicated that the total aberration and higher-order aberration mean values in the case group were slightly higher than those in the control group, and there was no statistical difference between them ($P > 0.05$) (Table 3).

Table 3.

Comparison of wavefront aberration parameters between case and control groups

	Case group (n = 32)	Control group (n = 38)	Test value	p
K1mm	7.61 ± 1.96	7.81 ± 1.22	Z= 1.00	0.61
K2mm	7.38 ± 1.95	7.55 ± 1.18	Z= 0.88	0.66
K1_axis	66.18 ± 79.87	100.39 ± 82.32	Z = 0.12	0.08
K2_axis	88.45 ± 26.19	88.50 ± 21.64	Z= 0.34	0.99
Cyl	-1.36 ± 0.62	-1.48 ± 0.67	t=0.75	0.46
S_R_3	3.99 ± 22.06	0.71 ± 14.05	Z = 0.49	0.45
S_R_5	-1.62 ± 3.49	-1.60 ± 2.14	Z = 0.71	0.97
S_R_7	-1.04 ± 4.18	-1.31 ± 2.61	Z = 0.60	0.74
C_R_3	-0.50 ± 2.40	-0.83 ± 1.63	Z = 0.38	0.51
C_R_5	-0.50 ± 2.40	-0.90 ± 1.66	Z = 0.26	0.41
C_R_7	-0.53 ± 2.33	-0.94 ± 1.63	Z = 0.24	0.40
A_R_3	2.03 ± 1.89	1.82 ± 1.58	Z= 0.88	0.63
A_R_5	2.44 ± 1.79	2.16 ± 1.52	Z = 0.43	0.49
A_R_7	1.87 ± 1.47	2.07 ± 1.32	Z = 0.66	0.53
RMS_3	0.89 ± 0.92	0.80 ± 0.64	t= 0.49	0.63
RMS_5	0.25 ± 0.17	0.25 ± 0.19	Z = 0.16	0.99
H_RMS_3	0.07 ± 0.07	0.05 ± 0.03	Z = 0.96	0.13
H_RMS_5	2.41 ± 3.04	2.62 ± 3.03	Z = 0.71	0.78

Correlation analysis

Pearson correlation analysis was used to compare the correlations between wavefront aberration parameters and other parameters in children and adolescents with diabetes mellitus. The results showed that the RMS values at 3-mm and 5-mm measurement ranges in the case group were significantly correlated ($P < 0.05$) with the curvature of the anterior and posterior surfaces of the lens, (Table 4).

Table 4.

Correlation between wavefront aberration parameters and other parameters in the case group (Pearson coefficient, P value)

	RMS_3	RMS_5	HRMS_3	HRMS_5
Age (years)	0.194, 0.278	0.266, 0.134	0.084, 0.640	0.130, 0.487
Best corrected visual acuity	-0.368, 0.121	-0.377, 0.112	-0.106, 0.666	-0.203, 0.419
Corneal endothelium cell count	-0.188, 0.302	-0.180, 0.324	0.006, 0.973	-0.109, 0.566
Non-contact tonometer	-0.035, 0.845	-0.080, 0.656	-0.059, 0.743	-0.043, 0.818
Eye axis	-0.039, 0.832	0.036, 0.846	0.122, 0.507	0.113, 0.554
Corneal diameter	-0.248, 0.172	-0.307, 0.087	-0.196, 0.283	-0.269, 0.151
Central corneal thickness	0.036, 0.843	0.084, 0.649	-0.041, 0.824	0.005, 0.979
Lens thickness	-0.140, 0.469	-0.137, 0.479	-0.290, 0.127	-0.183, 0.361
Anterior surface curvature of lens	-0.430, 0.014	-0.407, 0.021	-0.108, 0.557	-0.043, 0.820
Posterior surface curvature of lens	-0.373, 0.035	-0.368, 0.038	-0.072, 0.697	-0.036, 0.851
Anterior chamber depth	0.030, 0.870	0.035, 0.849	-0.055, 0.763	0.031, 0.869

Discussion

This study included diabetic children and adolescents, and controls with no impairment of binocular central vision. In contrast, although higher-order aberrations and total aberrations in children with diabetes were slightly higher than those in normal children, there was no significant difference, which was different from the findings of previous studies in adults. In adult studies, the total higher-order aberrations in diabetic patients were significantly higher than those in the normal group (Table 5). The reason for this difference is that children and adolescents are younger and have a shorter duration of diabetes than adults. The changes in higher-order aberrations and total aberrations in diabetic patients are closely related to their age. Some studies have also shown that higher-order aberrations and total aberrations increase with age in patients with insulin-dependent diabetes mellitus^[22] (Table 5). In this study, higher-order aberrations also increased with age, but because the subjects in this study were children, their age range was small, which may explain the absence of statistical difference in this study. Some studies on adults also reported the relevance of aberrations and diabetic macular edema, and in our study, diabetic macular edema was absent^[11]. Previous studies have shown that, the longer the duration of diabetes, the more serious are the changes in the tear film, anterior and posterior corneal surface, and lens in patients with diabetes^[8]. Because the total aberration and higher-order aberrations in the case group increased, the visual quality might have been affected.

Table 5.

A comparison between the main findings of previous studies on wavefront aberrations in adults with diabetes, and wavefront aberrations in children with diabetes in this study

	Age of diabetic patients	Best corrected visual acuity	Root mean square of higher-order aberration	Root mean square of total aberration
Valeshabad AK, et al.	53±15	0.30±0.25	0.28±0.11	0.40±0.15
Calvo-Maroto AM, et al.	42.29±9.19 (IDDM) 57.09±6.44 (NIDDM)	Not mentioned	0.634±0.228 (IDDM) 0.527±0.245 (NIDDM)	Not mentioned
Miháltz K, et al.	63.5±17.3	0.361±0.28	0.33±0.18	1.33±1.28
Shahidi M, et al.	52±12	Not mentioned	0.45±0.18	Not mentioned
This study	10.81±3.22	-0.03±0.09	0.07±0.07 (3 mm)	0.89±0.92 (3 mm)

The causes of declined visual quality in diabetic children and the factors leading to wavefront aberrations in diabetic children may be related to the cornea, tear film, lens, or retina. For example, the more serious the injury to the paracrine gland cells in diabetic eyes is, the less the basic secretion of tears will be, which will further reduce the stability of the tear film^[23,24]. A long-term increase or instability in the glucose content in the aqueous humor of diabetic patients will lead to an increase in lactic acid concentration, changes in corneal glucose metabolism, metabolic acidosis of corneal stroma, and changes in corneal endothelial cell morphology and function^[25]. However, in this study, we found that the RMS of aberrations in diabetic children was only related to the curvature of the lens, and there was a statistically significant relationship between these factors. This shows that the early change in lens is the main reason affecting the early wavefront aberrations in diabetic children. With the changes in osmotic pressure in diabetic patients, the lens permeability changes accordingly. Huntjens et al. found that the lens thickness is related to the duration of type 1 diabetes and the level of glycosylated hemoglobin^[26]. Some studies have shown that the lens thickness and curvature in type 1 diabetic patients are larger than those in normal individuals^[27], and that the refractive index shows a compensatory decrease. Therefore, we believe that for children who do not show central visual impairment but complain of poor visual quality, clinicians should focus on the subtle changes in their lenses. Some changes in lens transparency in children with diabetes mellitus are reversible and closely related to blood glucose control^[28]. Therefore, it is suggested that blood glucose should be strictly controlled in order to reduce the persistent damage to the lens in children with diabetes mellitus.

The limitations to this study include the single-center, cross-sectional design and the inability to obtain trends for wavefront aberration. Moreover, despite meeting the study's sample size requirements, the number of subjects included in the study was not large. This is mainly because the subjects were school students and the academic course is hectic during the semester, so we could only use the winter vacation in 2019 to conduct the study. Moreover, the subjects were included only after signing informed consent forms, wavefront aberration examinations took a long time, and the degree of cooperation among young children was poor.

Conclusions

For diabetic children, subtle changes in lens may lead to changes in wavefront aberrations and this may be the causes of visual impairment. These findings indicate the need to strengthen early screening and close follow-up of wavefront aberrations in diabetic children.

Declarations

Ethics approval and consent to participate

This study conforms to the ethical principles of the Helsinki Declaration, and all subjects signed informed consent forms. This study was approved by the Ethics Committee of Children's Hospital of Fudan University. The ethics number of this study is Fuerlunshen (2018) 01.

Consent for publication

Consent for publication has been obtained from all individuals.

Availability of data and materials

The datasets used during the current study are available from the corresponding author on reasonable request.

Competing interests

The authors declare that they have no competing interests.

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Authors' contributions

HZ and CY supervised the program. SW, YJ and TL analyzed and interpreted the patient data. SW, YJ, TL, AW and LG performed the examination of the eye, and SW was a major contributor in writing the manuscript. All authors read and approved the final manuscript.

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Reference

1. Patterson C, Guariguata L, Dahlquist G, et al. Diabetes in the Young-A Global View and Worldwide Estimates of Numbers of Children with Type 1 Diabetes. *Diabetes Res Clin Pract.* 2014;103:161-75.
2. Cho NH, Shaw JE, Karuranga S, et al. IDF Diabetes Atlas: Global Estimates of Diabetes Prevalence for 2017 and Projections for 2045. *Diabetes Res Clin Pract.* 2018;138:271-81.
3. Treatt J, Willimson JF, Huynh K, et al. Ocular Disease, Knowledge and Technology Applications in Patients with Diabetes. *Am J Med Scie.* 2013;345:266-70.
4. King H, Aubert RE, Herman WH. Global Burden of Diabetes, 1995-2025: Prevalence, Numerical Estimates, and Projections. *Diabetes Care.* 1998;21:1414-431.
5. Thibos LN, Applegate RA, Schwiegerling JT, et al. Standards for Reporting the Optical Aberrations of Eyes. *Refract Surg.* 2002;18:S652-60.
6. Wildsoet CF. Active Emmetropization-Evidence for its Existence and Ramifications for Clinical Practice. *Ophthal Physiol Opt.* 1997;17:279-90.
7. Thibos LN. Wavefront Data Reporting and Terminology. *J Refract Surg.* 2001;17:S578-83.
8. Manaviat MR, Rashidi M, Afkhami-Ardekani M, et al. Prevalence of Dry Eye Syndrome and Diabetic Retinopathy in Type 2 Diabetic Patients. *BMC Ophthalmol.* 2008;2:10.
9. Miháltz K, Kovács I, Weingessel B, Vecsei-Marlovits PV. Ocular Wavefront Aberrations and Optical Quality in Diabetic E Retina. 2016;36:28-36.
10. Calvo-Maroto AM, Pérez-Cambrodí RJ, García-Lázaro S, et al. A Pilot Study on Total, Corneal, and Internal Aberrations in Insulin-Dependent and Non-Insulin-Dependent Diabetes Mellitus P Graefes *Arch Clin Exp Ophthalmol.* 2015;253:645-53.
11. Shahidi M, Blair NP, Mori M, Zelkha R. Optical Section Retinal Imaging and Wavefront Sensing in D *Optom Vis Sci.* 2004;81:778-84.

12. Valeshabad AK, Wanek J, Grant P, et al. Wavefront Error Correction with Adaptive Optics in Diabetic R Optom Vis Sci. 2014;91:1238-43.
13. Jinran Fang, Yang Wei. Study on Wavefront Aberration in Patients with Diabetic Retinopathy of Different Degrees and Dry Eye S Int J Ophthalmol. 2018;18:950-53 [Chinese].
14. Fen Ye, Nong Tian, Yuhua Shi et al. Wavefront Aberration Analysis in Diabetic Patients with Dry E Yanke Xinjinzhan. 2012;32:356-58 [Chinese].
15. Calvo-Maroto AM, Pérez-Cambrodí RJ, García-Lázaro S, et al. A Pilot Study on Total, Corneal, and Internal Aberrations in Insulin-Dependent and Non-Insulin-Dependent Diabetes Mellitus P Graefes Arch Clin Exp Ophthalmol. 2015;253:645-53.
16. Lim M, Park L, Shin C, et al. Induction of Apoptosis of Beta Cells of the Pancreas by Advanced Glycation End-Products, Important Mediators of Chronic Complications of Diabetes Me Ann N Y Acad Sci. 2008;1150:311-15.
17. Schultz RO, Van Horn DL, Peters MA, et al. Diabetic Keratopathy. Trans Am Ophthalmol Soc. 1981;79:180-99.
18. Shahidi M, Blair NP, Mori M, Zelkha R. Optical Section Retinal Imaging and Wavefront Sensing in Diabetes. Optom Vis Sci. 2004;81:778-84.
19. Hod M, Kapur A, Sacks DA, et al. The International Federation of Gynecology and Obstetrics (FIGO) Initiative on Gestational Diabetes Mellitus: A Pragmatic Guide for Diagnosis, Management, and C Int J Gynaecol Obstet. 2015;131,S173-211.
20. Li B, Sheng M, Xie L, et al. Tear Proteomic Analysis of Patients with Type 2 Diabetes and Dry Eye Syndrome by Two-Dimensional Nano-Liquid Chromatography Coupled with Tandem Mass Spectrometry. Invest Ophthalmol Vis Sci. 2014;55:177-86.
21. Lane JD, Krumholz DM, Sack RA, et al. Tear Glucose Dynamics in Diabetes Mellitus. Curr Eye Res. 2006;31:895-901.
22. Geffen N, Topaz N, Kredy-Farhan L, et al. Phacoemulsification Induced Injury in Corneal Endothelial Cells Mediated by Apoptosis: In Vitro M J Cataract Refract Surg. 2008;34:2146-152.
23. Huntjens B, Charman WN, Workman H, et al. Short-Term Stability in Refractive Status Despite Large Fluctuations in Glucose Levels in Diabetes Mellitus Type 1 and 2. PLoS One. 2012;7:e52947.
24. He J, Xu X, Zhu J, et al. Lens Power, Axial Length-to-Corneal Radius Ratio, and Association with Diabetic Retinopathy in the Adult Population with Type 2 D Ophthalmology. 2017;124:326-35.
25. Park JH. Transient Bilateral Cataract during Intensive Glucose Control: A Case R J Med Case Rep. 2017;12;11:107.