

Blood Glucose Level Impact on Biometric Parameters, Refraction and Intraocular Pressure in Patients with Subcompensated Insulin-Requiring Type II Diabetes

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Abstract

Purpose: To study the relationship of biometric parameters, visual acuity, eye refraction and intraocular pressure (IOP) with blood glucose levels and glycated hemoglobin (HbA1c) in patients with subcompensated insulin-requiring type II diabetes mellitus.

Materials and Methods: Ophthalmic monitoring lasted 3 years, the experience of insulin therapy - 6 years. 32 patients (27 women and 5 men) with insulin-requiring diabetes mellitus and no severe general diabetic complications or concomitant eye pathology were monitored for 3 years. The patients' average age was 60.4 ± 5.3 years; average weight 94.3 ± 16.5 kg; average height 163.4 cm; average BMI (body mass index) was 29.93 kg/m², all received insulin treatment for 6 years. Patients determined the level of blood glucose themselves on a daily basis using individual "Accu-Check" and/or "OneTouch select" glucometers, supplemented by endocrinologist checks on scheduled examinations once a month. The level of glycated hemoglobin (HbA1c) was determined once every 3 - 6 months. The 3-year ophthalmic monitoring involved both eyes and included biomicroscopy, autorefractometry, pneumotometry, measurement of the anterior-posterior axis, the depth of the anterior chamber and lens thickness; pachymetry of the cornea in the central optical zone, and ophthalmoscopy. Visometry was performed according to ETDRS (Early Treatment Diabetic Retinopathy Study Research Group) requirements.

Results: The impact of blood glucose level on visual acuity (Spearman $R = 0.18/-0.23$, $t(N-2) = 1.07/-1.34$, $p = 0.1$) is higher than that of HbA1c (Spearman $R = 0.07/-0.15$, $t(N-2) = 0.4/-0.8$, $p = 0.65$). The higher the glucose level, the lower the depth of the anterior chamber and the shorter the APA. In contrast, the higher the level of HbA1c, the thicker the cornea in the central optical zone. Both the glucose and the HbA1c levels reveal a similar positive correlations with IOP. A refraction shift toward myopia from 42% to 55% was shown to correlate to HbA1c, and a corresponding reduction of hyperopia share was revealed.

Conclusion: In patients with subcompensated insulin-requiring diabetes mellitus type II, biometric parameters, refraction and intraocular pressure are determined by changes in the level of blood glycemia.

Keywords: Diabetes Mellitus Type II; Blood Glucose; Glycated Hemoglobin (HbA1c); Biometry Parameters; Refraction; Intraocular Pressure

Introduction

It is known that a good state of visual functions in many respects determines a high quality of life, which is why it is so important to monitor their changes in patients with diabetes mellitus (DM). This disease causes the development of pathological processes in various body systems, including the organ of vision, where primarily we are talking about diabetic retinopathy, which is thoroughly studied and fairly well controlled using ophthalmoscopy, fluorescence angiography and fundus photorecording. The effect of diabetes on the anterior segment of the eye is not so deeply studied and described in the literature, although diabetes is known to lead to changes in the cornea and lens, affecting visual acuity and refraction [1].

It was noted that reflux fluctuations in patients with diabetes are often associated with diabetes dysregulation and changes in blood glucose levels, which in turn leads to “jumps” in visual acuity [2-4]. It is also known that episodes of acute hyperglycemia can lead to the formation of transient posterior cortical cataracts [5,6].

The myopic shift is the first reaction of the eye to hyperglycemia, and the hyperopic shift is the reaction to a decrease in glucose after acute hyperglycemia, expressed in a temporary change in the curvature or thickness of the lens [7-11]. However, data on changes in refraction in diabetes are quite contradictory. Thus, researchers using Orbscan II and A-scan did not find a significant effect of acute hyperglycemia on the thickness and optical power of the cornea, the depth of the anterior chamber, the thickness of the lens and the length of the eye [12].

It is possible that blurred vision during episodes of acute hyperglycemia is associated not only with the lens, but also with moisture in the anterior and posterior chambers and the vitreous due to a change in their refractive power [13].

As for the literature data on the relationship of intraocular pressure (IOP) with blood glycemia, it was found that in patients with insulin-using diabetes mellitus (IPSD) type II there is no statistically significant relationship between these parameters. However, in patients with established glaucoma in the absence of proper glycemic control, an increase in IOP is possible [14]. It should be noted that all the above-mentioned changes in refraction, IOP, and biometric parameters in patients with type I or type II diabetes were detected either during decompensation or during stress tests with glucose. Information on the relationship of biometric indicators, refraction, and IOP with blood glucose and glycated hemoglobin (HbA1c) levels in patients with type II diabetes who use insulin was not found in the literature in the subcompensation phase.

Purpose of the Study

The purpose of the work was to identify the relationship of biometric indicators, visual acuity, refraction and IOP with blood glucose and HbA1c levels in patients with type II IPSD in the subcompensation phase.

Materials and Methods

During a routine ophthalmological monitoring, 32 patients (64 eyes) with insulin-requiring type II diabetes mellitus without severe general diabetic complications (84.4% of women and 15.6% of men) were examined for 3 years. The age of patients ranged from 50 to 70 years (average 60.42 ± 5.31 years). The weight of patients was within 94.33 ± 16.52 kg, growth averaged 163.4 cm, body mass index 29.93 kg/m^2 .

The experience of using insulin in patients was at least 3 years (on average 6 years). The initial level of blood glucose was 10.81 mmol/l, the initial level of glycated hemoglobin HbA1c - 9.03%, which confirmed the state of subcompensation.

Ophthalmological criteria for inclusion in the group of subjects were emmetropic refraction or ametropia of not more than 0.5 diopters, as well as the absence of a history of glaucoma, aphakia or artificial. The study group did not include patients with anterior-posterior axis (APA) length of the eye less than 22.0 mm and more than 24.5 mm, with a thickness of the cornea in the central optical zone (COZ)

of less than 500 microns and more than 600 microns, with anterior chamber depth (ACD) eyes less than 2.75 mm and more than 3.5 mm, with a lens thickness less than 3.6 mm and more than 5.0 mm.

During the first 2 years of monitoring, the patients were examined by an ophthalmologist four times, during the third year - once taking into account the requirements of the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS).

Blood glucose levels were determined by patients daily on their own using individual Accu-Check or OneTouch select glucometers, as well as an endocrinologist every month at routine examinations. The level of glycosylated hemoglobin HbA1c was determined one time in 3 - 6 months.

In the process, the following methods of ophthalmological research were used: visometry using the 20/200 ETDRS system from a distance of 4 m using the ESV-3000; determination of the axial length of the APA, ACD, the thickness of the cornea in the COZ, the thickness of the lens using an ultrasonic biometer-pachymeter TOMY AL-3000; eye biomicroscopy with a Reichert slit lamp; refractometry with a Humphrey 585 autorefractometer; ophthalmoscopy with a pupil width of 5 - 6 mm using a direct electric ophthalmoscope Heine Beta 2000; determination of true IOP (Po) on a Reichert XPERT NCT non-contact pneumotonometer.

Statistical processing of the results was carried out using the STATISTICA program, version 10. Initially, the data were classified according to the type of observed signs, checked for the nature of the distribution, and described accordingly with the calculation of 95% confidence intervals (CI). The accuracy of quantitative data was determined by the measurement accuracy of the instrument from which the readings were taken. Then, a comparison was made of the studied groups for possible differences and relationships. Differences or dependencies were considered significant if the obtained p value for a given criterion or test was below the critical significance level $\alpha = 0.05$. To solve the problem of pairwise comparisons of several groups, the procedure of a posteriori comparisons of means was used using the Newman - Kales q-test. In the case when the distribution of the trait was different from normal, a non-parametric analysis of the Kruskal-Wallis variations was used. Analysis of contingency tables was performed using the chi-square test (χ^2). In the event that the absolute frequencies in the cells of the frequency table were less than 10, criterion χ^2 was used with Yates correction for continuity. If the frequency in at least one cell of the table turned out to be less than 5, the Fisher exact two-sided criterion was the selection method. The dependencies between the studied variables were revealed by calculating the significant Pearson correlation coefficients r in the case of a linear relationship of quantitative characteristics, or Spearman's R, when this condition was not met.

Results and Discussion

During the entire observation period, there was a significant decrease in the level of glycosylated hemoglobin HbA1c and an almost constant level of glucose (Figure 1 and 2).

In the course of the study of biometric indicators, it was found that in patients with type II diabetes mellitus (insulin-requiring in sub-compensated phase) and an average insulin therapy experience of 6 years, the length of the APA was initially 22.92 ± 0.97 mm, ACD 2.98 ± 0.23 mm, Lens Thickness 4.65 ± 0.3 mm, the thickness of the cornea in the COZ 549 ± 35.5 μ m, that is, these indicators were within the average norm (Table 1).

The relationship of biometric indicators (APA, ACD, lens thickness, corneal thickness in the COZ), refractive indices, visual acuity and IOP with blood glucose and HbA1c. Evaluation of the ratio of biometric indicators with the level of blood glycemia showed that they are interconnected [15,16]. The frequency of reliable association of these indicators with HbA1c was 2 times higher than with glucose. At the first examination, a significant negative correlation was found between the level of blood glucose and the size of the APA of the left eyes: with a higher level of blood glucose, the APA on the left eyes and ACD on both eyes were less, i.e. there was a tendency to hypermetropization. A similar significant negative correlation was found between the length of the APA and ACD in both eyes and HbA1c, i.e. at a higher level of HbA1c, these indicators were lower. At the same time, an increase in HbA1c was accompanied by an increase in corneal thickness indices ($R_s = 0.19$, $p < 0.05$). At the same time, HbA1c proved to be a more informative indicator than blood sugar in relation to the thick-

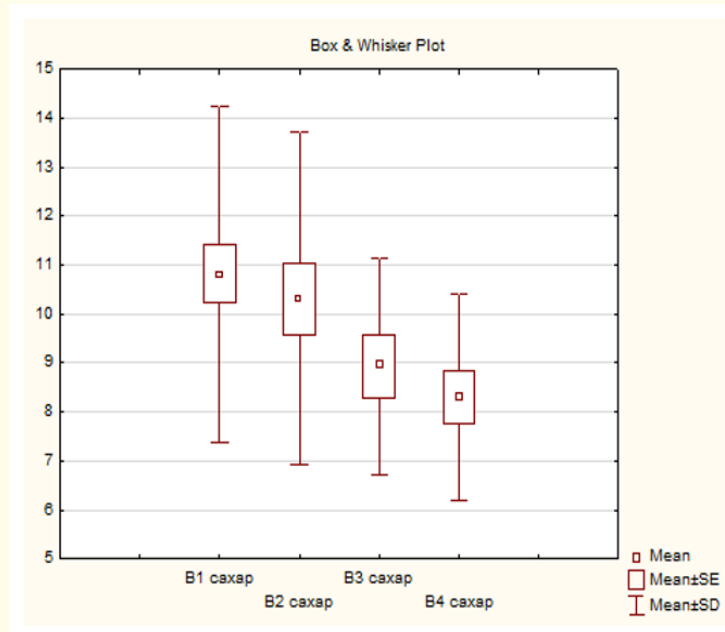


Figure 1: Dynamics of blood glucose level during 3-year observation period.

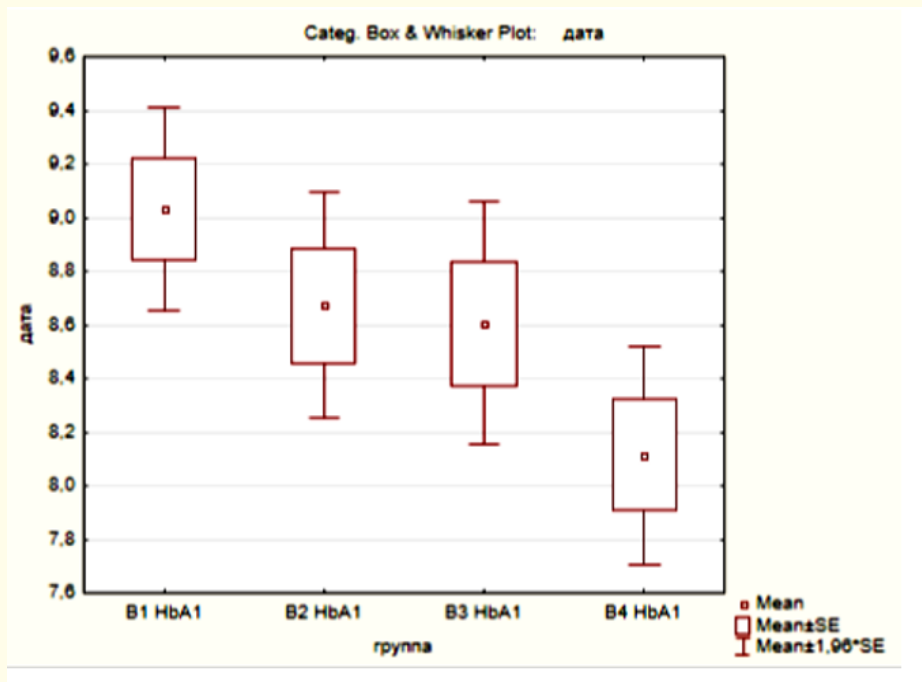


Figure 2: Dynamics of the glycosylated blood hemoglobin level.

Parameter	Eye	N	Average value	Confidence interval-95%	Confidence interval +95%	Min	Max	Standard error of the mean
Axial length	OD	34	22,92	22,59	23,26	21,71	26,11	0,17
	OS	34	22,82	22,49	23,15	21,47	26,80	0,16
Anterior chamber depth (ACD)	OD	32	2,98	2,89	3,08	2,59	3,65	0,05
	OS	33	2,98	2,89	3,06	2,46	3,47	0,04
Lens thickness	OD	32	4,66	4,55	4,77	4,25	5,26	0,053
	OS	33	4,62	4,49	4,75	3,40	5,36	0,065
Central corneal thickness	OD	34	548,79	536,40	561,18	483,0	637,0	6,09
	OS	34	554,18	541,23	567,12	490,0	650,0	6,36

Table 1: Patients initial biometrics data according to one-dimensional echography.

ness of the cornea. Fluctuations in blood glucose were not significantly associated with changes in corneal thickness in the COZ. It is likely that the ACD of the eye decreases both due to swelling of the lens and an increase in the thickness of the cornea (Table 2).

Blood glucose/HbA1c	Biometric parameters	Eye	N	Spearman R	t (N-2)	P - level
Blood glucose	Anterior-posterior length	OD	34	-0,18	-1,008	0,32
		OS	34	-0,25	-1,45	0,015
HbA1c		OD	34	-0,19	-1,096	0,028
		OS	34	-0,19	-1,098	0,028
Blood glucose	Anterior chamber depth	OD	32	-0,27	-1,53	0,013
		OS	33	-0,19	-1,13	0,026
HbA1c		OD	32	-0,22	-1,21	0,023
		OS	33	-0,28	-1,59	0,012
Blood glucose	Lens thickness	OD	32	0,054	0,29	0,771
		OS	33	-0,005	-0,03	0,973
HbA1c		OD	32	0,009	0,05	0,962
		OS	33	0,027	0,15	0,882
Blood glucose	Central corneal thickness	OD	34	0,07	0,43	0,674
		OS	34	0,1	0,6	0,551
HbA1c		OD	34	0,19	1,102	0,027
		OS	34	0,21	1,103	0,032

Table 2: The relationship of biometrics with blood glucose and blood glycated hemoglobin (visit 1).

The dynamics of refractive indices are shown in table 3. As the obtained data show, significant differences in refraction are observed at the beginning and at the end of monitoring. During the observation period, the myopia that took place at the beginning of the study intensified in the right eyes of patients, and in the left eyes hyperopia turned into weak myopia, i.e. there is a general significant trend towards a change in refraction towards myopia. A strict pattern in the magnitude and direction of the axis of the cylinder was not detected [16].

Visit	Parameter	Eye	N	Average value	Confidence interval-95%	Confidence interval+95%	Min	Max	Standard error of the mean	P - level
1	sph	OD	33	-0,30	-0,94	0,33	-6,25	3,75	0,03	0,046121
3			14	-1,05	-2,17	0,06	-5,75	0,75	0,12	
1		OS	34	-0,13	-0,78	0,51	-8,5	2,75	0,03	0,075181
3			15	-0,75	-1,98	0,48	-8,5	0,75	0,07	
1	cyl	OD	33	-0,02	-0,31	0,28	-1,75	2,75	0,04	0,015765
3			14	-0,19	-0,63	0,23	-1,75	1,0	0,09	
1		OS	34	0,11	-0,19	0,41	-2,75	2,50	0,05	0,095391
3			15	0,07	-0,50	0,63	-2,75	1,75	0,06	
1	ax	OD	33	73,00	51,42	94,58	0,0	180,0	10,6	0,080479
3			14	67,50	34,13	100,87	0,0	168,0	15,44	
1		OS	34	81,41	58,79	104,03	0,0	180,0	11,12	0,017114
3			15	102,9	68,63	137,23	0,0	180,0	15,99	

Table 3: Dynamics of indicators of total clinical refraction by constituent components throughout the entire observation period.a

The relationship of refractive indices with blood glucose is shown in table 4.

Visit	Blood glucose/HbA1c	Refractive indices	Eye	N	Spearman R	t (N-2)	P-level
1	Blood glucose	sph	OD	33	0,124287	0,69741	0,490745
			OS	34	0,151650	0,86790	0,391913
	HbA1c		OD	33	0,412439	2,52075	0,017070
			OS	34	0,226086	1,31293	0,019854
	Blood glucose	cyl	OD	33	0,296348	1,72760	0,040122
			OS	34	-0,096419	-0,54798	0,587506
	HbA1c		OD	33	0,384849	2,32156	0,027001
			OS	34	0,214710	1,24358	0,022686
Blood glucose	ax	OD	33	-0,207399	-1,18041	0,024814	
		OS	34	0,047951	0,27156	0,787701	
HbA1c		OD	33	0,130959	0,57006	0,030959	
		OS	34	0,082809	0,47006	0,641503	
3	Blood glucose	sph	OD	11	0,184762	0,56400	0,586534
			OS	12	-0,266911	-0,87582	0,401676
	HbA1c		OD	13	0,348202	1,23195	0,024365
			OS	14	0,193772	0,68421	0,506840
	Blood glucose	cyl	OD	11	-0,072616	-0,21842	0,831971
			OS	12	-0,346984	-1,16995	0,026915
	HbA1c		OD	13	0,207009	0,70177	0,497400
			OS	14	-0,055681	-0,19319	0,850044
	Blood glucose	ax	OD	11	0,782110	3,76533	0,004448
			OS	12	-0,525574	-1,95359	0,079275
	HbA1c		OD	13	0,299587	1,04145	0,320016
			OS	14	0,286188	1,03466	0,321229

Table 4: The relationship of refraction with blood glucose and HbA1c throughout the observation period.

At the first examination, a positive correlation was observed between the level of blood glucose and the size of the cylinder in the right eyes of patients [R = 0.296348; p = 0.040]; a negative correlation was found between blood glucose and the direction of the axis of the cylinder in the right eyes (R = -0.207; p = 0.024). A third examination revealed a positive correlation between blood glucose and refraction: the higher the glucose level, the more refraction shifted towards myopia. A negative correlation was found between the blood glucose level and sph of the left eyes of patients [R = -0.266911; p = 0.40].

A negative correlation was noted between the glucose content and the size of the cylinder, and the direction of the axis in the left eyes of the patients [R = -0.35; p = 0.02]; as well as the axis of the left eye OS [R = -0.53; p = 0.07] (the higher the blood glucose level, the lower these indicators).

As for the correlation of biometric data with the content of HbA1c, during the first examination, a positive correlation was found between this indicator and the magnitude of the spherical and cylindrical refractive components. At the third examination, a reliable positive correlation between HbA1c and the magnitude of spherical refraction was maintained, and the correlation was negative with the magnitude of cylindrical refraction. Thus, one way or another, all the parameters studied by us, were, either related to the HbA1c level either in the form of a positive or negative relationship. The visual acuity data at the beginning and at the end of the monitoring are shown in table 5. It can be seen from these data that it decreased slightly in both eyes of the patients, although this decrease was not statistically significant. Perhaps this decrease is due to the small shift of refraction mentioned above towards myopia.

Visit	Parameter	Eye	N	Average value	Confidence interval-95%	Confidence interval+95%	Min	Max	Standard error of the mean	P-level
1	Visual acuity numerator	OD	34	3,91	3,73	4,09	1,00	4,0	0,09	0,772148
			15	3,80	3,37	4,23	1,00	4,0	0,20	
1	Visual acuity numerator	OS	34	3,91	3,73	4,09	1,00	4,0	0,09	0,821628
			15	3,80	3,37	4,23	1,00	4,0	0,20	
1	Visual acuity denominator	OD	34	9,19	6,43	11,94	4,00	40,0	1,35	0,203212
			15	10,21	4,66	15,75	4,00	40,0	2,59	
1	Visual acuity denominator	OS	34	8,84	6,35	11,33	4,00	40,0	1,22	0,392128
			15	9,91	4,8	15,02	4,00	40,00	2,38	

Table 5: Dynamics of visual acuity (in numerator and denominator).

Data on the correlation between visual acuity and glucose and HbA1c are shown in table 6.

Visit	Blood glucose/HbA1c	Visual acuity indicator	Eye	N	Spearman R	t (N-2)	P-level
1	Blood glucose	Numerator	OD	34	0,186394	1,07321	0,291204
			OS	34	0,186394	1,07321	0,291204
	HbA1c		OD	34	0,079963	0,45379	0,653043
			OS	34	0,079963	0,45379	0,653043
	Blood glucose	Denominator	OD	34	-0,279722	-1,64814	0,010911
			OS	34	-0,231708	-1,34741	0,018731
HbA1c	OD		34	-0,148529	-0,84963	0,401843	
	OS		34	-0,155199	-0,88870	0,380794	
3	Blood glucose	Numerator	OD	12	0,087804	0,27874	0,786125
			OS	12	0,087804	0,27874	0,786125
	HbA1c		OD	14	0,206861	0,73243	0,477968
			OS	14	0,206861	0,73243	0,477968
	Blood glucose	Denominator	OD	12	0,071562	0,22688	0,825087
			OS	12	0,140310	0,44813	0,663609
	HbA1c		OD	14	-0,383455	-1,43827	0,017592
			OS	14	-0,539760	-2,22112	0,046345

Table 6: The relationship of visual acuity (numerator / denominator) with blood glucose and HbA1c during the observation period.

As can be seen from table 6, only a negative correlation was found between the denominator of visual acuity and both of these indicators (numerator and denominator) both at the beginning and at the end of monitoring.

Data on true IOP at the beginning of the study are shown in table 7.

Visit	Parameter	Eye	N	Average value	Confidence interval-95%	Confidence interval+95%	Min	Max	Standard error of the mean	P-level
1	IOP	OD	34	15,94	14,96	16,91	8,00	21,00	0,48	0,010806
3			15	14,85	13,49	16,2	11,00	19,00	0,63	
1	IOP	OS	34	16,06	15,14	16,98	10,00	21,00	0,45	0,003924
3			15	15,17	14,04	16,3	11,50	18,00	0,52	

Table 7: Dynamics of the level of true IOP (Po).

From these data it is seen that the IOP (Po) during the observation period statistically significantly decreased by about 1 mm.rt.st. - from 15.94 to 14.85 mm.rt.st. on the right eyes and from 16.06 to 15.17 mm.rt.st. on the left eyes.

The relationship between IOP and blood glucose and HbA1c levels during the observation period is shown in table 8 [15].

Visit	Blood glucose /HbA1c	Parameter	Eye	N	Spearman R	t (N-2)	P - level
1	Blood glucose	IOP	OD	34	0,21	1,22	0,232
			OS	34	0,24	1,42	0,175
	HbA1c		OD	34	0,25	1,52	0,014
			OS	34	0,31	1,88	0,037
3	Blood glucose	IOP	OD	12	0,25	0,83	0,43
			OS	12	0,46	1,66	0,012
	HbA1c		OD	14	-0,36	-1,34	0,027
			OS	14	-0,12	-0,44	0,6

Table 8: The relationship of IOP level with blood glucose level and HbA1c during the observation period.

The first examination revealed a reliable positive correlation between the level of glucose and HbA1c and the level of IOP in both eyes: the higher the level of glucose and HbA1c in the blood, the higher the IOP. During the monitoring period, a positive correlation was detected only in the right eyes of the examined patients.

Conclusion

1. In case of insulin-requiring type II diabetes mellitus in the stage of subcompensation, biometric indicators, refraction and IOP are determined by changes in blood glycemia.
2. Changes in the biometric parameters of the optical system of the eye, in particular, the thickness of the cornea in the central zone, as well as the shift of refraction towards myopia correlate mainly with the level of HbA1c in the blood.
3. An inverse correlation was revealed between the depth of the anterior chamber and the length of the anterior-posterior axis of the eye with the glucose level: the higher the glucose level, the smaller the anterior chamber and the shorter the anterior-posterior axis of the eye.
4. There is a direct correlation between IOP and glucose and HbA1c levels: the higher these indicators, the higher the IOP.

Conflict of Interests

There is no conflict of interests.

Financial Disclosure

No author has a financial or property interest in any material or method mentioned.

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