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To Study the Ocular Consequences in Children with Diabetes

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ABSTRACT

Background: Numerous well-known microvascular consequences of diabetes mellitus (DM), a systemic illness, include diabetic retinopathy (DR), neuropathy, and nephropathy. Lacrimal gland, cornea, and retina can all be affected by diabetes-related autonomic neuropathy. According to several studies, the prevalence of DR in young children ranges from 10% to 35%, however the risk of developing microvascular problems may rise during adolescence. Both the anterior and posterior parts of the eye can be impacted by diabetes mellitus (DM), a condition that has reached pandemic proportions. Even in affluent nations, diabetic retinopathy (DR) continues to be one of the main causes of blindness. Globally, it was estimated that 93 million people have DR and 28 million of those had DR that threatens their vision.

Aim: This study aims to investigate the diabetes-related ocular changes according to the glycosylated hemoglobin (HbA1c) level and duration of diabetes in children and compare the results with nondiabetic healthy children.

Material and Method: The Department of Ophthalmology undertook this prospective cross-sectional investigation. 42 consecutive Type 1 DM patients from a pediatric clinic of a state hospital were included in the study. The Ophthalmology Department consulted the patients as part of a program to screen for diabetic eye illness, and two youngsters were sent home because of their lack of cooperation during the examination. Thus, 40 kids with clinically confirmed Type 1 DM and 40 healthy, age- and gender-matched kids served as the study's controls. Each patient had an eye exam, a physical examination, and a review of their medical background and current medications. The following measurements were made: HbA1c level, best corrected visual acuity, intraocular pressure (IOP), central corneal thickness (CCT), tear break up time (BUT), Schirmer test, results of the dilated fundus examination, central retinal thickness (CRT), and total macular volume (TMV).

Results: The mean age of the patients with diabetes was 11.1 ± 2.1 years (mean ± SD, range: 4–18 years). The mean age of the healthy subjects was 11.22 ± 1.3 years. Twenty patients were male in the diabetic group (50 %), and 20 patients were female in the control group (50%). The mean duration of diabetes was 2.3 ± 2.1 (median was 3 years) and the mean HbA1c value was 8.5% ± 1.2% in the diabetic group. All eyes included in the analysis had a visual acuity of at least 20/20. Type 1 DM group exhibited significantly reduced Schirmer test, increased IOP, and decreased retinal thickness relative to the age-matched control group but no statistically significant difference was found for the BUT and for the CCT. The correlations between the age, duration, HbA1c, and IOP, BUT, Schirmer test, TMV, and CRT measurements did not reach statistical significance.

Conclusion: For the early diagnosis of problems, such as neuropathy-related DES, IOP abnormalities, and DR, more frequent screening may be beneficial. In order to track the development of DR, it is recommended that children with type 1 DM have at least an annual SD-OCT assessment of RNFL and macular thickness. For diabetic patients with long-term type 1 DM and/or greater HbA1c values, this period may be shortened. For the purpose of defining methods for the early diagnosis of pre-clinical retinopathy, additional prospective longitudinal comprehensive studies are required.

Keywords: Corneal thickness, Diabetic retinopathy, Dry eye syndrome, Type 1 DM.

INTRODUCTION

Adults with diabetes mellitus (DM) are known to experience a variety of ocular issues, such as microvascular paralytic strabismus, cataract, macular edema, and diabetic retinopathy (DR). In the United States, 12,000 to 24,000 new cases of diabetic retinopathy and macular edema progress to the final ocular consequence of blindness each year, making DM the main cause of blindness in persons 20 to 74 years old.[1] The Diabetic Retinopathy Study (DRS) and the Early Treatment of Diabetic Retinopathy Study (ETDRS) both showed

that treating diabetic macular edema and proliferative diabetic retinopathy early in people with DM decreased their likelihood of suffering moderate to severe vision loss.[2,3] As a result, there has been a strong focus on public health to establish ocular screening programs for people with DM, starting at a young age. A screening program must find a disease that is asymptomatic and has a therapy that is affordable; diabetic retinopathy typically satisfies these requirements.[4,5]

Lacrimal gland, cornea, and retina can all be affected by diabetes-related autonomic neuropathy. According to several studies, the prevalence of DR in young children ranges from 10% to 35%, however the risk of developing microvascular problems may rise during adolescence.[6,7] An anterior and posterior region of the eye must be carefully examined as part of a targeted screening program in order to find these microvascular problems.[8,9] Additionally, research indicate that Type 2 DM is frequently linked to thicker corneas and elevated intraocular pressure (IOP).[10,11] There is evidence that suggests neural alterations play a significant part in the emergence of DR in Type 2 DM patients.[12] In a recent study, it was also discovered that people with Type 1 DM and limited DR had thinner retinas than nondiabetic controls.[13] Therefore, the development of DR, dry eye syndrome (DES), and glaucoma, which may result in clinical or subclinical microvascular alterations, may be significantly influenced by diabetes-related neuronal abnormalities.

The American Academy of Ophthalmology (AAO)'s most recent recommendations urge all individuals with Type 1 DM to begin annual screening exams five years after receiving their diagnosis.[14] There is a lack of knowledge regarding the beginning and prevalence of other diabetic ocular problems in children as most research have concentrated on DR, and there are conflicting findings in the literature regarding the age at which DR is first diagnosed and how common it is in children. Some information is available, but not notably for the very young, regarding modifiable risk factors to prevent the development of ocular complications of DM. According to results from the Diabetes Control and Complications Trial (DCCT), children with type 1 DM between the ages of 13 and 17 who received intensive glucose control had a 53% lower risk of developing DR.[15,16] However, one study of DM in young children revealed that the onset of DM type 1 at a relatively young age (i.e., 5 years) would protect against the emergence of DR. The risk of DR appears to grow with longer duration of DM.[17] Children with type 2 DM, a population that is increasingly relevant to investigate given the rising frequency of children with this ailment, have even less knowledge on DR risk and incidence than children without the condition. Even in affluent nations, diabetic retinopathy (DR) continues to be one of the main causes of blindness. Globally, it was estimated that 93 million people have DR and 28 million of those had DR that threatens their vision.[18]

MATERIAL AND METHODS

The Department of Ophthalmology undertook this prospective cross-sectional investigation. 42 consecutive Type 1 DM patients from a pediatric clinic of a state hospital were included in the study. The Ophthalmology Department consulted the patients as part of a program to screen for diabetic eye illness, and two youngsters were sent home because of their lack of cooperation during the examination. Thus, 40 kids with clinically confirmed Type 1 DM and 40 healthy, age- and gender-matched kids served as the study's controls. By measuring the levels of glycosylated hemoglobin (HbA1c), venous blood samples from diabetic and nondiabetic participants were collected to assess their metabolic condition. It describes the typical blood glucose level during the last two to three months and illustrates how well diabetes treatment is working. Usually, HbA1c is 4-6.4%. Higher numbers indicate inadequate blood glucose control.

Inclusion criteria:

- Inclusion criteria were no previous known macular or other retinal changes, best-corrected Early Treatment DR Study (ETDRS) visual acuity of >1.0, refractive error within ± 6 diopters (D), and no ophthalmic or systemic disease other than Type 1 DM.

Exclusion criteria:

- Any eye condition that would affect the study's findings, such as a history of ocular surgery, laser treatment, chronic or recurrent inflammatory eye illnesses, intraocular trauma, or current use of any ophthalmic or systemic steroid, led to the exclusion of subjects from the study.

Study Criteria:

Each patient had an eye exam, a physical examination, and a review of their medical background and current medications. Age, gender, when DM first appeared, and the HbA1c level were noted. An ETDRS chart was used to evaluate visual acuity at a distance of 4 meters. A noncontact tonometer (Topcon CT 80A, Japan) was used to measure IOP. Each patient had a +90 D condensing lens-based dilated binocular indirect ophthalmoscopy along with slit lamp biomicroscopy. Tear film break-up time (BUT) and the Schirmer test were two of the tests used to validate the presence of dry eye. Slit lamp examination of the cornea and conjunctiva was performed. The time between a full blink and the appearance of dry patches in a fluorescein-stained tear film was used to measure BUT, and a time interval of 10 seconds (s) or less was deemed abnormal.

Using an ultrasonic pachymeter (IOPac Advanced, Heidelberg Engineering GmbH, Germany), the central corneal thickness (CCT) was determined. The Stratus OCTTM (software version 4.0.1, Model 3000, Carl Zeiss Meditec, Dublin, CA, USA) was used to perform optical coherence tomography (OCT) while the patient's pupil was dilated in order to quantify the central macular thickness. In the macula's center, six radial OCT scans were taken. The macula was separated into the fovea, which has a diameter of 1 mm, the pericentral area, which is a doughnut-shaped ring with an inner diameter of 1 mm and an outward diameter of 3 mm, and the peripheral area, which has an inner diameter of 3 mm and an exterior diameter of 6 mm. Six radial scans from the eyes were employed, and the mean thickness at the intersection point was used for analysis. The patients with OCT-detected total macular volumes (TMV) were also measured.

STATISTICAL ANALYSIS

Results were expressed as means ± standard deviations (SDs), and percentages with 95% confidence intervals. Descriptive statistics, Student's t-test, Mann–Whitney U-test, Chi-square test for comparison of the group parameters, and correlation analyses (Spearman analysis) were performed with SPSS statistical software 17.0.

RESULT: -

The mean age of the patients with diabetes was 11.1 ± 2.1 years (mean ± SD, range: 4–18 years). The mean age of the healthy subjects was 11.22 ± 1.3 years. Twenty patients were male in the diabetic group (50 %), and 20 patients were female in the control group (50%). The mean duration of diabetes was 2.3 ± 2.1 (median was 3 years) and the mean HbA1c value was 8.5% ± 1.2% in the diabetic group. All eyes included in the analysis had a visual acuity of at least 20/20. IOP was 15.4 ± 1.4 mmHg in the diabetic group and 13.5 ± 1.5 mmHg in the control group. Even though there was no diagnosis of glaucoma, IOP measurements were found significantly higher in the diabetic group than in the control group.

Table 1: Descriptive data from the diabetic and control groups

	Diabetic group	Control group
Mean age	11.1 ± 2.1	11.22 ± 1.3
IOP	15.4 ± 1.4	13.5 ± 1.5
Schirmer	13.4±2.82	18.6±2.704
BUT	12.1±2.197	11.1±1.66
CCT	444.3±38.17	554.3±35.6
TMV	5.53±0.532	5.01±0.477
CRT	151.18±23.729	180.18±13.26

Schirmer test was found to be 13.4 ± 2.8 mm in the diabetic group and 18.6 ± 2.7 mm in the control group. There was a statistically significant difference between the diabetic and control group for the Schirmer test. BUT was 12.1 ± 2.1 s in the diabetic group and 11.1 ± 1.6 s in the control group. There was no statistically significant difference between the diabetic and control group for the BUT.

TMV values were 5.53 ± 0.532 mm^3 and 5.01 ± 0.477 mm^3 in the diabetic and control groups, respectively. CRT values were 151.18 ± 23.729 µm and 180.18 ± 13.26 µm in the diabetic and control group, respectively. The measurements of TMV and CRT were found significantly lower in the diabetic group than in the control group.

Table 2: Correlation analysis of intraocular pressure, Schirmer test, central corneal thickness, tear break-up time, total macular volume, and diabetes mellitus-related variables

	IOP		Schirmer		CCT		BUT		TMV	
	R	P	R	P	R	P	R	P	R	P
Duration	0.1	0.07	0.02	0.71	0.080	0.432	−0.06	0.48	−0.01	0.932
HbA1c	−0.13	0.15	0.13	0.19	−0.283	0.006	0.08	0.37	0.106	0.305

In the diabetic group, the univariate regression analysis showed a statistically significant negative correlation between HbA1c and CCT. We analyzed the correlation between the age, duration, HbA1c and IOP, BUT, Schirmer test, and TMV measurements in the diabetic group but the correlations did not reach statistical significance.

DISCUSSION

As a systemic condition, DM causes a number of well-known ocular consequences, including DES, glaucoma, corneal abnormalities, and retinopathy in the anterior and posterior segments. In the current investigation, we compared the results with those from sex- and age-matched healthy controls to assess the metabolic status of children with Type 1 DM using a comprehensive anterior and posterior segment ophthalmologic examination.

A procedure that interferes with the tearing reflex pathways or that impairs the lacrimal gland's capacity to secrete can both cause dry eyes.[19] Diabetes may cause damage to the lacrimal gland's microvasculature, which, along with autonomic neuropathy, may impede the gland's ability to function. Tear production may be reduced due to corneal diabetic sensory neuropathy. Although some studies indicated a higher incidence of dry eye in diabetics, others failed to detect a significant decline in aqueous tear production or tear BUT among insulin-dependent diabetic patients.[20]

Holl et al.1998[21] reported one child who had received laser prior to their study but did not report the age of the patient at treatment or duration of DM. **Akil et al.2016**[22] investigated the alterations in the anterior and posterior segment findings of children with type 1 DM with and without DR and found that the measurements of total macular volume and central retinal thickness were significantly lower in the diabetic group than in controls. **Van Dijk et al.2010**[23] investigated which retinal layers are most affected by diabetes in patients with type 1 DM who have no or minimal DR and demonstrated that thinning occurs in the inner retinal layers, particularly the ganglion cell layer.

In a recent study, **Chen et al.2016**[24] indicated that the mean retinal, ganglion cell, and inner plexiform layer complex thickness measurements were significantly thinner than those of the age-matched control subjects. Goebbels discovered that in insulin-treated diabetic patients, there was neither a substantial reduction in the volume of aqueous tear flow nor an impaired tear BUT. They stated that there were more indications of conjunctival metaplasia and that the values on the Schirmer test had dramatically dropped.[25]

Binder et al.1989[26] reported that sicca symptoms affected some Type 1 diabetic patient only during the hyperglycemic phases. They came to the conclusion that this may be caused by excessive extracellular fluid osmolarity interfering with tear generation rather than being a long-term diabetic consequence.

Poorer glycemic control and prolonged diabetes have both been identified as independent risk factors for DR in children and adolescents.[27] Despite a mean HbA1c that remained consistently high and was greater than the HbA1c advised by the Diabetes Control and Complications Trial, newer investigations have found a decrease in the prevalence of DR.[15] However, most young diabetic patients are now treated with either multiple injections or insulin pumps as in our study. Therefore, as suggested by **Mohsin et al.2005**[28] the lower prevalence of DR observed in most recent studies may be partly due to fewer glucose excursions.

Lopes de Faria et al.2002[29] investigated whether an RNFL defect is present in patients with type 1 DM without clinical manifestations of DR and found that the mean superior RNFL thickness measurements are significantly lower in diabetic eyes compared to control eyes. **El Fayoumi et al.2016**[30] also investigated whether type 1 DM in children affects the RNFL and ganglion cell complex when compared to the control subjects by using Fourier domain OCT and found that in children with type 1 DM with no DR, the mean average RNFL and ganglion cell thickness was statistically significantly thinner.

According to various publications on neuroglial tissue death in DM and minor alterations in retinal function seen in DM prior to the formation of DR, the loss of retinal thickness in the early stages of DR may be explained by a loss of neural tissue.[27]

CONCLUSION:

In comparison to the age-matched control group, the type 1 DM group showed significantly lower Schirmer test, elevated IOP, and decreased retinal thickness. If not identified and treated in a timely manner, diabetic neuropathy and retinopathy in children with Type 1 DM may proceed to visual problems and ultimately blindness. For the early diagnosis of problems, such as neuropathy-related DES, IOP abnormalities, and DR, more frequent screening may be beneficial. In order to track the development of DR, it is recommended that children with type 1 DM have at least an annual SD-OCT assessment of RNFL and macular thickness. For diabetic patients with long-term type 1 DM and/or greater HbA1c values, this period may be shortened. For the purpose of defining methods for the early diagnosis of pre-clinical retinopathy, additional prospective longitudinal comprehensive studies are required.

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