Analysis of the Influence of Type of Diabetes Mellitus on the Development and Type of Glaucoma

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ABSTRACT

Aim: Main the goal of the research is to analyze the occurrence of glaucoma in patients with diabetes mellitus type 1 (DM type 1) and diabetes mellitus type 2 (DM type 2). Patients and methods: The study involved 140 patients, 34 with DM type 1 and 106 with DM type 2. In relation to the type of glaucoma to the patients are divided into two groups: Primary and Secondary glaucoma. According to the stage of diabetic retinopathy (DR) patients were analyzed in three groups: non-proliferative, preproliferative and proliferative DR. Since ophthalmological parameters were analyzed: best corrected visual acuity (BCVA), intraocular pressure (IOP), visual field (VF) of computerized perimetry, excavatio optic nerve (E/D) by optic coherent tomography (OCT). Results: Applying the test of quotient chance found that subjects with DM type 1 have a 5.94 times greater chance of developing secondary glaucoma, but is of primary (P <0.0001). In patients with DM type 2, where the chance of getting the subjects of secondary glaucoma 4.43 times larger than that of the primary (P = 0.0002). Conclusion: Patients with DM type have great chance of developing secondary glaucoma of the primary. Primary glaucoma more common in NPDR but secondary glaucoma more common in PDR.

Key words: Diabetes mellitus (DM), diabetic retinopathy (DR), primary and secondary glaucoma (Gl)

1. INTRODUCTION

Diabetes mellitus is the metabolic disease of carbohydrates, fats and proteins, which is caused by reduced secretion or insulin resistance. It differs Diabetes mellitus type 1 (type 1 DM) and Diabetes mellitus type 2 (type 2 DM). Basically type 1 DM is an autoimmune process that destroys the islets of Langerhans, in genetically susceptible individuals. According to recent studies infection enteroviruses is a precipitating factor for developing the disease (1). A 2011 report from the US Centers for Disease Control and Prevention (CDC) estimated that approximately 1 million Americans have type 1 DM. Type 1 DM is the most common metabolic disease of childhood. Every 400-600 children and adolescents has type 1 DM (2).

Type 2 diabetes mellitus consists of an array of dysfunctions characterized by hyperglycemia and resulting from the combination of resistance to insulin action, inadequate insulin secretion, and excessive or inappropriate glucagon secretion. In an update to its 2008 diabetes screening guidelines, the US Preventive Services Task Force (USPSTF) has issued draft guidelines recommending that all adults aged 45 or older be screened for abnormal glucose and type 2 diabetes. The new guidelines also recommend screening in younger adults with risk factors, including those with overweight or obesity or with a first-degree relative with diabetes, as well as women with a history of gestational diabetes or polycystic ovarian (3-11). Hyperglycemia-inducing damage to the endothelium of blood vessels, ischemia horioretine and significant changes in it with clinical signs: microaneurysms, dot and blot hemorrhages, flame shaped hemorrhages, retinal edema and hard exudates, cotton-wool spots, venous beading, intraretinal microvascular abnormalities, macular edema, preretinal hemorrhages, neovascularization, hemorrhage into the vitreous, fibrovascular tissue proliferation, traction retinal detachments. Classified as non-proliferative diabetic retinopathy (NPDR), Proliferative diabetic retinopathy (PreDR)) and Proliferative diabetic retinopathy (PDR). Approximately 700,000 persons in the United States have proliferative diabetic retinopathy, with an annual incidence of 65,000. A recent estimate of the prevalence of diabetic retinopathy in the United States showed a high prevalence of 28.5% among those with diabetes aged 40 years and older (12).

In diabetic eye may develop primary glaucoma (open or closed chamber angle), ocular hypertension and second-
ary glaucoma (uveal, post-traumatic, neovascular, postoperative, iatrogenic, phakic, at intubalbarnh tumor). Primary Open-angle glaucoma (POAG) is a multifactorial disease characterized by progressive retinal ganglion cell death and visual field loss. Focal and systemic vascular abnormalities have also been well documented in diabetic patients. The relationship between diabetes mellitus and POAG remains enigmatic in the literature. Although current studies support the role of vascular contributions to both diseases, the association between glaucoma and diabetes yields contrasting results (5). Although there are some hints for a correlation between diabetes and primary open angle glaucoma (POAG), it remains unclear in which way diabetes influences eye pressure (IOP) and glaucoma. Despite this, the main reason for neovascular glaucoma in diabetes is proven to be retinal ischemia due to diabetic vessel damage. Primary open angle glaucoma is more frequent than neovascular glaucoma, but neovascular glaucoma is very aggressive and difficult to treat (6).

The main purpose of the research is to analyze the occurrence of glaucoma in patients with diabetes mellitus type 1 (DM type 1) and diabetes mellitus type 2 (DM type 2).

2. PATIENTS AND METHODS

The research was conducted at the Eye Clinic, Clinical University Center Sarajevo in the period May 2012 - 2014. A prospective study included 140 patients with diabetes mellitus of that 34 patients had DM type 1 and 106 patients with DM type 2. In the study included patients insulin dependent and patients on oral antidiabetic. The patients according to the type of glaucoma (GL) divided into two groups: Primary and Secondary glaucoma. According to the stage of diabetic retinopathy patients were analyzed in three groups (non-proliferative, preproliferative, proliferative) diabetic retinopathy. Since ophthalmological parameters were analyzed: best corrected visual acuity (BCVA), intraocular pressure (IOP), visual field (VF) of computerized perimeter, excavaio optic nerve (E/D) by optic coherent tomography (OCT). In addition ophthalmology examination is implied binocular slit-lamp direct and indirect ophthalmoscopes and gonioscopy.

3. RESULTS

DM type 2 was predominant in male and female. There is statistically significant difference in the age structure of respondents with diabetes type 1 and type 2.

The analysis of the age structure of the respondents found that there is a statistically significant difference in the age structure of respondents with DM type 1 and DM type 2.

Applying the test quotient chances (odds ratio) found that subjects with DM type 1 have 5.94 times higher chance to have secondary glaucoma than the primary. Similar results were obtained in patients with diabetes type 2, and the chance to have a secondary glaucoma 4.43 times higher than primary glaucoma. The analysis of visual acuity patients studied groups was no significant difference in the number of respondents in relation to the category of visual acuity. Most of the respondents had IOP <20mmHg. OCT findings in the total sample.

4. DISCUSSION

A sample of 140 patients, 34 patients with DM type 1 and 106 patients with DM type 2. The Poland epidemiologic study aimed to analyze the changes in incidence rates of DM type among children ages 0-14 years from 1989 to 2012 in this region. The overall incidence rate increased 3.8 times, confirm that Poland currently has one of the highest incidence rates of pediatric DM type 1 in Europe (9). A 2011. Centers for Disease Control and Prevention (CDC) report estimated that nearly 26 million Americans have diabetes. Additionally, an estimated 79 million Americans have prediabetes. In 2014, the CDC
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Table 5. The frequency of different types of glaucoma in the total sample tested

| Glaucoma Type                  | Total | IOP <=20 mmHg | 21 - 22 mmHg | >22 mmHg |
|--------------------------------|-------|---------------|--------------|----------|
| Type 1 DM                      | 280   | 212           | 106          | 62       |
| Odds ratio                     | 4.4321| 2.0474 to     | 9.5945      |          |
| Z statistic                    | 3.779 |               |              |          |
| Significance level             | P < 0.0001|                |              |          |

Table 6. Best corrected visual acuity patients

| IOP     | Number | %     |
|---------|--------|-------|
| <20 mmHg| 166    | 59.2  |
| 21 - 22 mmHg | 8     | 2.8   |
| >22 mmHg | 106    | 37.8  |

Table 7. Intraocular pressure (IOP) patients in the total sample

| IOP     | Number | %     |
|---------|--------|-------|
| <20 mmHg| 166    | 59.2  |
| 21 - 22 mmHg | 8     | 2.8   |
| >22 mmHg | 106    | 37.8  |

Table 8. The excavatio of the optic nerve, on the basis of objective indicators Cup/Disc Area Ratio

| Scotomas visual field | Cup/ Disk Area Ratio | < 0.3 | 0.4 - 0.5 | > 0.5 |
|-----------------------|----------------------|-------|-----------|-------|
| Centrocecal scotoma   | Total                | 158   | 56.4      | 39    |
| Paracentral scotoma   | 13.92                | 59    |
| Diffuse depression    | 29.6                 | 124   |
| Normal findings       | 44.2                 | 124   |

Table 9. Results of computerized perimetry patients total sample

Chi square test was found statistically significant difference - ss (X^2 = 27.134, p = 0.001) between the analyzed groups. The CDC estimated that in 2010 year, 79 million Americans aged 20 years or older had prediabetes - 35% and 50% of those aged 65 years or older (11, 12). The patient with DM type 1 NPDR developed in 11 eyes, PreDR in 14 eyes, and PDR in 27 eyes. In this groups we had a primary glaucoma in 4 cases in the context of NPDR, and 12 eyes with PreDR, secondary glaucoma we had in 15 eyes with PreDR and 24 eyes with PDR (Table 3). In patients with DM type, NPDR developed at 40 eyes, PreDR at 61 and PDR in 89 eyes. Primary glaucoma is registered in 12 eyes with NPDR, and 7 eyes with PreDR and Secondary glaucoma was found in 13 eyes with PreDR and 27 cases in the PDR (Table 4).
Primary glaucoma is more common answer at non-proliferative diabetic retinopathy, while the secondary glaucoma more common in proliferative diabetic retinopathy (Table 3 and 4). Cruz-Ingo Y et al. suggest that Puerto Rico patients between 40 to 79 years of age with diabetic retinopathy have an increased risk of developing open-angle glaucoma with each subsequent decade (8). Klemm M, Gesser C. In his article communicated that Primary open angle glaucoma is more frequent than neovascular glaucoma, but neovascular glaucoma is very aggressive and difficult to treated (6, 8). Applying the test of refraction chances (odds ratio) found that subjects with DM type 1 have a 5.94 times greater chance of developing secondary glaucoma, but is of primary (P <0.0001). Similar results were obtained in patients with DM type 2, where the chance of getting the subjects of secondary glaucoma 4.43 times larger than that of the primary (P = 0.0002) (Table 5).

Apreutesei NA et al. in the study „Glaucoma evolution in patients with diabetes“, the presence that of non-proliferative diabetic retinopathy influenced (only marginally statistically) the glaucomatous disease progression (14). Noma H. et al. amounts that was also a significant correlation between the vitreous levels of sVEGFR-1 and sVEGFR-2. These results suggest that the vitreous levels of sVEGFR-1 and sVEGFR-2 are dependent on VEGF in patients who have iris neovascularisation (INV) with or without neovascular glaucoma (NVG) (15).

In patients with DM type 1, no clinically significant retinopathy can be seen in the first 5 years after the initial diagnosis of diabetes is made. After 10 - 15 years, 25 - 50% of patients show some signs of retinopathy. This prevalence increases to 75 - 95% after 15 years and approaches 100% after 30 years of diabetes. Proliferative diabetic retinopathy (PDR) is rare within the first decade of DM type 1 diagnosis but increases to 14 - 17% by 15 years, rising steadily thereafter. In patients with DM type 2, the incidence of diabetic retinopathy increases with the disease duration. Of patients with type 2 diabetes, 23% have nonproliferative diabetic retinopathy (NPDR) after 11-13 years, 41% have NPDR after 14-16 years, and 60% have NPDR after 16 (16). As part of a complete ophthalmological examination is followed by visual acuity patients, who are the VO divided into four groups. There were no statistically significant (ss) in the number of respondents by category VO (Table 6). Were analyzed and values of IOP in the total sample. IOP was usually below 20 mmHg, which was statistically significant (X² = 135.08, p = 0.001) (Table 7).

We analyzed excavation of the optic nerve, on the basis of objective indicators Cup/Disc Area Ratio. OCT finding in the total sample recorded 29.6% of cases with the excavation of the optic nerve greater than 0.5, and in 13.9% of cases had the excavation of 0.4-0.5. These data indicate a significant damage of the optic nerve in patients with DM for DR and GL (Table 8). Results of computer perimeter point to falling sensibilities in 29.6% of patients, the occurrence of paracentral scotoma 14.6% and 11.4% patients had centrocecal scotoma. These findings also point to the obvious damaged visual field in patients with DM, DR IGL (Table 9).

5. CONCLUSION
The analysis of changes in the eye in 140 patients with diabetes mellitus, we conclude that there was no statistically significant difference in relation to the sex of respondents. DM type 1 was the most common in the age group of 36-45 years, and DM type 2 in the age group of 46-55 years. Primary glaucoma was more common in NPDR and secondary glaucoma occurs more frequently in the PDR. Applying the test of quotient chance (odds ratio) found that subjects with DM type 1 have a 5.94 times greater chance of developing secondary glaucoma, but is of primary. Similar results were obtained in patients with DM type 2 where the chance of getting the subjects of secondary glaucoma 4.43 times larger than that of the primary.

CONFLICT OF INTEREST: NONE DECLARED.

REFERENCES
1. Hsiao-Chuan L, et al. Enterovirus infection is associated with an increased risk of childhood type 1 diabetes in Taiwan: A nationwide population-based cohort study. Diabetologia. 2014;67(10):2125-34.
2. U.S. Department of Health and Human Services, Centers for Disease Control and Prevention. 2011. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed January 28, 2011.
3. USPSTF. Public comment on draft recommendation statement and draft evidence review: screening for abnormal glucose and type 2 diabetes mellitus. US Preventive Services Task Force. Available at http://www.uspreventiveservicestaskforce.org/Announcements/News/Item/public-comment-on-draft-recommendation-statement-and-draft-evidence-review-screening-for-abnormal-glucose-and-type-2-diabetes-mellitus. Accessed Oct 14 2014.
4. Tucker ME. USPSTF: Screen everyone 45 and older for abnormal glucose. Medscape Medical News [serial online]. Oct 6 2014;Accessed Oct 14 2014. Available at http://www.medscape.com/viewarticle/832850.
5. Gerber AL, Harris A, Siskey B, Lee E, Schab TJ, Huck A. Vascular Dysfunction in Diabetes and Glaucoma: A Complex Relationship Reviewed. J Glaucoma. 2014 Sep 26. [Epub ahead of print]
6. Klemm M, Gesser C. The relevance of diabetes for patients with glaucoma. Clin Monbl Augenheilkd. 2014;231(2):116-20.
7. Parlaske-TA, Chrounkova NR, Dasydova HG, Okhotsimskaia TD, Beznos OV, Grigor’ev AV. Level of tear endothelin-1 and plasminogen in patients with glaucoma and proliferative diabetic retinopathy. Vestn Oftalmol. 2013;129(4):20-3.
8. Cruz-Iliño Y, Izquierdo NJ, García O, Pérez RI Anc Med PR. Open-angle glaucoma in patients with diabetic retinopathy at the Puerto Rico Medical Center. 2012;104(4):610-3.
9. Chobert A, Polanska J, Deja G, Jarosz-Chobert P. Incidence of type 1 diabetes among Polish children aged 0-14 years from 1999-2012. Acta Diabetol. 2014 Nov 8. [Epub ahead of print]
10. U.S Department of Health and Human Services, Centers for Disease Control and Prevention. 2011. National diabetes fact sheet: national estimates and general information on diabetes and prediabetes in the United States, 2011. Available at http://www.cdc.gov/diabetes/pubs/pdf/ndfs_2011.pdf. Accessed January 5, 2012. Hackethal V 2 in 5 American Adults Will Develop Diabetes. Medscape Medical News. Available at http://www.medscape.com/viewarticle/829883. Accessed August 13, 2014.
11. Gregg EW, Zhao X, Abigail AL, et al. Trends in lifetime risk and years of life lost due to diabetes in the USA, 1985—2011: a modelling study. The Lancet Diabetes & Endocrinology. Available at http://www.thelancet.com/journals/landia/article/PIIS2213-8587(14)701615/fulltext. Accessed August 13, 2014.
12. Zhang X, Sadine JB, Chou CF, Cotch MF, Cheng YJ, Geiss LS, et al. Prevalence of diabetic retinopathy among US adults aged 18 years and older: trends from 1999-2010. Diabetes Care. 2014;37(7):e134-40. [Epub ahead of print]
13. Schmidt D, Schmetterer L, Garbüler G, Popa-Cherechusa A. Gender Differences in Ocular Blood Flow. Curr Eye Res. 2014:1-12. [Epub ahead of print]
14. Apreutesei NA, Chisiletta D, Motas OJ. Glaucoma evolution in patients with diabetes. Rev Med Chir Soc Med Nat Iasi. 2014;118(4):649-56.
15. Noma H, Mimura T, Yasuda R, Shimura M. Vascular endothelial growth factor and its soluble receptors-1 and -2 in iris neovascularization and neovascular glaucoma. Ophthalmologica. 2014;232(2):10.
16. Bragge P, Girvan RL, Chau M, Forbes A, Taylor HR. Screening for Presence or Absence of Diabetic Retinopathy: A Meta-analysis. Arch Ophthalmol. 2011;129(4):435-44. Grand multiparity: Risk factors and