The Possible Association between Diabetes Mellitus and Pseudoexfoliation Syndrome in Egyptian Population

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Abstract

Background: Unknown is the precise chemical make-up of the fibrillar substance. It is believed that it is secreted multifocally by the ciliary epithelium, iris pigment epithelium, and peripheral anterior lens epithelium. Pseudoexfoliation syndrome has been associated with ischemic heart disease (IHD), arterial hypertension(AH), and type 2 diabetes. Certain illnesses, such as pseudoexfoliation, may be more common in people with diabetes mellitus. Diabetic patients had a higher prevalence of PEX than people without diabetes, according to Psilas.

Objectives: to determine the relationship between diabetes mellitus and pseudoexfoliation syndrome.

Patient and methods: The ophthalmology department at Qena University Hospital was the site of this study. The patients were divided into two groups.

Results: A PXF diagnosis was associated with a significantly higher probability of DM. In terms of Binary Logistic Regression, pseudoexfoliation and DM displayed a significant correlation.

Conclusion: There was a strong correlation between pseudoexfoliation syndrome and diabetes mellitus. Patients diagnosed with PXF are 4.6 times more likely to be diabetic than subjects with no PXF.

Keywords: Diabetes Mellitus; Pseudoexfoliation Syndrome; Pseudoexfoliation.

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Introduction

Pseudoexfoliation syndrome (PEX) was first described by Lindberg in **(1917)** and is characterized by the deposition of a distinctive fibrillar substance in the anterior part of the eye. It is typically associated with pseudoexfoliation glaucoma, a common type of secondary open-angle glaucoma around the globe **(Ritch et al., 1994).**

The exact chemical nature of the fibrillar material is still unclear after intensive research. It is hypothesized that it is secreted multifocally by the ciliary epithelium, peripheral anterior lens epithelium, and iris pigment epithelium **(Dickson et al., 1979).**

Pseudoexfoliation syndrome aetiology and pathogenestis are still unknown , but it is thought to be a systemic biochemical process **.(Schlotzer and Schrehardt et al., 2006).**

It has been discovered that pseudoexfoliation syndrome is related to diabetes mellitus, arterial hypertension (AH), and ischemic heart disease (IHD). In 2016, 422 million people were discovered to have diabetes worldwide, making it a common condition. Accounting for the shifting age structure of the global population, the prevalence of diabetes among adults is 8.5%, nearly double the rate of 4.7% in 1980 **(World Health Organization, 2016)**.

In this work, we would like to see if there is an increased prevalence of DM in patients with PEX.

Aim of Work was to find the correlation between pseudoexfoliation syndrome and diabetes mellitus

Patients and Methods

This was a case control study curried out at ophthalmology department Qena University Hospital. On 110 patients All patients enrolled in the study underwent complete ocular examination.

Patients were divided into two groups: Based on the following criteria, PXE syndrome has been diagnosed in patients in Group 1: about 55 patients (about 110 eyes) as as the patients were examined for both eyes. Pseudoexfoliative material (PXF) in cilliary processes and zonules, Pseudoexfoliative material dispersed on corneal endothelium, flecks of exfoliative material across the anterior chamber, and white, greyish exfoliation material on the anterior lens capsule and/or pupillary edge are all symptoms of glaucoma. Group 2 about 55 patients (about 110 eyes) consists of age-matched controls whom haven't PXE syndrome. As in (**Figs.1,2.3**). Some figures that explain the subject of the study.

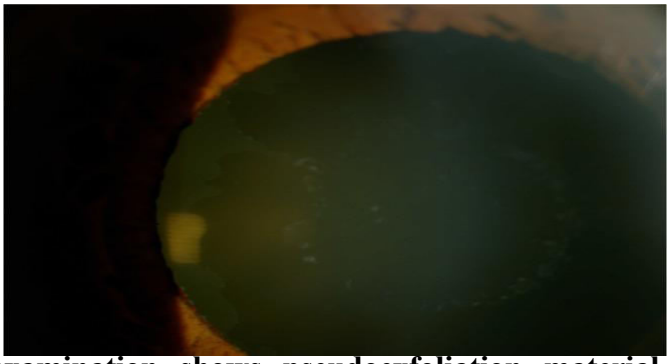

Fig.1. Slit-lamp examination shows pseudoexfoliation material on the lens surface in distinct zones: a central disk, peripheral zone, and clear intermediate zone (**Tekin et al., 2019**).

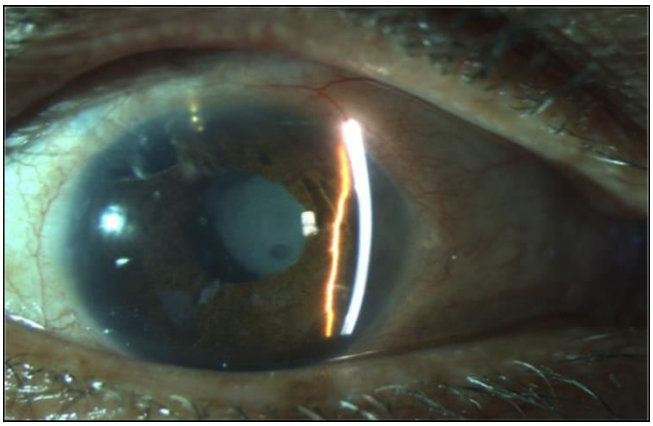

Fig.2. Lens subluxation is observed in a patient who underwent trabeculectomy surgery due to pseudoexfoliation glaucoma (**Tekin et al., 2019**).

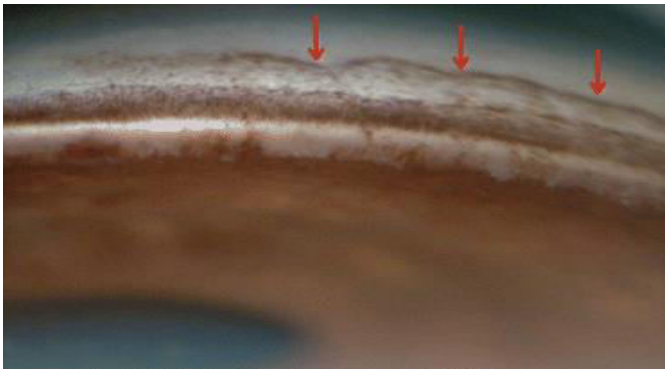

Fig.3. The Sampaolesi's line (red arrow) above the Schwalbe's line (**Figus et al., 2016**).

Each diseased participant in both groups was tested to diagnose the DM. Patients will be diagnosed with DM if they have one or more of the following criteria: 1- HbA1c ≥ 6.5%, 2-Fasting plasma glucose (FPG) is 7mmol/L (126mg/dl) or higher, 3-Plasma glucose 2h after 75 g glucose load (2hpG) is 11.1 mmol/L (200mg/dl) or higher, 4-Random venous plasma glucose concentration ≥ 11.1mmol/L. and 5-Patients already on treatment.

Inclusion criteria: Phakic patients above the age of 50 whom visited the outpatient ophthalmology clinic at Qena University Hospital, age: ≥ 50 years old, sex: male and female were included in the study, residence from Egyptian population in upper Egypt (Qena) and risk factors: Optic disc changes, visual field changes, increased cup disc ratio, increased intra ocular pressure and associated ocular diseases.

Exclusion criteria: Patients with previous intraocular surgery **and** patients under the age of 50.

Ethical consideration: Obtaining an informed written consent from all patients that were included in this study. Obtaining approval from the ethical committee of Faculty of Medicine, Qena University.

Statistical analysis

Data was collected and entered into Microsoft Access for analysis using the social science statistical package (SPSS inc., Chicago, version 16.0).

Results

A total of 110 patients with 220 eyes were examined (55 patients in each group) were enrolled in our study. Group I included patients diagnosed with pseudoexfoliation (PXF), while group II included healthy subjects.

In group I, 21 patients (38.2%) had unilateral disease, while 34 patients (61.8%) had bilateral disease. In the unilateral group, the right eye was affected in 14 (66.7%) patients, and the left eye was affected in 7 (33.3%) patients. In the bilateral group, 20 (58.8%) patients had symmetrical disease, and 14 (41.2%) patients had asymmetrical disease

As shown in (**Table.1**): all participants were divided into three categories in relation to age as: those under 60, those between 60 and 70, and those over 70.

There was no statistically significant variation as regard age, gender **(Fig.4)**. Residency and occupation between groups.

Table 1. Patient Characteristics (N = 110)

Variables	Group I (N = 55)		Group II (N = 55)		P value*
	Frequency	Percentage	Frequency	Percentage	
Age (years)					.171
Less than 60	19	34.5	13	23.6	
60 – 70 years	22	40.0	19	34.5	
More than 70	14	25.5	23	41.8	
Gender					.654
Female	12	21.8	14	25.5	
Male	43	78.2	41	74.5	
Residence					.001
Rural	38	69.1	20	36.4	
Urban	17	30.9	35	63.6	
Occupation					.001
Outdoor	40	72.7	22	40.0	
Indoor	15	27.3	33	60.0	

* Chi-square test.

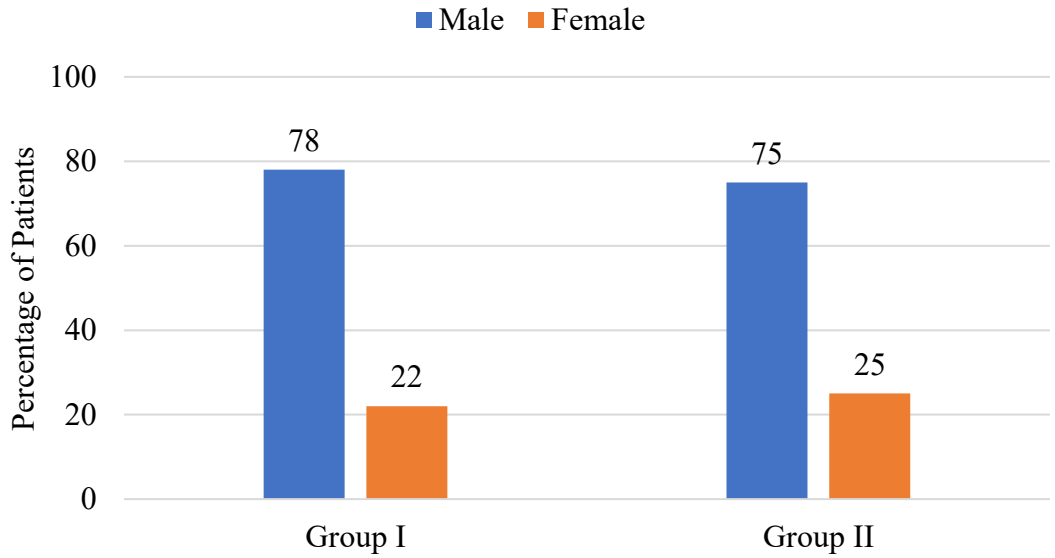

Fig. 4: Gender Distribution

No statistically significant difference was found between groups in terms of gender (Chi-square test, P = .654).

As shown in (**Table.2)**, patients with PXF had lower visual acuity and higher IOP compared to healthy individuals. On the other hand, no significant difference was observed between groups regarding prevalence of glaucoma and cataract.

Table 2. Ocular Characteristics (N = 110)

Variables	Group I (N = 55)		Group II (N = 55)		P value*
	Frequency	Percentage	Frequency	Percentage	
Visual Acuity					.003
6/6	4	7.3	20	36.4	
6/12	9	16.4	7	12.7	
6/24	9	16.4	8	14.5	
6/30	33	60.0	20	36.4	
High IOP					.002
No	19	34.5	35	63.6	
Yes	36	65.5	20	36.4	
Glaucoma					.644
No	42	76.4	44	80.0	
Yes	13	23.6	11	20.0	
Cataract					.055
No	26	47.3	36	65.5	
Yes	29	52.7	19	34.5	

* Chi-square test.

In group I, 36 (65.5%) patients had high IOP, while 19 (34.5%) had normal IOP. In group II, 20 (36.4%) had high IOP, while 35 (63.6%) had normal IOP (**Fig.5**). Patients with PXF had significantly higher IOP compared to the control group.

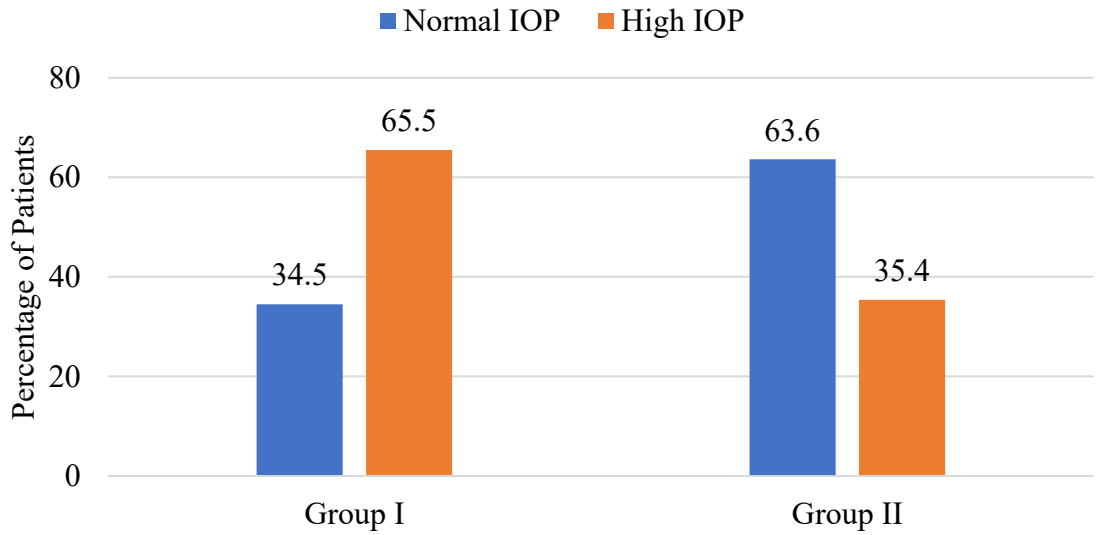

Fig.5. IOP

In group I, 33 (60%) patients had a VA of 6/30, nine (16.4%) had VA of 6/24, nine (16.4%) had VA of 6/12, and four (7.3%) had VA of 6/6. In group II, 20 (36.4%) had VA of 6/6, seven (12.7%) had VA of 6/12, eight (14.5%) had VA of 6/24, and 20 (36.4%) had VA of 6/36 (**Fig.6**).

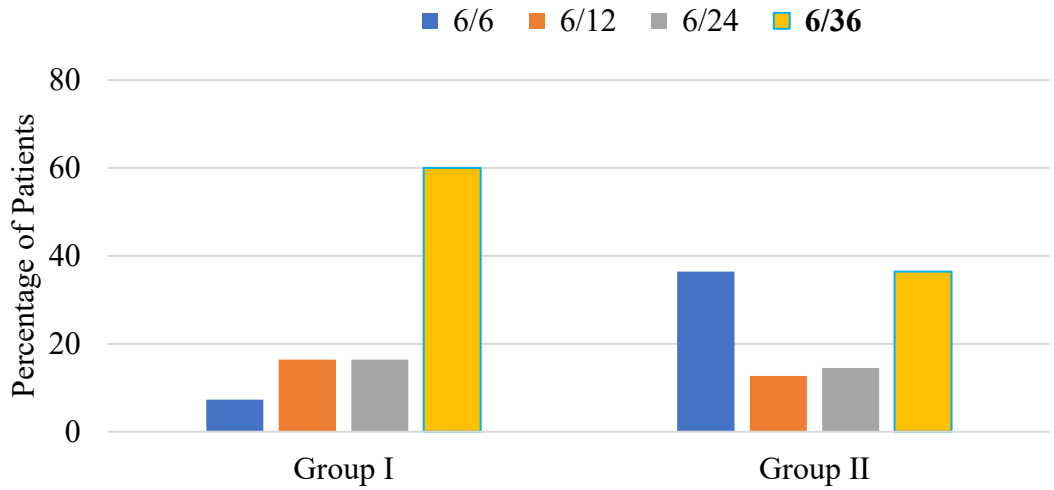

Fig. 6. Visual Acuity. Patients with PXF had significantly lower visual acuity compared to the control group (Chi-square test, P = .003).

Disease laterality, symmetry, and location are summarized in (**Table.3**). In group I, 21 patients (38.2%) had unilateral disease, while 34 patients (61.8%) had bilateral disease.

Among patients with PXF, 37 (67.3%) had PXF at the pupillary border, 12 (21.8%) had PXF at lens capsule and 6 (10.9%) had PXF at both pupillary border and lens capsule . **(Fig.7)**.

Table 3. Disease Characteristics in Group I (N = 55)

Variables	Frequency	Percentage
Unilateral	21	38.2
Rt Eye	14	66.7
Lt Eye	7	33.3
Bilateral	34	61.8
Symmetrical	20	58.8
Asymmetrical	14	41.2
Location		
Pupillary border	37	67.3
Lens capsule	12	21.8
Both	6	10.9

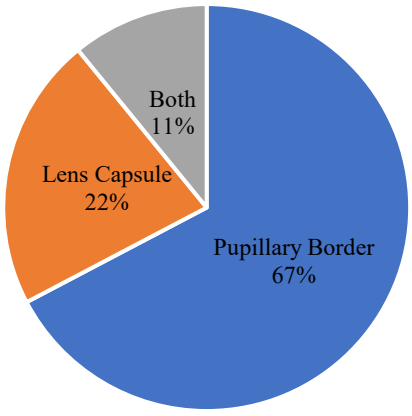

Fig.7. Disease Location

As demonstrated in (**Table.4**), the prevalence of DM was significantly higher among patients diagnosed with PXF. Besides, group I had higher mean values of glycemic parameters, including RBS, postprandial blood sugar and HbA1c (the mean HbA1c was 6.4 ± 1.1% (range, 5.1 – 9.4) **(Fig. 8)**. The prevalence of DM was significantly higher among patients diagnosed with PXF (Chi-square test, $P = .00$). Besides, group I had higher mean values of glycemic parameters, including RBS, postprandial blood sugar and HbA1c (Independent sample t test, $P < .05$).

Table 4. Comparing Prevalence of Diabetes between Groups

Variables	Group I (N = 55)	Group II (N = 55)	P value
Diagnosed with DM	39 (71%)	19 (35%)	.000*
FBG (mg/dl)	157 ± 42	128 ± 39	.000**
PPG (mg/dl)	257 ± 95	191 ± 57	.000**
HbA1c (%)	7.1 ± 1.0	6.4 ± 1.1	.005**

FBG: fasting blood glucose; PPG: postprandial glucose.* Chi-square test; ** independent sample t test.

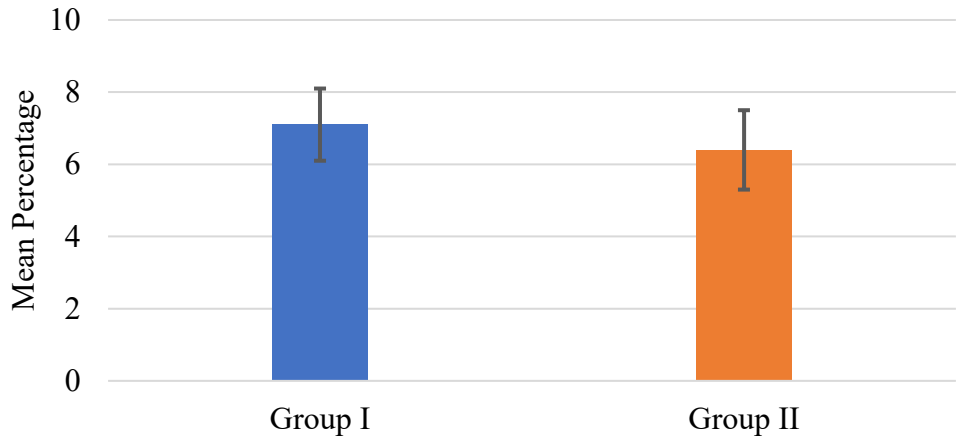

Fig. 8. HbA1c levels among the study groups

The (**Table.5),** clarified that By running a Spearman correlation analysis, a significant correlation was observed between PXF and DM. To determine the odds ratio, a binary logistic regression model was conducted. As demonstrated, patients diagnosed with PXF are 4.6 times more likely to be diabetic than subjects with no PXF.

Table 5. Binary Logistic Regression

Variables	B	SE	Wald	P value	Exp (B)	95% CI Exp (B)	
						Lower	Upper
PXF	1.530	0.411	13.889	.000	4.618	2.066	10.327
Constant	-0.639	0.284	5.079	.024	0.528		
B: estimated coefficient; SE: standard error; Exp (B): exponential value of B or odds ratio; CI: confidence interval.							

Cases of the study that explain different types of Pseudoexfoliation syndrome:

Case 1 (Fig.9).

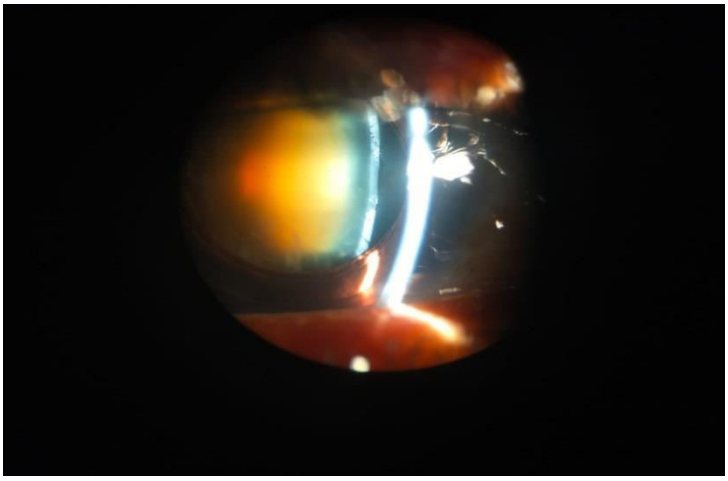

Fig. 9 . Diabetic Female patient aged 65 years old with PXF (dandruff material on the pupillary margin)

Case 2: (Fig.10).

Fig.10 . Male patient aged 55 years old with PXF (narrow angle of Anterior chamber) IOP was 27 mmHG when measured Has nuclear and Posterior sub capsular cataract

Case 3: (Fig.11).

Fig.11. Female patient aged 70 years ago with fibrillary material on the anterior lens capsule

Discussion

Pseudoexfoliation syndrome (PEX) is an age-related systemic microfibrillopathy characterized by the progressive deposition of whitish-gray extracellular material

PEX is most typically seen in adults over the age of 50. In fact, various epidemiological studies have determined that, in all populations, the disease's occurrence is negligible in the middle-aged population (49-54 years), and the disease's prevalence grows substantially with age **(Tekin et al.,(2019)**.

This was case control study conducted at ophthalmology department Qena University Hospital. All patients enrolled in the study underwent complete ocular examination. Then patients were divided into two groups: *Group1: included 55 patients who were diagnosed with PXE syndrome. *Group2: include 55 age matched controls that do not have PXE syndrome. The trial lasted somewhere between six and twelve months. Regarding demographic data the mean age of group 1 was 64.8 + 8.7 years (range, 50 – 80) while the mean age of group 2 was 66.7 + 8.6 years (range, 50 – 80).

Each set of patients were divided into three age categories: those under 60, those between 60 and 70, and those over 70. For either age or sex, there were no statistically significant differences between the groups.

Our results were supported by study of **Fani et al.(2021)**, which claimed that their examined patients were split into four categories,. Each group consisted of ten patients. Those in Group I, which serves as the control group, lack pseudo exfoliation and diabetes mellitus, while those in Groups II, III, and IV have both disorders. Group I also included those who have both conditions. The study included 40 eyes from 40 people between the ages of 65 and 86, with a mean age of 77.4 5.5 years (mean standard deviation) and a gender ratio of 57.5%. Between the groups analyzed,

There was no statistically significant difference. In terms of ocular characteristics, The current study found that patients with PXF had lower visual acuity and higher IOP when compared to healthy individuals. However, there was no appreciable difference in the prevalence of cataracts and glaucoma between the groups. In a **Topouzis et al. (2009)** study, found that PXF is the most frequently identified cause of open-angle glaucoma. Intraocular pressure (IOP) increases frequently.

Many patients with Pseudoexfoliation syndrome will develop glaucoma. Glaucoma will be more difficult to treat and will have a higher probability of treatment failure than primary open-angle glaucoma. With the same high IOP, those with PXF were three times more likely to develop glaucoma than those without PXF (above 21 mmHg).

Using the same glaucoma criteria, only two studies in the Middle East revealed glaucoma prevalence among PXF patients. Whereas **Al-Bdour et al. (2010)** found a 33.1% incidence in Jordan,

Shazly et al. (2011) observed a 30.3% prevalence of PXF glaucoma in Egypt (2008). Nevertheless, **Vazquez and Ferreiro et al. (2016)** It was revealed that, while the danger of severe complications has been significantly reduced due to the use of current microsurgical techniques and special instrumentation, it is still higher than in normal eyes after cataract extraction. This is because intraoperative and postoperative complications of cataract surgery are more likely when there is pseudo exfoliation.

According to the current study, group I contained 21 patients (38.2%) with unilateral disease and 34 (61.8%) with bilateral disease. In the unilateral group, 7 (33.3%) patients had left eye involvement while 14 (66.7%) patients had right eye involvement. 20 (58.8%) of the patients in the bilateral group had symmetrical disease, whereas 14 (41.2%) had asymmetrical illness.

PXF impacted 37 patients (67.3%) at the pupillary boundary, 12 patients (21.8%) at the focal point container, and 6 patients (10.9%) at both the pupillary line and focal point case.

While **Jammal et al. (2021)** discovered that 25.4% of PXF patients experienced pseudo exfoliation glaucoma, a greater proportion than most studies have recorded. Any comparison of glaucoma rates between studies may be hampered by differences in research design and population included the definition of glaucoma, the inclusion of only patients with high intraocular pressure, and the overall prevalence of glaucoma among different ethnicities. It is worth noting that population-based studies have reported lower rates of glaucoma (2.8-15.2%) than hospital-based studies, with the reasoning being similar to that for lower PXF rates in population-based studies, as study cohorts attending a hospital are more likely to manifest PXF and glaucoma.

Also, According to **Shazly et al. (2012),** only two researches in the Middle East reported on glaucoma prevalence among PXF patients using the same criteria of glaucoma. PXF glaucoma was found in 30.3% of Egyptians. In any case, there is a more probability of transformation to glaucoma over the long run in PXF eyes and in the clinically typical eye in individuals with clinically one-sided PXF.

Our results were supported by study of **Psilas et al. (1991)** as they reported that the prevalence of PEX was 23.7% in non-diabetic patients and 11 % in diabetic patients with statistically significant difference between them

Similarly, in a population-based survey performed by **Nouri-Mahdavi et al. (1999)** a random sample of people aged 50 or above from Falavarjan city (near our area), central Iran, was examined for signs of PEX. 806 eyes in 405 cases (210 women and 195 men) were examined. Seventy-seven eyes of 53 cases showed pseudo exfoliative deposits.

There are also research with statistically significant findings. In a Greek study conducted by **Konstas et al. (1998),** whereas diabetes was 3.5 times more common in the PEX group than in the control group, despite the fact that the average age in the first group was much greater. Diabetes was substantially less common in cataract patients who had PEX than in those who did not have PEX., as per **Shingleton et al. (2003).**

In contrary to our results, studies **Praveen et al., (2011); Sekeroglu et al., (2008)** they reported that DM rates did not vary between patients with and without PEX. In **Spečkauskas et al., (2012),** A small number of DM patients were studied, and there was no significant difference in glycemia, treatment approaches, or DM rate when PEX was present. The differences between their studies and ours may be explained by differences in sample size and duration of study, as well as better diabetes control.

Conclusion

There was a substantial relationship between pseudo exfoliation syndrome and diabetes mellitus. Individuals with PXF are 4.6 times more likely to be diabetic than patients without PXF.

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