Original Research Article

Association between pseudoexfoliation syndrome and dyslipidemia: A case control study

Afshan Sumaiya Qazi[1], Sheikh Asma Bashir[1], Imtiyaz Ahmad Lone[1]*

[1]*Dept of Ophthalmology, SKIMS Medical College, Srinagar, Jammu and Kashmir, India*

ARTICLE INFO

ABSTRACT

Background: Pseudoexfoliation syndrome, also known as PEX 1, is a systemic micro fibrillopathy associated with ageing that is brought on by the gradual buildup of extracellular white and grey matter on various ocular and extra ocular structures. It is deposited in extra-ocular tissues such the heart, blood vessels, meninges, liver, and lungs. Numerous investigations have shown a connection between PEX and glaucoma. A person with PEX is typically thought to be at risk for acquiring glaucoma, and vice versa.
Atherosclerosis is facilitated by dyslipidemia, which is an increase in plasma cholesterol, triglycerides (TGs), or both, or a low HDL level. A potential risk factor for the progression of cardiovascular disease is dyslipidemia. Numerous investigations have discovered abnormal lipid profiles in pseudoexfoliation syndrome patients, including elevated levels of triglycerides, cholesterol, and LDL. Due to the straight association between lipid levels, atherosclerosis, and cardiovascular risk, patients with PEX are shown to be at an elevated risk of cardiovascular and cerebrovascular events.
Objective: To study the correlation between dyslipidemia and pseudoexfoliation syndrome in patients above 50 years of age and compare it with age matched controls.
Materials and Methods: This case control study was conducted from November 2020 to November 2022 at SKIMS Medical College and Hospital, Srinagar and included 150 patients with PEX above 50 years of age and compared with age matched controls.
Results: In this study mean total cholesterol among cases was 176.88±34.76 mg/dl versus 172.94±51.51 mg/dl in controls. P-value for total cholesterol was statistically insignificant (0.438). Mean triglyceride level among cases was 180.11±54.70 mg/dl while as mean triglyceride level among controls was 163.14±46.21 mg/dl and P-value was found to be statistically significant. Mean LDL level among cases was 104.57±32.80 mg/dl while as in controls mean was 82.70±27.60 mg/dl. P-value for LDL levels was found to be statistically significant. Mean HDL levels among cases was found to be 41.93±8.94 mg/dl while as in controls mean was 39.67±13.73 mg/dl. P-value for HDL levels was statistically insignificant (0.09). Mean VLDL levels among cases was found to be 25.34±19.52 mg/dl while as in controls mean was 27.66±14.36mg/dl. P-value for VLDL levels was statistically insignificant (0.242).
Conclusion: There is significant correlation between dyslipidemia and pseudoexfoliation syndrome in patients above 50 years of age.

1. Introduction

Pseudoexfoliation syndrome is often referred to as PEX1, PES, or PXS. PEX is a systemic micro fibrillopathy associated with ageing that develops as extracellular grey and white material gradually builds up on various ocular and

* Corresponding author.
E-mail address: imtiyazalone@yahoo.co.in (I. A. Lone).

extra-ocular structures. [1–3] The anterior chamber structures, trabecular meshwork, central disc of the lens, zonular fibres, anterior hyaloid face, pupillary edge and anterior iris, and on occasion the cornea, are among the ocular structures where it is deposited. [4,5] Based on slit lamp examination of white flaky deposits on the anterior lens surface and pupillary border, the syndrome's precise clinical diagnosis is made. It is deposited in extra-ocular tissues such as the heart, meninges, liver, and blood vessels. [6–9] Although it is thought that PEX and glaucoma are connected, there are cases of both people who have PEX without glaucoma and those who have glaucoma without PEX. A person with PEX is typically thought to be at risk for acquiring glaucoma, and vice versa. Dyslipidemia is elevation of plasma cholesterol, triglycerides (TGs) or both or a low HDL level that contributes to the development of atherosclerosis. According to the American Heart Association classification, dyslipidemia is defined as total cholesterol exceeding 5.2 mmol/L (200 mg/dl), LDL exceeding 3.4 mmol/L (130 mg/dl), HDL below 0.9 mmol/L (35 mg/dl), or triglycerides exceeding 1.7 mmol/L (150 mg/dl), or any combination of these. Dyslipidemia may increase the risk of cardiovascular disease progression

Many studies have found deranged lipid profile in patients with pseudoexfoliation syndrome which includes increased triglycerides, cholesterol and LDL levels. Some studies have found decreased HDL levels and few are inconclusive about HDL levels in pseudoexfoliation syndrome. Additionally, research have revealed that patients with PEX had higher systolic and diastolic blood pressure as well as thicker intima media. Patients with PEX are found to be at increased risk of cardiovascular and cerebrovascular accidents because of linear relationship between lipid levels, atherosclerosis and cardiovascular risk. Patients with pseudoexfoliation who have dyslipidemia have a higher risk of systemic vascular disorders, endothelial dysfunction, and decreased antioxidant defense.. Further evaluation was needed to prove an association between pseudoexfoliation and dyslipidemia in our population.

Following were objectives of our study

1. To investigate the relationship between pseudoexfoliation syndrome and dyslipidemia in people over 50 years of age.
2. To have a regular follow-up of patients having altered lipid levels with pseudoexfoliation syndrome (PEX) for subsequent development of pseudoexfoliative glaucoma (PEG).
3. To advice patients having deranged lipid profile with pseudoexfoliation syndrome to consult general physician for focused cardiovascular examination.

2. Materials and Methods

After receiving approval from the hospital's ethics council, the case-control study was carried out at SKIMS Medical College Hospital Srinagar from November 2020 to November 2022. All the patients with age >50 years who visited Ophthalmology OPD for different Ophthalmic ailments were evaluated for presence of pseudoexfoliative material by slit lamp biomicroscopy and those found positive for PEX were evaluated for any deranged lipid profile. Similar number of age matched controls were also evaluated for dyslipidemia.

2.1. Inclusion criteria

All patients with pseudoexfoliation syndrome and age matched controls, age > 50 years and apparently healthy individuals with no known cardiovascular or cerebrovascular illness or diabetes mellitus were included in this study.

2.2. Exclusion criteria

Age < 50 years (pesudoexfoliation being less common in younger age group), patients with known cardiovascular or cerebrovascular illness or diabetes mellitus and those refuses to participate in the study were excluded.

2.3. Statistical analysis

The gathered information was put into a Microsoft Excel spreadsheet, which was then exported to the data editor of SPSS Version 20.0 (SPSS Inc., Chicago, Illinois, USA). Categorical variables were summed up as frequencies and percentages, whereas continuous variables were expressed as Mean SD. Bar and line diagrams were used to illustrate the data graphically. For comparing continuous variables, the Student's independent t-test or Mann-Whitney U-test was used, depending on what was practical. For comparing categorical variables, either the Fisher's exact test or the chi-square test was used, depending on the situation. Statistical significance was defined as a P-value 0.05.

3. Results

In all, 150 participants, 150 cases and 150 controls, ranging in age from 50 to 90 years, were included in this study. The mean age of the cases was 67.1+8.94 years, while that of the controls was 65.7+8.71 years. Majority of cases i.e. 41.3% in this study were aged between 61-70 years In this study, majority of the patients were from rural areas i.e. 59% among cases and 62% among controls. In this study, history of smoking was present in around 27% of cases and 35% of controls.

In this study mean total cholesterol among cases was 176.88±34.76mg/dl versus 172.94±51.51mg/dl in controls. P-value for total cholesterol was statistically insignificant

(0.438).

Mean triglyceride level among cases was 180.11±54.70mg/dl while as mean triglyceride level among controls was 163.14±46.21 mg/dl and P-value was found to be statistically significant.(Figure 1)

Mean LDL level among cases was 104.57±32.80 mg/dl while as in controls mean was 82.70 ±27.60 mg/dl. P-value for LDL levels was found to be statistically significant.(Figure 2)

Mean HDL levels among cases was found to be 41.93±8.94mg/dl while as in controls mean HDL levels were 39.67±13.73mg/dl. P-value for HDL levels was statistically insignificant (0.09). (Figures 3 and 4)

Mean VLDL levels among cases was found to be 25.34±19.52 mg/dl while as in controls mean was 27.66±14.36 mg/dl. P-value for VLDL levels was statistically insignificant (0.242).
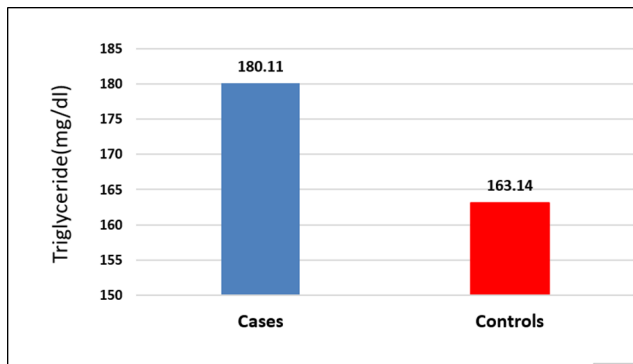

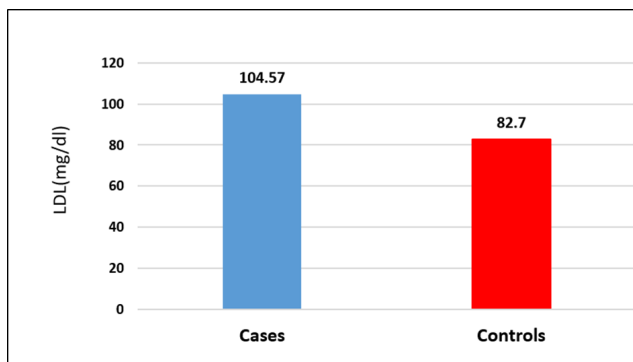**Figure 1:** Triglyceride levels among cases and controls

Figure 2: LDL levels among cases and controls

4. Discussion

In this study, a total of 150 Cases and 150 controls were enrolled who were aged between 50 to 90 years with a mean age of 67.1+8.94 years in cases and 65.7±8.71 years in controls. Majority of cases i.e., 41.3% in this study were aged between 61-70 years. There was a little male
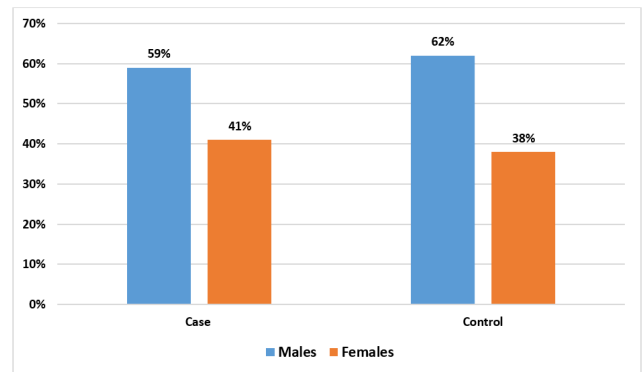

Figure 3: Male and female distribution among cases and controls
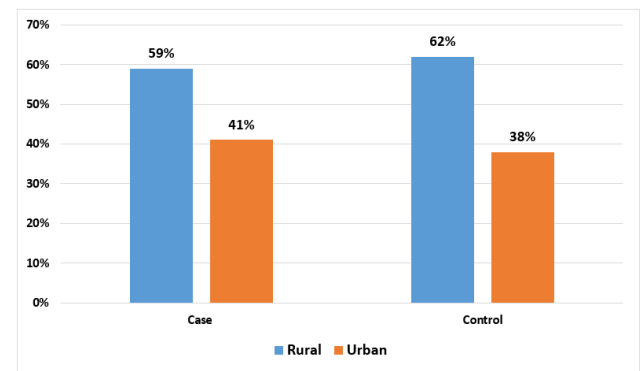

Figure 4: Demographic distribution among cases and controls

predominance in this study with 61% males versus 39% females among cases and 57% males versus 43% females among controls which corresponds with the study conducted by Masoumi et al.[10] in which gender of 58% of the patients was male, and 42% were female with an average age of 62.7 years and also with the study conducted by Nouri & Kouchaki.[11] in which gender of 58% of the patients was male and of 42% were female with an average age of 62.7years.

In this study mean triglyceride level among cases was 180.11±54.70 mg/dl while as mean triglyceride level among controls was 163.14±46.21 mg/dl and P-value was found to be statistically significant. Mean LDL level among cases was 104.57±32.80 mg/dl while as in controls mean LDL was 82.70 ±27.60 mg/dl and P-value was found to be statistically significant. Altintaş et al.[12] found a positive association between pseudoexfoliation syndrome and hyperlipidemia, as was found in the present study. In a study conducted by Masoumi et al.[10] mean triglyceride level in PEX patients was 181.64±21.23 mg/dl and the mean LDL levels were 138.86±13.27 mg/dl, which also correlated with the present study. In a study conducted by Nouri & Kouchaki.[11] The mean triglyceride level in PEX patients was 181.64±21.23 mg/dl, the mean cholesterol level was

221.31±32.12 mg/dl and the mean LDL 138.86±13.27 mg/dl, these results were also in line with the present study. Abay RN et al.[13] also concluded higher triglyceride glucose index in patients with PEX, correlating with present study in terms of higher triglycerides. In the study conducted by Bengi ece kurtul et al.[14] high LDL levels were found in PEX patients which were also similar to present study.

Our findings are however different from the research conducted by Hanna Lesiewska et al.[15] and Davari MH et al.[16] where no association was found between pseudoexfoliation syndrome and dyslipidemia.

In Mirza E et al.[17] study, PEX was also found to be positively associated with the risk for CAD among subjects 50 years or older. In the study done by Citirik et al.[18] the number of patients with PEX among CAD(+) patients was substantially larger than controls. In all, 28 of 50 CAD (+) patients and only 12 of 50 CAD (-) patients had PEX. Hence PEX was significantly associated with CAD (P=0.001). In the same study when all patients were regrouped according to the presence of PEX, patients with PEX did not differ from patients without PEX in terms of age (P=0.360) and sex (P=0.507), but the prevalence of CAD was higher (P=0.001) and fundoscopic findings of vascular diseases were significantly more prominent (P=0.0001) in PEX (+) patients. Our study also aimed at preventing cardiovascular risk in PEX patients and the study concluded that all patient with PEX have statistically significant association with Hyperlipidemia and needs cardiovascular evaluation.

In the study performed by French et al.[19] there were 6,046 case patients with pseudoexfoliation; approximately half were diagnosed with pseudoexfoliation glaucoma. Also as per study conducted by Yildirim N et al.[20] the incidence of glaucoma was found to be 26%in PEX patients and 1.7% in non-PEX participants and a statistically significant difference was observed (P<0.001). As per their study such patients require early treatment to prevent complications like glaucoma, however our study emphasized early treatment of dyslipidemia to prevent pseudoexfoliation and PEX-related glaucoma. Overall motive from both studies concluded early management of PEX to prevent ophthalmic and systemic manifestations of PEX.

5. Conclusion

In the present study mean triglyceride levels and mean LDL levels among patients with pseudoexfoliation syndrome was found to be significantly higher compared to age matched controls. Thus, it is concluded from the study that there is significant correlation between dyslipidemia and pseudoexfoliation syndrome in patients above 50 years of age and patients having deranged lipid profile with pseudoexfoliation syndrome should be advised to consult general physician for focused cardiovascular examination.

6. Source of Funding

None.

7. Conflict of Interest

None.

References

1. Ritch R, Schlötzer-Schrehardt U. Exfoliation syndrome. *Surv Ophthalmol* . 2001;45(4):265–315.
2. Ringvold A. Epidemiology of the pseudo-exfoliation syndrome. *Acta Ophthalmol Scand*. 1999;77(4):371–5.
3. Forsius H. Exfoliation syndrome in various ethnic populations. *Acta Ophthalmol Suppl*. 1988;184:71–85.
4. Gartaganis SP, Georgakopoulos CD, Mela EK, Exarchou A, Ziouti N, Assouti M, et al. Matrix metallo proteinases and their inhibitors in exfoliation syndrome. *Ophthalmic Res*. 2002;34(3):165–71.
5. Gartaganis SP, Patsoukis NE, Poulos DKN, Georgiou CD. Evidence for oxidative stress in lens epithelial cells in pseudo- exfoliation syndrome. *Eye (Lond)*. 2007;21(11):1406–11.
6. Schlotzer-Schrehardt UM, Koca MR, Naumann GO, Volkholz H. Pseudoexfoliation syndrome. Ocular manifestation of a systemic disorder. *Arch Ophthalmol*. 1992;110(12):1752–6.
7. Streeten BW, Li ZY, Wallace RN, Eagle RC, Keshgegian AA. Pseudoexfoliative fibrillopathy in visceral organs of a patient with pseudoexfoliation syndrome. *Arch Ophthalmol*. 1992;110(12):1757–62.
8. Schlotzer-Schrehardt U, Kuchle M, Hofmann-Rummelt C, Kaiser A, Kirchner T. Latent TGF-beta 1 binding protein (LTBP-1); a new marker for intra and extra ocular PEX deposits. *Klin Monbl Augenheilkd* . 2000;216(6):412–9.
9. Mardin CY, Schlotzer-Schrehardt U, Naumann GO. Early diagnosis of pseudoexfoliation syndrome. A clinical electron microscopy correlation of the central, anterior lens capsule. *Klin Monbl Augenheilkd* . 1997;211(5):296–300.
10. Masoumi R, Ojaghi H, Zamanian T. Relationship between PseudoExfoliation Syndrome (PEX) and Hyperlipidemia in Patients Over 40 Years Visiting Ardabil City Hospital. *J Ophthalmol & Vis Sci*. 2016;1(1):1011.
11. Nouri M, Koucheki B. Related factors with Glaucoma and IOP in patients suffering from PEX in Feyz and Farabi hospitals in Esfahan 1998-1999. *Bina*. 2001;6:214–22.
12. Altintaş O, Maral H, Yüksel N, Karabaş VL, Dillioğlugil MO, Cağlar Y, et al. Homocysteine and nitric oxide levels in plasma of patients with pseudoexfoliation syndrome, pseudoexfoliation glaucoma, and primary open-angle glaucoma. *Graefes Arch Clin Exp Ophthalmol*. 2005;243(7):677–83.
13. Abay RN, Katipoğlu Z. The correlation between pseudoexfoliation syndrome and the Triglyceride-Glucose index. *Graefes Arch Clin Exp Ophthalmol*. 2022;260(12):3903–8.
14. Kurtu BE, Kurtu A, Ozer PA, Kabatas EU, Ertugrul GT. Serum Lipid Levels in Pseudoexfoliation Syndrome. *Semin Ophthalmol* . 2017;32(3):281–4.
15. HLesiewska, Łukaszewska-Smyk A, z-Sypniewska GO, Krintus M, Mańkowska-Cyl A, Malukiewicz G, et al. Chosen Vascular Risk Markers in Pseudoexfoliation Syndrome: An Age-Related Disorder. *J Ophthalmol*. 2017;2017:5231095.
16. Davari MH, Kazemi T, Heydari B, Sukhtanlu F, Bizhaem SK. The association between pseudoexfoliation and metabolic syndrome, a case control study. *New Front Ophthalmol*. 2018;4(4):1–3.
17. Mirza E. Atherogenic indices in pseudoexfoliation syndrome. *Eye (Lond)*. 2019;33(12):1911–26.
18. Citirik M, Acaroglu G, Batman C, Yildiran L, Zilelioglu O. A possible link between the pseudoexfoliation syndrome and coronary artery disease. *Eye (Lond)* . 2007;21(1):11–5.
19. French DD, Margo CE, Harman LE. Ocular pseudoexfoliation and cardiovascular disease: a national cross-section comparison study. *N Am J Med Sci*. 2012;4(10):468–73.

20. Yildirim N, Yasar E, Gursoy H, Colak E.   Prevalence of pseudoexfoliation syndrome and its association with ocular and systemic diseases in Eskisehir. 2017;10(1):128–34.

Author biography

Afshan Sumaiya Qazi, Postgraduate Scholar

Sheikh Asma Bashir, Postgraduate Scholar

Imtiyaz Ahmad Lone, Professor