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Association of ocular psuedoexfoliation syndrome with ischemic heart disease, systemic hypertension, and diabetes mellitus Type II in Bundelkhand region: A cross-sectional study

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ABSTRACT

Background: Studies exploring the links between ischemic heart disease (IHD), arterial hypertension (AH), diabetes mellitus (DM), and pseudoexfoliation syndrome (PEX) have yielded no clear evidence and attributing PEX to any one particular disease. **Aims and Objectives:** The present study was undertaken to determine the prevalence of PEX syndrome and its association with IHD, AH, and DM at our center. **Materials and Methods:** The study comprised of participants (n = 102) having IHD, AH and DM. Demographic details and clinical history in detail were written down in a structured proforma. Participants in the study were examined for the diagnosis of PEX syndrome with slit lamp bi microscopy as well as direct and indirect ophthalmoscopy. For numerical variables, descriptive statistics comprised mean and standard deviation, and for categorical variables, the percentage of various categories. To compare categorical variables, Chi-square (χ^2) test was utilized. **Results:** The prevalence of PEX in our study came out to be 17.64% (18 of the 102). Patients of PEX were in the age group of 61–70 years, that is, 8 (44.44%) and were males, that is, 11 (61.11%). The percentage of systemic hypertension patients who had PEX syndrome was 35.29% with statistical significant association ($\chi^2 = 10.9$; P = 0.001). The percentages of IHD and DM patients with PEX syndrome were 11.76% ($\chi^2 = 1.214$; P = 0.270) and 5.88% ($\chi^2 = 3.718$; P = 0.053), respectively, the statistical association was a non-significant one. **Conclusion:** People above 40 years should undergo routine ophthalmological examinations for the detection of PEX Syndrome. Patients diagnosed with hypertension should be given a thorough ophthalmological examination to rule out PEX syndrome.

Key words: Prevalence; Slit lamp; Indirect ophthalmoscopy; Systemic hypertension

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INTRODUCTION

Pseudoexfoliation syndrome (PEX) is a systemic microfibrillopathy associated with aging that is brought on by extracellular debris that gradually builds up and deposits over different tissues.[1] Lindberg originally identified it in a Finnish population in 1917. He noted the typical observations of white or grey flakes on the anterior lens capsule, glaucoma in around 50% of eyes, and an increase in the prevalence of the ailment with advancing age.[2]

Different intraocular cell types including the pre-equatorial lens epithelium, non-pigmented ciliary epithelium, trabecular endothelium, corneal endothelium, vascular endothelial cells, and nearly all cell types of the iris seem to secrete PEX fibrils multifocally.

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Unusual elastin fibrils detected by electron microscopy in the heart, lung, liver, kidney, gallbladder, and meninges[3] gave rise to the notion that the PEX might be a part of a systemic illness.[4] The broad distribution of exfoliation fibers led to a search of probable systemic comorbidities in patients with the PEX.[5] It was hypothesized that PEX might contribute to greater morbidity mainly from systemic vascular disorders such as ischemic heart disease (IHD), arterial hypertension (AH), or cerebrovascular disease or from an ocular pathology such as a cataract, glaucoma, or age-related macular degeneration.[3]

The prevalence of PEX worldwide ranges from 0.5% in people aged <60 years to 15% in those aged ≥60 years.[6] The prevalence of PEX depending on hospital records from India ranges from 1.87% to 13.5%.[7] PEX is more prevalent among elderly population, with most cases occurring in the late 60s and early 70s. Studies on the links between PEX and IHD, systemic AH, and diabetesmellitus (DM) have yielded mixed results, and no clear evidence attributing PEX to any one particular systemic disease has yet been established.[5,8] There is a paucity of literature about PEX syndrome in the Bundelkhand region of India.

Aims and objectives

This study was undertaken with the objective of determining the prevalence of PEX syndrome in the region and its association with IHD, systemic hypertension, and DM Type II.

MATERIALS AND METHODS

This was a cross-sectional hospital-based study that comprised 34 cases each of IHD, DM Type II, and systemic hypertension, amounting to 102 participants in total, who reported to the department of ophthalmology at our tertiary care center, from April 2021 to June 2022 (15 months duration) for various complaints and were found to have these co-morbid conditions. Ethical clearance for the study was taken from Institution Ethics Review Committee and the study adhered to the principles of declaration of Helsinki. We limited the sample size for the study to 102 participants, after taking into the consideration the time and resources available at our disposal. Non-probability purposive sampling was used to recruit patients for the study. We included patients who fell under the age group 45–75 years and were known cases of IHD, DM Type II and systemic hypertension. The above comorbidities in all the participants were mutually exclusive. Only those participants who were willing to participate in the study and gave their written and informed consent were considered for the study. We excluded patients who were below the age of 45 years and above the age of 75 years, with aphakia, luxated lens, and phthisis after eye globe injury, with other ocular disorder such as uveitis, retinal detachment, or retinal vascular disorders, gave history of ocular trauma and recent ocular surgery (<6 months), pregnant, or lactating, with bilateral pseudophakia, with congenital or developmental cataract, having occupation in which they are exposed to infrared radiation, with complicated cataract, known cases of primary open angle glaucoma (POAG), and primary angle closure glaucoma. Up until the required sample size was met, patients were recruited for the study. Demographic information and a detailed history of the patient was taken a written down in proforma designed for the study.

Procedure followed to select the AH, IHD, and DM cases:

Case of Systemic Hypertension (AH): Participants were asked to sit still for 5 min before their blood pressure was taken. Blood pressure was measured 3 times with a 2-min interval between measurements, using a sphygmomanometer. Hypertension was diagnosed if the systolic blood pressure was 140 and/or the diastolic blood pressure was 90 mmHg or higher, or if drugs were used during the past 2 weeks.

Case of IHD: IHD was determined according to a documented history of myocardial infarction or electrocardiogram readings that indicate the ischemic changes.

DM Type II: The presence of DM was determined if responders gave a positive answer to the following question: "Has a doctor ever told you that you have diabetes?," This basically indicates to the fact that patient is a K/C/O of DM Type II or fasting glycemia of 5.5 mmol/l or more, or HbA1C >6.5%.

Every participant in the study underwent a slit lamp (Haaag Streit Koeniz) examination to check for the presence of pseudoexfoliation deposits. Then, the fundus examination of every participant was done using direct and indirect ophthalmoscopy. Eye drops containing 5–10% of phenylephrine and 1% of tropicamide were used to dilate the pupils of subjects with open angles. If phenylephrine was contraindicated, 1% of homatropine eye drops were used instead. The anterior lens capsule was examined for PEX deposits under dilatation. The anterior lens surface and pupillary ruff were inspected under high magnification. PEX was diagnosed if typical pseudoexfoliative material was present on the anterior lens capsule and/or pupillary margin in either one or both eyes.

Statistical analysis

The Statistical Package for the Social Sciences was used to analyze the data for Windows, version 21.0. For numerical variables, descriptive statistics comprised mean and standard deviation, and for categorical variables, they included the percentage of various categories. To compare categorical variables, the Chi-square (χ^2) test was utilized.

RESULTS

The maximum number of participants in the study, that is, 36 (35.29%), were from the age group of 45–50 years. Further, it was observed that the maximum number of PEX syndrome patients were in the age group of 61–70 years, that is, 8 (44.44%). This difference was statistically not significant based on our study (Table 1). Higher numbers of males, that is, 64, were part of the study, and also PEX syndrome was present in greater proportion, that is, 11 (61.11%) in males in our study (Table 1). The overall prevalence of psuedoexfoliation syndrome in our study came out to be 17.64%, that is, 18 of the 102 study participants had PEX syndrome. The number of participants was equal among the 102 study participants, 34 for each systemic disease in which the association of PEX was determined. After analyzing the data, it was discovered that the majority of PEX syndrome patients (12 out of 18) had systemic hypertension (Figure 1), followed by IHD (six out of 18) (Figure 2) and DM Type II (two out of 18) (Table 2 and Figure 3). The percentage of systemic hypertension patients who had PEX syndrome was 35.29%. The number is higher when compared with the rest of the variables taken into account in the study. The difference was statistically significant (χ^2=10.9; P=0.001). The percentages of IHD and DM patients with PEX syndrome were 11.76% and 5.88%, respectively, and the statistical association was a non-significant one (P>0.05).

Table 1: Prevalence of pseudoexfoliation syndrome according to overall, gender, and age-group (n=102)

Variable	Pseudoexfoliation syndrome				χ^2	P-value
	Present		Absent			
	n	%	n	%		
Age (in years)						
45–50	5	13.89	31	86.11	2.504	0.644
51–55	2	15.38	11	84.62		
56–60	3	15.79	16	84.21		
61–70	8	25.81	23	74.19		
71–75	0	0.00	3	100.00		
Gender						
Male	11	17.19	53	82.81	0.025	0.874
Female	7	18.42	31	81.58		

Table 2: Association of IHD, Systemic Hypertension (AH), and DM with pseudoexfoliation syndrome (n=102)

Comorbidity	Pseudoexfoliation syndrome				χ^2	P-value
	Present		Absent			
	n	%	n	%		
IHD						
Present	4	3.9	30	29.4	1.214	0.270
Absent	14	13.7	54	52.9		
Systemic hypertension						
Present	12	11.8	22	21.6	10.9	0.001
Absent	6	5.9	62	60.8		
DM						
Present	2	2.0	32	31.4	3.718	0.053
Absent	16	15.7	52	51.0		

IHD: Ischemic heart disease, AH: Arterial hypertension, DM: Diabetes mellitus

DISCUSSION

The PEX prevalence found in our study population was higher than the PEX prevalence reported in studies from South India (Aravind Comprehensive Eye Survey: age: 40+ years; PEX prevalence: 6.0%),[9] from Australia (PEX prevalence, in white Australians: 3.0%; indigenous Australians: Age: 40+ years: 5.9%),[10] and from North China (age: 50+ years; PEX prevalence: 5.8%).[11] These differences in the prevalence may reflect actual variations brought on by ethnic, genetic, and the demographical attributes of the geographical region concerned. Variations can also be due to different methods of measurement employed and the methodology used to ascertain the diagnosis of PEX syndrome. The differences in study design, sampling techniques, population size, and the age distributions in the sampled populations, among many others, might also be contributing factors for these variations. Our research showed that the prevalence of PEX cases increased in tandem with the participants' ages. The study conducted by Arnarsson et al.,[12] discovered higher prevalence rates as people aged: 2.5% of participants in the 50–59 age group had PEX, compared to 40.6% of people who were 80 years or older. Similar to our study, studies by, McCarty and Taylor,[13] Arvind et al.,[14] Miyazaki et al.,[15] Damji et al.,[16] Anastasopoulos et al.,[17] and Sufi et al.,[18] found that the prevalence of PEX markedly increased with age.

In our study, maximum number of participants was male. The prevalence of PEX syndrome was also higher in males than the female participants in the study. However, this difference was not statistically significant. Studies have revealed varying gender difference in prevalence of PEX. Male preponderance was also seen in studies done by McCarty and Taylor,[13] and Sufi et al.,[18] who reported a male preponderance in a study of PEX in eye camps in Kashmir, but Hiller et al.,[19] also reported female preponderance.

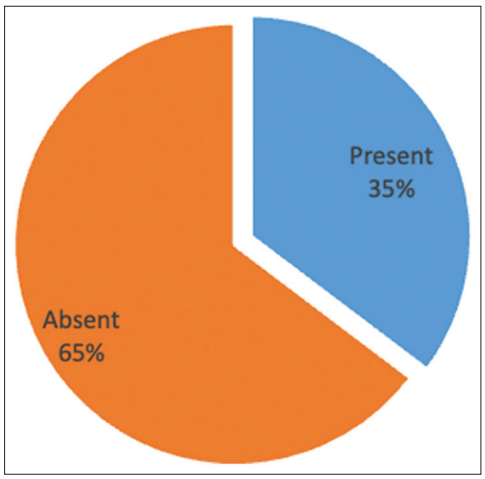

Figure 1: Prevalence of PEX among AH cases

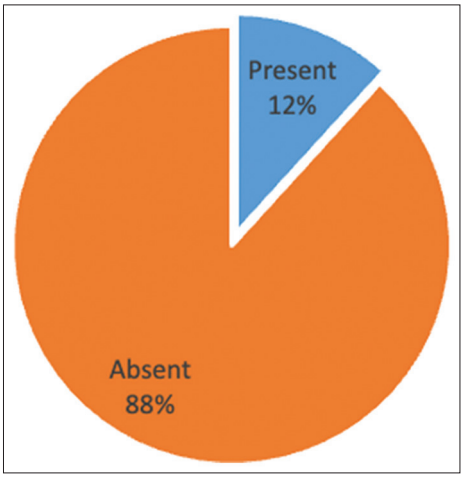

Figure 2: Prevalence of PEX among cases

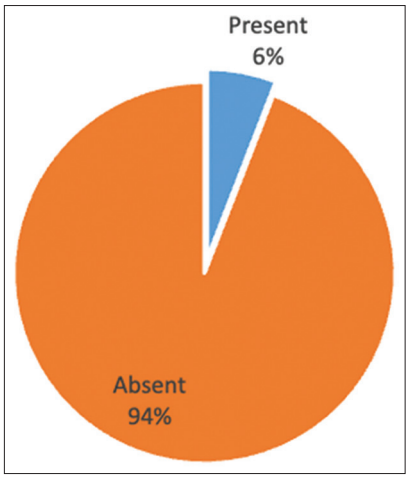

Figure 3: Prevalence of PEX among cases

We observed no statistically significant association between these and PEX syndrome in our investigation in our study. Similar to our findings, the registry data of POAG and exfoliation glaucoma patients in Finland and Norway found out that there is no proof that IHD rates vary in the two groups of patients (Tarkkanen et al.;[5] Ritland et al.[20]). A study in India included a sample of just 160 participants, and another study in Croatia comprised relatively young 50-year-old subjects; both were hospital-based investigations (Praveen et al.;[21] Brajković et al.[22]) that support the idea that PEX and IHD are not related. A population-based study from Spain found that PEX increased the OR for cardiovascular disease by 2%, but this increase was not statistically significant.[23] A study conducted to determine a statistical association between PEX and IHD in Icelandic families with three or more individuals aged 70 or older and at least one member with PEX found the result to be statistically insignificant.[24]

These seem to be in opposition to case–control research where ES was more prevalent in 50 patients sent for coronary angiography than in controls with matching ages and sexes (Citirik et al.).[25]

In our study, a statistically significant association between the PEX syndrome and systemic hypertension was observed. These findings were consistent with the findings of the two prior population-based investigations on systemic hypertension and PEX syndrome. According to these research studies, patients with PEX had a higher prevalence of systemic hypertension.[15,26] Several other research studies (Tarkkanen et al.;[5] Praveen et al.;[21] Viso et al.;[23] Brajković et al.;[22] Allingham et al.,[24] Citirik et al.[25]) found no appreciable difference between the rates of AH in PEX and non-PEX groups.

The proportion of PEX syndrome patients among DM II was marginal, the association between them too was not statistically significant. Similar to our study, a study done by Praveen et al.,[21] also showed no difference in diabetes rates between patients with and without PEX. In two more trials of various size and design, the result revealed no difference in the occurrence of DM between patients with and without ES. (Brajković et al.;[22] Allingham et al.[24]).

Limitations of the study

This was a study conducted in our medical college, a tertiary health care setting, as it was not feasible to conduct the study in the community setting due to constraints like time, cost, facility, etc. There might be a possibility of missing cases of PEX syndrome from the community, leading to an underreporting of the prevalence of the syndrome in the area. True prevalence that can be extrapolated to the entire population can only be obtained through a population-based house to house survey.

CONCLUSION

From our study, we can conclude that the prevalence of the PEX syndrome is noteworthy in the population age group of 45–70 years, that the cases of the syndrome increased with increasing age, and that males were more susceptible to the syndrome. Systemic hypertension was statistically significant with PEX. As the age of the study participants increases, the cases of PEX syndrome increase too. As a result, we believe that people over the age of 40 should have routine ophthalmological examinations to detect early changes in the eyes that can predict the development of PEX Syndrome later in life. Systemic hypertension is statistically associated with PEX. Patients who present to the hospital after being diagnosed with hypertension should be given a thorough ophthalmological examination to rule out PEX syndrome.

However, IHD and Type II DM were not found to be associated with PEX.

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JK- Definition of intellectual content, literature survey, prepared first draft of manuscript, implementation of study protocol, data collection, data analysis, and manuscript preparation; **AG**- Concept, design, clinical protocol, manuscript preparation, editing, and manuscript revision; **NT** and **AP**- Design of study, literature survey, statistical analysis and interpretation, manuscript preparation, and review and submission of article.

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