The association between pseudoexfoliation and metabolic syndrome, a case control study

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Abstract

Introduction: Pseudoexfoliation Syndrome (PXS) is a systemic disease which is characterized by creation of fibro-granular materials in the anterior segment of the eye. PXS is also known as a risk factor for vascular blockages in the arteries and veins of the retina. Given the existing information about PXS, the present study was done to perform a comparative study on the prevalence of metabolic syndrome in patients suffering PXS with control group

Methods: This case-control study was performed on 50 patients with PXS and 35 healthy people who are with patients referred to other clinics that were matched by sex and age with case groups. PXS was diagnosed with slit lamp by an ophthalmologist. Subjects checked for clinical examinations including blood pressure, height, weight, waist circumference by standard methods. A 12 hours fasted blood sample taken for determining Triglyceride, Cholesterol, HDL, LDL, and Fasting Blood Sugar. Metabolic syndrome defined according to the (NCEP ATP III) criteria. Data were entered into SPSS (Version22) and analyzed using chi-square test. Significance level of P was considered ≤0.05

Results: The mean age of participants were 70.24 ± 8.04 years, (71.34 ± 9.96 years in case and 68.68 ± 3.53 years in control groups) of whom 51.8% were male. Prevalence of metabolic syndrome was 36% in case and 28.6% in control group (p=0.47). Abnormal blood sugar in case group was more than control group (p-value<0.05, 132.96 ± 52.56 in case vs 104.20 ± 17.72 in control).

Conclusion: In this study, there is no significant correlation between the prevalence of metabolic syndrome and PXS that need to do various studies with larger sample sizes.

Introduction

In recent years, non-communicable diseases (NCD) in most countries have increased considerably [1]. Among diseases categorized as NCD, Diabetes mellitus (DM), obesity, and dyslipedimia are the most prevalent ones which have major effects on the level of health and quality of human life. Metabolic syndrome is a combination of dyslipidemia, hypertension, resistance to insulin, and obesity; this combination is a basic pathophysiology for atherosclerosis [2].

Metabolic syndrome is accompanied by higher risk of cardio-vascular diseases [3], stroke [4], skeletal system disorders such as osteoarthritis [5], eye disorders such as glaucoma, age-related cataract and age-related macular degeneration [6-8], as well as many other clinical conditions.

Recently researchers have suggested that there is a relationship between metabolic syndrome components and PXS. PXS is in fact progressive accumulation of abnormal extracellular febrile materials in anterior structure of the eye next to a non-ocular organ such as the skin or connective tissue of visceral organs [9-10]. Moreover, PXS is also known as a risk factor for vascular blockages in the arteries and veins of the retina, optic nerve and the auditory nerve. The relationship of PXS with vascular occlusions and other early retinal vascular disease has been also confirmed [11]. PXS is also known responsible for asymptomatic diastolic dysfunction in myocardium [12]. Dyslipidemia is also known as a risk factor in occurrence of cataract and the relationship of high blood cholesterol and triglyceride with age related cataract has been confirmed [13].

Based on literature regarding the potential role of PXS and components of metabolic syndrome, there is disagreement among scholars [14]. Therefore, the present study aims to do a comparative investigation on the prevalence of metabolic syndrome in patients suffering PXS with control group.

Methods

This study was a case-control which was done in ophthalmology clinic of Vali-e-Asr hospital from 2013 to 2014. Cases were selected from patients referring to ophthalmology clinic of Vali-e-Asr hospital. Participants who had inclusion criteria were selected and entered into the study after they were examined by an ophthalmologist using slit lamp. Control group was selected from the partners (healthy people who are with patients) referred to other clinics that were matched by sex and age with case groups. Exclusion criteria included steroid and anabolic hormones use.

Before implementation of the design, its protocol was approved in Ethics committee of University of Medical Sciences with code IR. BUMS.reC.1394.358. Then all subjects were informed about the objectives of the plan and they would give informed consent after

which they entered into the study. In this study patients who had been diagnosed by an ophthalmologist using slit lamp were included. Measurement of blood pressure, height, weight and waist circumstance were all done by a standard method. Then 5 cc of blood was taken from the right brachial vein after10-12 hours fasting was sent to Imam Reza hospital to measure blood glucose and serum lipid.

Data entered to SPSS (Version 22) and using descriptive statistics, chi-square and t-test for analyzing data. P-value as 0.05 was considered as statistically significant.

Results

In total, 85 people including 35 people in control group and 50 in case group entered into the study. There was no significant difference between age (71.34 ± 9.96 years in case and 68.68 ± 3.53 years in control groups, p=0.1) and sex (50% male in case group and 54.3% in control, p=0.4) of the two groups.

As shown in Table 1, mean FBS, cholesterol level, triglyceride, systolic and diastolic blood pressure were higher in PXS group compared to control group and only difference of FBS and systolic blood pressure were significant (p=0.003, p=0.04). Frequency of normal FBS was 48%, pre-diabetic 26%, and diabetic 26%.

Prevalence of dyslipidemia was 65.9% in the present study. Prevalence of dyslipidemia was higher in control group compared to PXS patients, but the difference was not significant (p=0.4). Prevalence of hypertension was 34.1% (36% in PXS patients and 31.4% in control group) which didn't show a significant difference (p=0.421).

Mean BMI was 24.10 ± 4.20. Prevalence of overweight and obesity was 14% and 10% in PXS group and 42.9% and 14.3% in control group which was statistically significant (p=0.012). Prevalence of metabolic disorder was 36% in PXS group and 28.6% in control group which was not statistically significant (p=0.316).

Prevalence of metabolic syndrome and its component according to metabolic definition show in Table 2. Prevalence of abnormal blood sugar was 48% (66% in PXS pateints and 38% in control group) respectively which showed a significant difference (p<0.05).

Discussion

In total, the results of the study showed that prevalence of metabolic syndrome was 36% in PXS group which doesn't have statistically difference with control group. Based on metabolic syndrome components, only prevalence of abnormal blood glucose was significantly higher in PXS group than control group.

Miyazaki *et al* and Citirik *et al.* [14,15] indicated in their study that frequency of DM in PXS patients was lower than normal people, but

Table 1. Comparing the mean values measured in the case and control group

Variables	Cases	Controls	P-value (T-test)
FBS	132.9 6 ± 52.56	104.20 ± 17.72	0.003*
Chol	191.74 ± 36.23	188.11 ± 42.02	0.72
TG	150.98 ± 79.72	137.48 ± 55.61	0.390
HDL	44.52 ± 11.54	48.14 ± 12.36	0.170
LDL	105.74 ± 29.67	111.88 ± 38	0.405
SBP	131.60 ± 23.46	122.71 ± 11.90	0.04*
DBP	78.12 ± 10.62	75.85 ± 7.71	0.124

FBS: Fasting Blood Sugar, Chol: Cholesterol, TG: Triglyceride, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, SBP: Systolic Blood Pressure, DBP: Diastolic Blood Pressure
*statistically significant

Table 2. The effect of various factors on psedoexfoliation

Variable	Odd ratio (95% CI)	Control	Cases	P-value
Metabolic syndrome	1.4 (0.55, 3.57)	10 (28.6)	18 (36)	P=0.47
Abnormal TG	0.8 (0.33, 1.97)	15 (42.9)	19 (38)	P=0.6
Abnormal HDL	1.9 (0.82, 4.80)	13 (37.1)	27 (54)	P=0.12
Abnormal FBS	2.91 (1.19, 7.12)	14 (40)	33 (66)	P=0.01
Abnormal BP	0.9 (0.39, 2.22)	16 (45.7)	22 (44)	P=0.8
Abnormal WC	0.54 (0.17, 1.68)	8 (22.9)	7 (14)	P=0.29

TG: Triglyceride, HDL: High Density Lipoprotein, FBS: Fasting Blood Sugar, BP: Blood Pressure, WC: Waist Circumstance

these findings were not statistically significant and was disagree with the present study. In the study of You *et al* and Jonas *et al,* [16,17] there was no significant relationship between DM and PXS. Speckauskas *et al.* [18] showed that prevalence of DM was 7.4% in PXS patients and 6.8% in others and the observed difference was not statistically significant.

Although prevalence of dyslipidemia was higher in control group than PXS group, but the difference was not significant. Along with our results, Miyazaki *et al.* [14] showed that prevalence of dyslipidemia was higher in PXS patients compared to normal people, but they have not found a significant difference either. In the study of You *et al.* [17] although there has been a significant relationship between HDL level and PXS, there has been no significant relationship between the levels of triglyceride, cholesterol, and LDL with PXS. Consistent with the results of the present study, Jonas *et al.* [16] showed that presence of PXS didn't have a significant relationship with HDL (p=0.74) and Cholesterol (p=0.20). Consistent with the results of the present study, in the study of Turkylmaz *et al.* [19] mean level of total cholesterol was higher in case group compared to control group, while mean level of HDL was lower and mean level of LDL and triglyceride was higher in case group than control group; however, none of these differences have been significant.

Mean systolic and diastolic blood pressure and also prevalence of hypertension was higher in case group compared to control group, that systolic blood pressure was statistically significant. Like the results of the present study, Romero-Aroca *et al.* [20] indicated that despite higher prevalence of hypertension in PXS patients, there was no significant difference between two groups (OR=1.441). Consistent with the results of the present study, Miyazaki *et al.* [14] in a study performed in Japan found that prevalence of hypertension was significantly higher in PXS patients (50.2% compared to 42%, p<0.05) and hypertension in people suffering this syndrome was 1.41 times more than normal people. You *et al* and Jonas *et al.* [16,17] indicated that overall prevalence of PXS was significantly related to higher systolic and diastolic blood pressure. Despite the result of this study and other studies done in this regard, Citirik *et al.* [15] have shown that prevalence of hypertension in PXS patients was less than normal people, but this difference was not statistically significant. These contradictory results can be attributed to selection of method or small sample size.

In the present study, prevalence of overweight and obesity was statistically higher in control group compared to PXS group. Along with this study, You *et al.* and Jonas *et al.* [14,17] reported prevalence of PXS was significantly associated with lower BMI and body weight. According to Miyazaki *et al.* [14] mean BMI was higher in PXS patients compared to normal people, although this finding was not statistically significant, it was against our results. Different results in these studies or sometimes observing results without scientific justification such as higher prevalence of BMI in normal people could be due to small sample size.

In investigating literature there was no study which had investigated association of metabolic syndrome and PXS. However, different studies have investigated the effects of different components of metabolic syndrome and its complications regarding PXS. Prevalence of coronary disease was investigated as one of metabolic syndrome complications [21-24]. In Andrikopoulos *et al.* [11] study, the prevalence of coronary diseases was 19.1% in PXS patients and 11.5% in normal people respectively. As it has been mentioned, regarding the effect of metabolic syndrome components on PXS, there are different confirming studies [14,16,17,20].

Conclusion

In total, it concluded that despite high prevalence of metabolic syndrome and its components in PXS patients, there is no significant relationship except abnormal blood glucose. It is suggested that in the future studies a bigger sample size is considered, while presence or absence of heart coronary diseases or cerebrovascular accidents and other risk factors should be also evaluated.

Acknowledgement

References

1. Kazemi T, Nik M1 (2015) "World heart day 2014", Significance of cardiovascular diseases in east of Iran. *J Res Med Sci* 20: 423. [Crossref]

2. Tabatabaei-Malazy O, Qorbani M, Samavat T, Sharifi F, Larijani B, et al. (2014) Prevalence of dyslipidemia in Iran: a systematic review and meta-analysis study. *Int J Prev Med* 5. [Crossref]

3. Nikolopoulou A, Kadoglou NP (2012) Obesity and metabolic syndrome as related to cardiovascular disease. *Expert Rev Cardiovasc Ther* 10: 933-939. [Crossref]

4. Farooqui AA (2013) Metabolic syndrome: an important risk factor for stroke, Alzheimer disease, and depression: *Springer Science & Business Media.*

5. Eymard F, Edwards M, Parsons C, Cooper C, Petit-Dop F, et al. (2014) Impact of components of the metabolic syndrome on knee osteoarthritis progression in the SEKOIA study. *Osteoarthritis and Cartilage* 22: S376.

6. Ghaem Maralani H, Tai BC, Wong TY, Tai ES, Li J, et al. (2015) Metabolic syndrome and risk of age-related macular degeneration. *Retina* 35: 459-466. [Crossref]

7. Park Y-H, Shin JA, Han K, Yim HW, Lee W-C, et al. (2014) Gender difference in the association of metabolic syndrome and its components with age-related cataract: the Korea National Health and Nutrition Examination Survey 2008-2010. *PLoS One* 9: e85068. [Crossref]

8. Kim M, Jeoung JW, Park KH, Oh WH, Choi HJ, et al. (2014) Metabolic syndrome as a risk factor in normal-tension glaucoma. *Acta Ophthalmol* 92: e637-643. [Crossref]

9. Conway RM, Schlötzer-Schrehardt U, Küchle M, Naumann GO (2004) Pseudoexfoliation syndrome: pathological manifestations of relevance to intraocular surgery. *Clin Exp Ophthalmol* 32: 199-210. [Crossref]

10. Ritch R, Schlötzer-Schrehardt U (2001) Exfoliation syndrome. *Surv Ophthalmol* 45: 265-315. [Crossref]

11. Andrikopoulos G, Mela E, Georgakopoulos C, Papadopoulos G, Damelou A, et al. (2009) Pseudoexfoliation syndrome prevalence in Greek patients with cataract and its association to glaucoma and coronary artery disease. *Eye* 23: 442-447. [Crossref]

12. Akdemir MO, Sayin MR, Armut M, Akpinar I, Ugurbas SH (2014) Pseudoexfoliation syndrome and coronary artery ectasia. *Eye (Lond)* 28: 594-599. [Crossref]

13. Heydari B, Kazemi T, Zarban A, Ghahramani S (2012) Correlation of cataract with serum lipids, glucose and antioxidant activities a case-control study. *West Indian Med J* 61: 230-234. [Crossref]

14. Miyazaki M, Kubota T, Kubo M, Kiyohara Y, Iida M, et al. (2005) The prevalence of pseudoexfoliation syndrome in a Japanese population: the Hisayama study. *J Glaucoma* 14: 482-484. [Crossref]

15. Citirik M, Acaroglu G, Batman C, Yildiran L, Zilelioglu O (2007) A possible link between the pseudoexfoliation syndrome and coronary artery disease. *Eye (Lond)* 21: 11-15. [Crossref]

16. Jonas JB, Nangia V, Matin A, Bhojwani K, Sinha A, et al. (2013) Pseudoexfoliation: normative data and associations. The central India eye and medical study. *PloS one* 8: e76770. [Crossref]

17. You QS, Xu L, Wang YX, Yang H, Ma K, et al. (2013) Pseudoexfoliation: normative data and associations: the Beijing eye study 2011. *Ophthalmology* 120: 1551-1558. [Crossref]

18. Speckauskas M, Tamosiunas A, Jašinskas V (2012) Association of ocular pseudoexfoliation syndrome with ischaemic heart disease, arterial hypertension and diabetes mellitus. *Acta ophthalmologica* 90.

19. Türkyilmaz K, Oner V, CiÃ§ek Y, Kurt A, DurmuÅŸ M (2014) Systemic arterial stiffness in patients with pseudoexfoliation glaucoma. *J Glaucoma* 23: e108-111. [Crossref]

20. Romero-Aroca P, Masip-Serra R, Martínez-Salcedo I, Salvat-Serra M, Fernández-Ballart J, et al. (2011) High prevalence of pseudoexfoliation syndrome and its complications in Tarragona in northeast Spain. *Eur J Ophthalmol* 21: 580. [Crossref]

21. Gami AS, Witt BJ, Howard DE, Erwin PJ, Gami LA, et al. (2007) Metabolic syndrome and risk of incident cardiovascular events and death: a systematic review and meta-analysis of longitudinal studies. *J Am Coll Cardiol* 49: 403-414. [Crossref]

22. Bayturan O, Tuzcu EM, Lavoie A, Hu T, Wolski K, et al. (2010) The metabolic syndrome, its component risk factors, and progression of coronary atherosclerosis. *Arch Intern Med* 170: 478-484. [Crossref]

23. Eddy D, Schlessinger L, Heikes K (2008) The metabolic syndrome and cardiovascular risk: implications for clinical practice. *Int J Obes (Lond)* 32: S5-S10. [Crossref]

24. Strange RC, Shipman KE, Ramachandran S (2015) Metabolic syndrome: A review of the role of vitamin D in mediating susceptibility and outcome. *World J Diabetes* 6: 896-911. [Crossref]