Ocular associations of metabolic syndrome

Rupali Chopra, Ashish Chander, Jubbin J. Jacob
Departments of Ophthalmology and Medicine, Christian Medical College, Ludhiana, India

ABSTRACT

Metabolic syndrome is a cluster of diseases including central obesity, dyslipidemia, hyperglycemia, and high blood pressure. People with metabolic syndrome have been shown to be at an increased risk of developing cardiovascular disease, beyond the risk associated with individual components of the syndrome. The association of diabetes and hypertension with retinopathy, cataract, and raised intraocular pressure is well known. This review highlights the association of metabolic syndrome, including all its components, with various ocular conditions such as retinopathy, central retinal artery occlusion, cataracts, and raised intraocular pressure.

Key words: Cataract, central retinal artery occlusion, intraocular pressure, metabolic syndrome, retinopathy

INTRODUCTION

Almost all patients with diabetes/pre-diabetes and concomitant cardiovascular disease (CVD) risk factors of hypertension, obesity, and dyslipidemia also have insulin resistance.[1] The clustering of these risk factors in a single patient has been termed the metabolic syndrome. The components of metabolic syndrome include abdominal obesity, diabetes, glucose intolerance, dyslipidemia, high blood pressure, and hyperuricemia.[2] The association of diabetes and hypertension with ocular conditions such as retinopathy,[3] cataract,[4] and raised intraocular pressure (IOP)[5,6] is well known. Metabolic syndrome is increasingly being recognized as a distinct identity and this review is an attempt to highlight the association between metabolic syndrome and various ocular conditions such as non-diabetic retinopathy, cataract, and primary open angle glaucoma.

DIAGNOSTIC CRITERIA FOR METABOLIC SYNDROME

According to the National Cholesterol Education Program (NCEP) guidelines, the metabolic syndrome is based on the presence of three of the following five risk factors[7]:

• Abdominal obesity (waist circumference >40 inches in men, >35 inches in women)
• Plasma triglycerides 150 mg/dL
• Plasma high density lipoprotein (HDL) cholesterol <40 mg/dL in men and <50 mg/dL in women
• Blood pressure 130/85 mmHg
• Fasting plasma glucose 110 mg/dL.

Epidemiology

The syndrome is increasingly being recognized as a distinct entity affecting a large proportion of US adult population.[8] The prevalence of metabolic syndrome as defined by the NCEP guidelines has been estimated using the National Health and Nutritional Examination Survey (NHANES) database.[8] Based on the data from NHANES collected between 1999 and 2002, the prevalence of metabolic syndrome is 34.5%.[9] The prevalence of metabolic syndrome in our country ranges from 20 to 55%. Much higher prevalence is seen among people in urban areas and those from higher socioeconomic strata.[10]

OCULAR ASSOCIATIONS OF METABOLIC SYNDROME

Retinal microvascular signs

Persons with metabolic syndrome are known to be at risk of developing large vessel atherosclerotic disease.[11] Characteristics of large and small vessel disease such
as inflammation and endothelial dysfunction have been reported to be associated with metabolic syndrome.\textsuperscript{[13]} The association of diabetes and hypertension with retinopathy and other microvascular changes is well known.\textsuperscript{[3]} Recent studies have shown that these retinal vascular signs are also associated with systemic markers of inflammation and endothelial dysfunction.\textsuperscript{[13]} In a population-based cross-sectional study involving 11,265 persons, retinal photographs were taken and graded for the presence of retinal microvascular signs. The data showed that persons with metabolic syndrome were significantly more likely to have retinopathy, arteriovenous nicking, focal arteriolar narrowing, smaller retinal arteriolar diameters, and larger retinal venular diameters than people without the syndrome, independent of age, gender, race, education, cigarette smoking, and alcohol consumption. With the exception of retinopathy, most associations were significant even in people without diabetes or hypertension, suggesting that factors other than hyperglycemia and high blood pressure (i.e. dyslipidemia, obesity, and inflammation) may explain the occurrence of these retinal lesions.\textsuperscript{[14]}

In another study conducted among Japanese adults, the various components of the metabolic syndrome were found to be associated with retinal microvascular signs: a larger waist circumference was associated with wider venular diameter and retinopathy lesions; a higher blood pressure level was associated with focal arteriolar narrowing, arteriovenous nicking, enhanced arteriolar wall reflex, and narrower arteriolar diameter; and a higher triglyceride level was associated with enhanced arteriolar wall reflex. Overall, persons with the metabolic syndrome were more likely to have retinopathy (odds ratio 1.64, 95% CI: 1.02–2.64) and wider venular diameter of 4.69 μm (95% CI: 1.20–8.19 μm) than persons without the metabolic syndrome in this study.\textsuperscript{[13]}

The association between metabolic syndrome and retinopathy was also studied in persons 40 years of age and older with gradable fundus photographs in the NHANES III. However, in this population-based cross-sectional study, there was no evidence of an association between the metabolic syndrome and retinopathy independent of diabetic status.\textsuperscript{[18]} Thus, prospective studies are warranted to determine the causal link between metabolic syndrome and the risk of retinopathy and other microvascular changes.

Obesity, one of the major components of metabolic syndrome, has been shown to be associated with retinopathy signs in the general and non-diabetic population.\textsuperscript{[17]} In the Hoorn Study in the Netherlands, waist–hip ratio was independently associated with a number of incident retinopathy signs including retinal hemorrhages, microaneurysms, hard exudates, and cotton wool spots in the non-diabetic general population, although the association with body mass index (BMI) failed to achieve a statistical significance.\textsuperscript{[18]} Vasoproliferative factors such as vascular endothelial growth factor (VEGF) have been proposed to have a role in the pathogenesis of diabetic retinopathy.\textsuperscript{[19]} The concentrations of serum angiogenic factors such as VEGF have been observed to be elevated in obese humans.\textsuperscript{[20]} These findings provide a potential link between obesity and retinopathy. Moreover, oxidative stress also contributes to development of diabetic retinopathy by inducing overexpression of VEGF.\textsuperscript{[21]} Obesity increases oxidative stress because of its associated hyperleptinemia.\textsuperscript{[22]}

Central retinal artery occlusion

It is one of the most sudden and dramatic events seen by the ophthalmologist. Patients usually present with a sudden painless loss of vision. The appearance of a cherry-red spot in the fundus is the main characteristic. The cherry-red spot appears because soon after the obstruction of the blood flow to the inner retina, the normally transparent retina becomes opaque and blocks the brownish-red color from the underlying choroid, which is still supplied by blood. Because the retina overlying the foveola is relatively thin, however, the normal color of the choroid is still visible in this area.

Possible risk factors for the development of central retinal artery occlusion (CRAO) [Figure 1] are arteriosclerosis, chronic atrial fibrillation, congestive heart failure, cerebrovascular accident, systemic hypertension, myocardial infarction, diabetes mellitus, primary open angle glaucoma, and rheumatic heart disease.\textsuperscript{[23]}

Our literature search reveals two case reports of CRAO wherein the patients met all the five NCEP criteria of...
metabolic syndrome. The pro-inflammatory markers were found to be raised in both the cases. Low-grade inflammation has been identified as a pivotal pathogenic factor for development of atherosclerosis and has been shown to predict myocardial infarction and stroke in patients with preexisting CVD. Increased C-reactive protein (CRP) is associated with an increase risk of CVD. CRP may also be an important marker for complications of metabolic syndrome such as CRAO. The most common risk factors for CRAO are present in metabolic syndrome. Thus, metabolic syndrome can result in CRAO causing profound visual loss. Other than these isolated case reports, our literature search did not reveal any prospective studies linking metabolic syndrome with CRAO. However, obesity has been recognized as a significant risk for retinal vein occlusion in few studies. Moreover, retinal venous and arterial occlusions are known to be associated with hypertension, diabetes mellitus, and hyperviscosity syndromes. There is evidence supporting association of obesity with diabetes, hypertension, and hypercoagulable disorders, thus providing a possible association between obesity and retinal occlusive diseases.

Age-related maculopathy
The relationship between age-related maculopathy (ARM) and obesity has been investigated in several studies. The Age Related Eye Disease Study (AREDS) has reported a cross-sectional association between higher BMI and more advanced ARM as documented from fundus photographs. Obesity increases systemic oxidative stress secondary to hyperleptinemia, and oxidative stress is known to play an important role in the pathogenesis of ARM.

Age-related cataract
Cataract, a leading cause of blindness and poor vision, is a major public health problem worldwide, particularly in Asia, home to half of the world’s population. Diabetes and hyperglycemia have long been recognized as risk factors for cataract. Various studies conducted in the Western and Asian populations have shown an association between metabolic syndrome and cataract. In the Singapore Malay Eye Study, the prevalence of cataract increased with increasing number of metabolic syndrome components in both men and women. In this study, metabolic syndrome and two of its principal components, diabetes and high BP, were significantly associated with cataract, assessed from lens photographs in a standardized manner. Coexisting diabetes and high BP were associated with fourfold higher odds of cataract. Serum triglycerides, HDL, and BMI were not found to be associated with cataract in this study. Mechanisms linking diabetes and hyperglycemia to cataract formation include advanced glycation of lens proteins and hyperosmotic effects of sorbitol on lens fibers formed through the aldose reductase pathway. The mechanism linking hypertension and cataract is not clear. Inflammation and endothelial dysfunction could possibly play a role in the association between hypertension and cataract.

Amongst the Western studies, Tan et al. have shown that metabolic syndrome is associated with all the three types of cataract (nuclear, cortical, and posterior subcapsular) in an elderly cohort of Australians in the Blue Mountain Eye study. Paunksnis et al. have also reported an association between cataract and metabolic syndrome among middle-aged European men and women. Further, metabolic syndrome, its components, and their combination were found to be associated with an increased risk of cataract extraction in an Italian hospital population and among Swedish women aged <65 years.

Obesity, an important component of metabolic syndrome, has been proposed to be a risk factor for cataract development, though the exact mechanisms are unclear. The Physicians Health Study, a randomized trial of 22,071 healthy male American physicians aged 40–84 years, reported both overall obesity, measured as BMI, and abdominal obesity as independent risk factors for cataract. Prospective data from Framingham Eye Study also demonstrate an independent association between greater BMI and higher incidence of cortical cataract and posterior subcapsular opacities. Several pathophysiological mechanisms have been proposed to explain the association of obesity and cataract. Leptin, a cytokine expressed and secreted mainly by adipocytes, is involved in the molecular mechanisms underlying cataract formation. Individuals with obesity are likely to have hyperleptinemia and leptin resistance. Thus, hyperleptinemia associated with obesity may promote cataract formation. These studies highlight the importance of tackling metabolic syndrome and its components for the prevention of cataract.

Primary open angle glaucoma
IOP is the only modifiable risk factor for primary open angle glaucoma. IOP is determined by the balance between aqueous humor secretion and outflow. Many cross-sectional and longitudinal epidemiological studies have reported association of elevated IOP with cardiometabolic risk factors such as type 2 diabetes mellitus, hypertension, and concurrent atherosclerotic disease, thereby suggesting a common underlying mechanism linking elevated IOP to various cardiometabolic factors. Chang et al. analyzed the clinical data of 1112 patients undergoing health checkup and concluded that participants with metabolic syndrome had significantly higher IOP than those without metabolic syndrome. Each additional component of metabolic syndrome was associated with
a mean increase in IOP of 0.33 mm Hg. Their findings were consistent with those reported by Oh et al.\[^{49}\] in the Korean population.

The mechanism by which metabolic syndrome is associated with IOP is currently unknown. Recent research has revealed some pathophysiological links such as sympathetic stimulation, endocannabinoid overactivity, and aquaporins. Sympathetic hyperstimulation is a common feature of obesity, hypertension, and insulin resistance.\[^{49}\] Stimulation of oculociliary sympathetic nerve also increases IOP.\[^{50}\]

Similarly, endocannabinoid overactivity contributes to the development of abdominal obesity, dyslipidemia, and hyperglycemia. In rodents, endocannabinoid receptors have been found in the trabecular meshwork where they regulate aqueous outflow and thus influence IOP.\[^{51}\] Aquaporin is a family of small membrane proteins that transport water and small molecules. They are present in various human tissues including trabecular meshwork in the eye, adipose tissue, liver, and pancreas. Aquaporins have been shown to increase aqueous fluid secretion across ciliary epithelium and regulate IOP.\[^{52}\]

Unexpectedly, aquaporin knockout mice were obese and developed severe insulin resistance, pointing toward another possible link between IOP and metabolic syndrome.\[^{53}\]

Population-based data from several studies have demonstrated independent cross-sectional association between obesity and ocular hypertension. The Beaver Dam Eye Study reported a significantly positive association of IOP with several factors including BMI.\[^{54}\]

Obesity exerts an effect on IOP by causing excessive intraorbital adipose

| Table 1: Associations of metabolic syndrome with eye disorders |
|---------------------------------|-----|---------------------------------|
| **Author**                      | **Study, year** | **Title**                                  | **Inference**                                                                 |
| Metabolic syndrome and retinopathy |             |                                              |                                                                                 |
| Wong et al.                     | 2004 | Associations between the metabolic syndrome and retinal microvascular signs | Individuals with metabolic syndrome were significantly more likely to have retinopathy, arteriovenous nicking, focal arteriolar narrowing, smaller retinal arteriolar diameters, and larger retinal venular diameters |
| Kawasaki et al.                | The Funagata Study, 2008 | The metabolic syndrome and retinal microvascular signs in a Japanese population | Metabolic syndrome was found to be associated with retinal microvascular signs like focal arteriolar narrowing, arteriovenous nicking, enhanced arteriolar wall reflex and narrower arteriolar diameter |
| Keenan et al.                   | 2009 | Retinopathy in non-diabetic persons with the metabolic syndrome | There was no evidence of an association between the metabolic syndrome and retinopathy independent of diabetic status |
| Van leiden et al.               | Hoorn Study, 2003 | Risk factors for incident retinopathy in a diabetic and non-diabetic population | Waist–hip ratio is associated with incident retinopathy signs |
|                                | Age Related Eye Disease Study, 2001 | Risk factors associated with macular degeneration | Higher BMI is associated with more advanced age-related maculopathy |
| Metabolic syndrome and cataract |             |                                              |                                                                                 |
| Sabanayagam et al.             | Singapore Malay Eye Study, 2011 | Metabolic syndrome components and age-related cataract | Metabolic syndrome is significantly associated with age-related cataract |
| Tan et al.                     | Blue Mountain Eye Study, 2008 | Influence of diabetes and cardiovascular disease on long-term incidence of cataract | Metabolic syndrome is associated with all three type of cataract – nuclear, cortical, and posterior subcapsular |
| Paunksnis et al.               | 2007 | Relationship between cataract and metabolic syndrome in middle-aged European men and women | Metabolic syndrome and its components are associated with metabolic syndrome |
| Galeone et al.                 | 2010 | Metabolic syndrome and age-related cataract extraction: A case–control study in Italy | Metabolic syndrome is associated with increased risk of cataract extraction |
| Metabolic syndrome and primary open angle glaucoma |             |                                              |                                                                                 |
| Chang et al.                    | 2010 | Association of intraocular pressure with metabolic syndrome and novel cardiometabolic risk factors | Participants with metabolic syndrome had significantly higher IOP than those without metabolic syndrome |
| Oh et al.                      | 2005 | Elevated intraocular pressure is associated with insulin resistance and metabolic syndrome | Elevated intraocular pressure is associated with metabolic syndrome in Korean population |
tissue, increased blood viscosity, increased episcleral venous pressure, and impairment of aqueous outflow facility.\(^{[55]}\) Also, obesity has been shown to cause vascular endothelial dysfunction and autonomic dysfunction.\(^{[56]}\) This may cause abnormal ocular blood flow and perfusion instability leading to impaired vascular supply to the optic nerve head and glaucomatous changes.\(^{[57]}\) Data from various studies is summarized in Table 1.

**Miscellaneous**

Obesity has also found to be related to oculomotor nerve palsy and recurrent lower lid entropion.\(^{[58,59]}\) Obstructive sleep apnea syndrome, a comorbid condition related to obesity, which has been associated with papilledema,\(^{[60]}\) and floppy eyelid syndrome.\(^{[61]}\)

**Conclusion**

The prevalence of the metabolic syndrome is rapidly increasing worldwide due to the sedentary lifestyles. Its association with various ocular manifestations such as non-diabetic retinopathy, CRAO, cataract, and primary open angle glaucoma suggests that an epidemic of metabolic syndrome can have far-fetched ocular consequences as well. Amelioration of metabolic syndrome may have a therapeutic role in preventing these ocular conditions. However, most of the studies done in this regard were cross-sectional studies, and thus a causal relationship cannot be proven. Prospective, interventional studies are required to determine the causal association between metabolic syndrome, its components, and various ocular manifestations such as retinal microvascular signs, cataract, and primary open angle glaucoma.

**References**

1. Bonora E, Kiechl S, Willeit J, Oberhollenzer F, Egger G, Targher G, et al. Prevalence of insulin resistance in metabolic disorders: The Bruneck Study. Diabetes 1998;47:1643-9.
2. Meigs JB. Invited commentary: Insulin resistance syndrome? Syndrome X? Multiple metabolic syndrome? A syndrome at all? Factor analysis reveals patterns in the fabric of correlated metabolic risk factors. Am J Epidemiol 2000;152:908-11.
3. Wong TY, Klein R, Klein BE, Tielsch JM, Hubbard LD, Nieto FJ. Retinal microvascular abnormalities and their relations with hypertension, cardiovascular disease and mortality. Surv Ophthalmol 2001;46:59-80.
4. Tan JS, Wang JJ, Mitchell P. Influence of diabetes and cardiovascular disease on the long term incidence of cataract: The Blue Mountains eye study. Ophthalmic Epidemiol 2008;15:317-27.
5. Mitchell P, Smith W, Chey T, Healy PR. Open angle glaucoma and diabetes: The Blue Mountain eye study, Australia. Ophthalmology 1997;104:712-18.
6. Dielemans I, Vingerling JR, Algra D, Hofman A, Grobbee DE, de Jong PT. Primary open angle glaucoma, intraocular pressure, and systemic blood pressure in the general elderly population. Ophthalmology 1995;102:54-60.
7. National Cholesterol Education Program (NCEP) Expert panel on the Detection, Evaluation and Treatment of high blood cholesterol in adults (Adult Treatment Panel III). Third report of the National Cholesterol Education Program (NCEP) Expert panel on the Detection, Evaluation and Treatment of high blood cholesterol in adults (Adult Treatment Panel III). Final report. Circulation 2002;106:3143-421.
8. Ford ES, Giles WH, Dietz WH. Prevalence of the metabolic syndrome among US adults: Findings from the third National Health and Nutrition Examination Survey. JAMA 2002;287:356-9.
9. Ford ES. Prevalence of the metabolic syndrome defined by the International Diabetes Federation among adults in the US. Diabetes Care 2005;28:2745-9.
10. Misra A, Khurana L. Obesity and the metabolic syndrome in developing countries. J Clin Endocrinol Metab 2008;93 (11 Suppl 1):S9-30.
11. Golden SH, Folsom AR, Coresh J, Sherratt AR, Szlo M, Brancati FL. Risk factor groupings related to insulin resistance and their synergistic effects on subclinical atherosclerosis: The Atherosclerosis Risk in Communities Study. Diabetes 2002;51:3069-76.
12. Duncan BB, Schmidt MI, Pankow JS, Boerwinkle E. Low grade systemic inflammation and the development of type 2 diabetes: The Atherosclerosis Risk in Communities Study. Diabetes 2003;52:1799-805.
13. Klein R, Sherratt AR, Klein BE, Chambless LE, Cooper LS, Hubbard LD, et al. Are retinal arteiolar abnormalities related to atherosclerosis? The Atherosclerosis Risk in Communities Study. Arterioscler Thromb Vasc Biol 2000;20:1644-50.
14. Wong TY, Duncan BB, Golden SH, Klein R, Couper DJ, Klein BE, et al. Associations between the metabolic syndrome and retinal microvascular signs: Atherosclerosis Risk in Communities Study. Invest Ophthalmo Vis Sci 2004;45:2949-54.
15. Kawasaki R, Tielsch JM, Wang JJ, Wong TY, Mitchell P, Tano Y, et al. The metabolic syndrome and retinal microvascular signs in a Japanese population: The Funagata Study. Br J Ophthalmol 2008;92:161-6.
16. Keenan JD, Fan AZ, Klein R. Retinopathy in non diabetic persons with the metabolic syndrome: Findings from the Third National Health and Nutrition Examination Survey. Am J Ophthalmol 2009;147:934-44.
17. Cheung N, Wong TY. Obesity and eye diseases. Surv Ophthalmol 2007;52:180-95.
18. Van Leiden HA, Dekker JM, Moll AC. Risk factors for incident retinopathy in a diabetic and non diabetic population; the Hoorn study. Arch Ophthalmo 2003;121:245-51.
19. Aiello LP, Avery RL, Arrigg PG. Vascular endothelial growth factor is associated with visceral fat accumulation in human obesity subjects. Diabetologia 2003;46:1483-8.
20. Miyazawa S, Takahashi K, Bujo H. Elevated serum vascular endothelial growth factor in ocular fluid of patients with diabetic retinopathy and other retinal disorders. N Engl J Med 1994;331:1480-7.
21. Caldecott RB, Bartoli M, Behzadian MA. Vascular endothelial growth factor and diabetic retinopathy: Role of oxidative stress. Curr Drug Targets 2005;6:511-24.
22. Bouloumine A, Marummo T, Lafontan M. Leptin induces oxidative stress in human endothelial cells. FASEB J 1999;13:1231-8.
23. Mangat HS. Retinal artery Occlusion. Surv Ophthalmol 1995;40:145-56.
24. Kosanovic-Jakovcic N, Petrovic L, Risnic D, Milenkovic S, Danica M.
Metabolic syndrome and central retinal artery occlusion. Vojnosanit Pregl 2005;62:935-8.

25. Celic SP, Petkovic T, Stankovic-Babic GL, Mrsic JM. Central retinal artery occlusion in a patient with Metabolic Syndrome X. J Ophthalmol Vis Res 2010;5:57-60.

26. Alexander RW. Inflammation and coronary artery disease. N Engl J Med 1994;331:468-9.

27. Haverkate F, Thompson SG, Pyle SD, Gallimore JR, Pepys MB. Production of C-reactive protein and risk of coronary events in stable and unstable angina. European concerted Action on Thrombosis and Disabilities Angola Rectorius Study Group. Lancet 1997;349:462-6.

28. Backhouse O, Parapia L, Mahomed I. Familial thrombophilia and retinal vein occlusion. Eye 2000;14:13-7.

29. Lahey JM, Kearney JJ, Tune M. Hypercoagulable states and central retinal vein occlusion. Curr Opin Pulm Med 2003;9:385-92.

30. Abramson N, Abramson S. Hypercoagulable: Clinical assessment and treatment. South Med J 2001;94:1013-20.

31. Risk factors associated with age related macular degeneration. A case control study in the age related eye disease study: Age Related Eye Disease Study Report Number 3. Ophthalmology 2000;107:2224-32.

32. Congdon NG, Friedman DS, Lietman T. Important causes of visual impairment in the world today. JAMA 2003;290:2057-60.

33. Sabanayagam C, Wang JJ, Mitchell P, Tan ES, Aung T, et al. Metabolic syndrome components and age related Cataract: The Singapore Malay Eye Study. Invest Ophthalmol Vis Sci 2011;52:2397-404.

34. Stitt AW. Advanced glycation: An important pathological event in diabetic and age related ocular disease. Br J Ophthalmol 2001;85:746-53.

35. Klein BE, Klein R, Lee KE, Knudtson MD, Tsai MY. Markers of inflammation, vascular endothelial dysfunction and age related cataract. Am J Ophthalmol 2006;141:116-22.

36. Paunkanis A, Bojarskiené F, Cimbalaš A, Cerniauskiene LR, Luksiene M. Endothelin–I plasma concentration in children and adolescents with atherogenic risk factors. Kardiol Pol 2004;61:329-38.

37. Galeone C, Petracci E, Pelucchi C, Zucchetto A, Lai VC, Tavani A. Metabolic syndrome, its components and risk of age related cataract extraction: A case control study in Italy. Ann Epidemiol 2010;20:380-4.

38. Lindblad BE, Hakansson N, Philipson B, Wolk A. Metabolic syndrome components in relation to risk of cataract extraction: A prospective cohort study of women. Ophthalmology 2008;115:1649-54.

39. Glynn RJ, Christen WG, Manson JE, Bernheimer J, Hennekens CH. Body mass index. An independent predictor of cataract. Arch Ophthalmol 1995;113:1131-7.

40. Hiller R, Podgor MJ, Sperduto RD, Nowroozi L, Wilson PW, Calton T, et al. A longitudinal study of body mass index and lens opacities. The Framingham Studies. Ophthalmology 1998;105:1244-50.

41. Gomez-Ambrosi J, Salvador J, Frühbeck G. Is hyperleptinemia involved in the development of age related lens opacities? Am J Clin Nutr 2004;79:888-9.

42. Narin F, Atebak ME, Karakulcu M, Narin N, Kurtoglu S, Gumus H, et al. The association of plasma homocysteine levels with serum leptin and apolipoprotein B levels in childhood obesity. Ann Saudi Med 2005;25:209-14.

43. Lazoza C, Garcia-Feijoo J, Castillo A, Perea J, Martinez-Casa JM, Garcia-Sanchez J. Impact of intraocular pressure after filtration surgery on visual field progression in primary open angle glaucoma. Eur J Ophthalmol 2007;17:357-62.

44. Civan MM, Macknight AD. The ins and outs of aqueous humour secretion. Exp Eye Res 2004;78:625-31.

45. Lee JS, Lee SH, Oum BS, Chung JS, Cho BM, Hong JW. Relationship between intraocular pressure and systemic health parameters in a Korean population. Clin Experiment Ophthalmol 2002;30:237-41.

46. Memarzadeh F, Ying-Lai M, Aziz SP, Varma R. Associations with intraocular pressure in Latinos: The Los Angeles Latino Eye Study. J Ophthalmol 2008;2008:146:69-76.

47. Chang YC, Lin JW, Wang LC, Chen HM, Hwang JJ, Chuang LM. Associations of intraocular pressure with the metabolic syndrome and novel cardiometabolic risk factors. Eye 2010;24:1037-43.

48. Oh SW, Lee S, Park C, Kim DJ. Elevated intraocular pressure is associated with insulin resistance and metabolic syndrome. Diabetes Metab Res Rev 2005;21:434-40.

49. Mancia G, Bousquet P, Eigozi JL, Esler M, Grassi G, Julius S, et al. The sympathetic nervous system and the metabolic syndrome. J Hypertens 2007;25:909-20.

50. Belmonte C, Bartels SP, Liu JH, Neufeld AH. Effects of stimulation of the ocular sympathetic nerves on IOP and aqueous humor flow. Invest Ophthalmol Vis Sci 1987;28:1649-54.

51. Jarvinen T, Pate DW, Laine K. Cannabinoids in the treatment of glaucoma. Pharmacol Ther 2002;95:203-20.

52. Verkman AS. Role of aquaporin water channels in eye function. Exp Eye Res 2003;76:137-43.

53. MacDougall OA, Burant CF. Obesity and metabolic perturbations after loss of aquaporin 7, the adipose glycerol transporter. Proct Natl Acad Sci U S A 2005;102:10759-60.

54. Klein BE, Klein R, Linton KL. Intraocular pressure in Latinos: The Los Angeles Latino Eye Study. Invest Ophthalmol Vis Sci 1992;33:2224-8.

55. Shiode Y, Kawase Y. A new approach to stratified normal intraocular pressure in a general population. Am J Ophthalmol 1986;101:714-21.

56. Glowinska B, Urban M, Hryniewicz A, Peczynska J, Florya B, Hwisch M. Endothelin–I plasma concentration in children and adolescents with atherogenic risk factors. Kardiol Pol 2004;61:329-38.

57. Broadway DC, Drance SM. Glaucoma and vasospasm. Br J Ophthalmol 1998;82:862-70.

58. Teuscher AU, Meineberg O. Ischaemic oculomotor nerve palsy. Clinical features and vascular risk factors in 23 patients. J Neurol 1985;232:144-9.

59. Raina J, Foster JA. Obesity as a cause of mechanical entropion. Am J Ophthalmol 1996;122:123-5.

60. Purvin VA, Kawasaki A, Yee RD. Papilledema and obstructive sleep apnea syndrome. Arch Ophthalmol 2000;118:1626-30.

61. McNab AA. The eye and sleep. Clin Exp Ophthalmol 2005;33:117-25.

Cite this article as: Chopra R, Chander A, Jacob JJ. Ocular associations of metabolic syndrome. Indian J Endocr Metab 2012;16:S6-11.

Source of Support: Nil, Conflict of Interest: None declared.