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Associations of primary open-angle glaucoma and metabolic syndrome: A review

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Abstract

Objective: We aim to review the available literature on the relationship between Metabolic Syndrome and the development of primary open-angle glaucoma.

Methods: A bibliographic search of articles published in English using PubMed, LILACS, MEDLINE, BIREME Internet search sites, and Scopus databases. For the search, the following terms were used: glaucoma, open-angle, metabolic syndrome, Systemic Hypertension, Diabetes Mellitus, Obesity, Dyslipidemia, and risk factors.

Findings and conclusions: Primary Open Angle Glaucoma (POAG) is one of the leading causes of irreversible blindness. Timely diagnosis is essential for preventing vision loss, which has made risk factors of interest in public health for achieving early screening for glaucoma, especially for those with higher risk. The literature has shown a clear relationship between several components of Metabolic Syndrome (MetS) in isolation from POAG, and the etiological factors that explain this relationship have been established. However, some of these studies have yet to show a statistically significant relationship. More studies are required to show whether there is a significant relationship between the components of Metabolic Syndrome and POAG.

Keywords: Open Angle Glaucoma; Metabolic Syndrome; Systemic Hypertension; Diabetes Mellitus; Obesity; Dyslipidemia; Risk factors

1 Introduction

Primary open-angle glaucoma (POAG) is one of the leading causes of irreversible blindness worldwide. It is a disease that is asymptomatic for an extended period, leading to irreversible visual loss in advanced stages. It is essential to understand the associated risk factors and thus be able to identify patients who require special care in timely detection. Regarding epidemiology, it is estimated that approximately 60 million people worldwide have glaucomatous optic neuropathy; of these, about 8.4 million people have blindness (2). Studies report that the age-standardized prevalence of blindness and vision loss due to glaucoma decreased between 1990 and 2017. This can be explained mainly by the revolution in diagnostic methods such as optical coherence tomography (OCT), OCT angiography, and automated perimetry, which has made early detection of asymptomatic patients possible in countries where access to such technology is possible (3). The prevalence of glaucoma in Colombia in 2005 was 1.1%, more common in women (female ratio 2.1:1), contributing to 2.7% of the total visual disability in that period (4).

Risk factors for POAG development are increased intraocular pressure (IOP), family history of glaucoma, advanced age, blood pressure (BP), and metabolic syndrome (MetS), among others (1). MetS comprise a group of diseases and signs with high cardiovascular risk, such as hyperglycemia, high BP, dyslipidemia, and abdominal obesity (5). In addition to

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cardiovascular risk, MetS have been associated with glaucomatous optic neuropathy and its most prevalent risk factor, elevated intraocular pressure (IOP)(6).

Several articles have studied the relationship between POAG, IOP, MetS, or some of its components; however, there is still contradictory evidence (5). Some studies have shown that Systemic Hypertension (SH) and Type 2 Diabetes Mellitus (T2DM) have an independent association with POAG (1). However, other studies have not shown an association between T2DM and POAG or systemic arterial hypertension and POAG (1, 7).

According to epidemiological data, different prevalences have been established worldwide that depend on the criteria used for their diagnosis. An article about the global epidemic of metabolic syndrome shows that, for example, a national survey in Iran in 2007 showed the prevalence of MetS was 37.4% based on International Diabetes Federation (IDF) definition. In another Middle Eastern country, Tunisia, the prevalence was 45.5% based on IDF criteria. However, in all the Middle Eastern countries, the prevalence was much higher among women than men (8).

According to the National Health and Nutrition Examination Survey in an article published in 2017, the United States witnessed a 35% increase in metabolic syndrome prevalence since the appearance of the term in the 1980s till 2012 (9).

In a study published in 2017, which included 18 types of research involving approximately 57,000 adults in 51 Asian countries, the prevalence ranged between 12% and 49%. It was higher in women and residents of urban áreas (10).

A systematic review in 2011 shows that the general prevalence of MetS in Latin-American countries was 24,9 (range: 18,8-43,3%). MetS were slightly more frequent in women (25, 3 %) than in men (23,2 %), and the age group with the highest prevalence of MetS consisted of those over 50 years of age (11).

A meta-analysis with 15 studies in Mexico estimated the prevalence of MetS, based on different criteria, as follows: (IDF) criteria 54% (95% CI 0.44-0.63), and World Health Organization (WHO) 31% (95% CI 0.04-0.81). According to the Der Simonian-Laird random-effects model, a pooled prevalence of MetS in Mexico was 41% (95% CI 0.34-0.47) (12).

A Secondary Analysis of SABE Colombia in 2015 concluded that MetS was present in 54.9% of the study population, with a higher prevalence among females than males (59.8% vs. 47.3%) using the International Diabetes Federation criteria (13).

On the other hand, a Colombian cross-sectional study made in 2018 evidenced a prevalence of 35.4% in a population of 68,288 subjects who participated in a public program follow-up of chronic diseases, with a presence in all areas of Medellin, Colombia (14).

With this previous data, this article aims to review the literature about the association that has been found between POAG and components of MetS.

2 Material and methods

A bibliographic search of articles published in English using PubMed, MEDLINE, LILACS, BIREME Internet search sites, and Scopus databases. For the search, the following terms were used: glaucoma, open-angle, metabolic syndrome, Systemic

3 Results and discussion

The most common definition for Metabolic Syndrome based on IDF (International Diabetes Federation) 2006 is Waist > 94 cm (men) or > 80 cm (women) along with the presence of two or more of the following: 1. Blood glucose greater than 5.6 mmol/L (100 mg/dl) or diagnosed diabetes 2. HDL cholesterol < 1.0 mmol/L (40 mg/dl) in men, < 1.3 mmol/L (50 mg/dl) in women, or drug treatment for low HDL-C 3. Blood triglycerides > 1.7 mmol/L (150 mg/dl) or drug treatment for elevated triglycerides 4. Blood pressure > 130/85 mmHg or drug treatment for hypertension (8).

According to the current literature, glaucoma can vary according to race, intraocular pressure (IOP), age, and family history, among other risk factors (1,2,4). To date, there are other factors under study, such as SH, T2DM, Dyslipidemia, increased Body Mass Index (BMI), and abdominal obesity, that could contribute to the development of POAG.

Population-based studies have shown that Systemic Hypertension (SH) and T2DM are independently associated with open-angle glaucoma (1,4,15).

Oh, and colleagues showed that men and women with SH and fasting hyperglycemia had significantly higher Intraocular Pressure (IOP) levels than subjects without these risk factors. They evidenced that men with abdominal obesity and women with high triglycerides also had elevated IOP levels ($p<0.05$), but apart from these results, there was no other significant association between IOP and the other components of the metabolic syndrome (16). Jaen-Diaz and colleagues demonstrated an association between hyperlipidemia and POAG (17).

People with elevated systolic and diastolic blood pressure are at higher risk of developing POAG, with a higher probability of those who take medications. It has been shown that people with high BP, or those taking antihypertensive medications, have a higher prevalence of POAG, regardless of IOP (17).

Several studies have shown an association between obesity and high IOP (22). The Beaver Dam Eye Study found a significantly positive association between IOP and high Body Mass Index (BMI) since obesity could cause an excess of intra-orbital adipose tissue, generating a possible Secondary IOP rise (16, 18).

People with a BMI greater than or equal to 30 kg/m2 are more likely to develop POAG, given a relationship between higher BMI and higher IOP elevation (18, 23).

Additionally, it has been shown that obesity causes vascular endothelial dysfunction and autonomic dysfunction, which can cause alteration in ocular blood flow with perfusion instability and poor vascular supply to the optic nerve, which contributes to glaucomatous changes (18).

According to a study in Korea, people with a BMI > or = 30 kg/m2 have a higher probability of developing POAG than those with a statistically significant BMI between 18.5 and 22.9 (HR, 1.35; 95% CI, 1.16 to 1.56) (15).

However, other studies have shown that the prevalence of POAG was lower in the obese population, even showing that a lower BMI was related to a higher prevalence of glaucoma, according to a study in India. These results may be due to different sociodemographic characteristics and differences in the definition of Mets and insulin resistance (18, 21).

In a study conducted in Korea by Younhea Jung et al., they showed that high levels of fasting plasma glucose had a higher risk of developing POAG (95% CI: 1.13-1.29 for fasting blood glucose greater than 100 mg /dL, and 95% CI: 1.36-1.74 for fasting blood glucose greater than 126 mg/dL) (15).

Some studies have described that people with high fasting plasma glucose levels have a higher risk of developing POAG (HR 3.26; 95% CI: 3.01-3.53) and an even higher risk in people with a previous diagnosis of T2DM under medication and without current treatment (18, 24).

In a longitudinal prospective cohort study in Korea, an association was found between people with elevated Systolic BP (140) and Diastolic DBP (90) who were more likely to have POAG (HR 1.68; 95% CI: 1.53 to 1 .84). And those who had a previous diagnosis of Systemic Hypertension under treatment were more likely to develop POAG (HR 2.83; 95% CI: 2.61 to 3.08) (15).

Newman-Casey et al. conducted a study with a population from various communities in the United States; they showed the frequency of POAG among people with high Blood Pressure, T2DM, hyperlipidemia, as well as different combinations of these conditions, people with T2DM alone showed a 35% increased risk of developing POAG (adjusted HR=1.35 [95% confidence interval (CI) 1.21–1.50]), and those with Systemic hypertension alone had a 17% increased risk of develop OAG (adjusted HR = 1.17 [95% CI: 1.13–1.22]). For people with Systemic hypertension together with T2DM, the risk was more significant than the risk of each of these conditions individually (adjusted HR = 1.48 [95% CI 1.39-1.58]), showing that those patients with hyperlipidemia alone showed a 5% lower risk of developing POAG (adjusted HR = 0.95 [95% CI 0.91–0.98]) and people with the three conditions high BP, DM and hyperlipidemia had a 26% higher risk of developing POAG (adjusted HR = 1.26 [95% CI: 1.22–1.31]) relative to those without any of these conditions (1).

Chang et al. performed a cross-sectional study seeking the association of IOP with metabolic syndrome components. They concluded that male patients, BMI, waist circumference, systolic and diastolic BP, fasting glucose, triglycerides, and fibrinogen levels were positively associated with increased IOP. The same study also reported that metabolic syndrome was associated with an increase in IOP of 0.78 mm Hg (95% CI): 0.37-1.19, each one breaking down the BMI

(95% CI): 0.48, P = 0.0001; waist circumference (95% CI): 0.37, P = 0.0001; SBP (95% CI): 0.29, P = 0.001; DBP (95% CI): 0.45, P = 0.0001; fasting glucose (95% CI): 0.35, P = 0.0001 (22).

Son et al., in a case-control study of 28,754 participants, showed differences in the risk of high IOP according to the different metabolic syndrome combinations. The multiple logistic regression analysis, adjusted for age and sex, concluded that having a combination of four blood pressure components, high-density lipoproteins, triglycerides, and fasting glucose, had a higher IOP. The study revealed that the presence of more components of MetS had a statistically significant higher risk of increased IOP (P < 0.001) (25).

Younhea Jung et al. showed that people with a more significant number of MetS components were more likely to develop POAG ([HR, 1.77; 95% CI, 1.66 to 1.89], [HR, 2.74, 95% CI, 2.54 to 2.96] and [HR, 4.17, 95% CI, 3.68 to 4.72] for one, two, and three components, respectively) (15).

Rasoulinejad et al., in a case-control study with 200 Iranian subjects comprising 100 controls and 100 patients with clinically documented POAG examined by an ophthalmologist, contrasted with MetS components, show that the prevalence of MetS in the glaucoma group was 53% compared to 38% in the control group. MetS were significantly higher in patients with glaucoma (p=0.037) and were associated with an increased odds ratio for IOP higher than 21 mmHg (OR: 1.72; 95% CI: 1.03- 2.79, p = 0.034). In this study, there was no association between abdominal obesity and glaucoma (26).

Other studies, such as the one by Kim et al., found that metabolic syndrome was not significantly associated with normal-tension glaucoma. (27) In the SiMES study, Tan et al. found that although diabetes, hyperlipidemia, and BMI were associated with a modest increase in IOP, they were not associated with glaucomatous optic neuropathy (7). Other studies, including the Rotterdam study, found no significant association between T2DM and glaucoma. He concludes that treatment of metabolic abnormalities has not been shown to improve glaucoma control so far(28).

4 Conclusion

Primary Open Angle Glaucoma (POAG) is one of the leading causes of irreversible blindness. Timely diagnosis is essential for preventing vision loss, which has made risk factors of interest in public health for achieving early screening for glaucoma, especially for those with higher risk.

The literature has shown a clear relationship between several components of the MetS in isolation from POAG, and the etiological factors that explain this relationship have been established. However, some of these studies have yet to show a statistically significant relationship.

More studies are required to show whether there is a significant relationship between the components of Metabolic Syndrome and POAG.

Compliance with ethical standards

Disclosure of conflict of interest

Authors declare no conflict of interest.

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