

## Original Research Article

# Association between components of metabolic syndrome and elevated intraocular pressure

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## ABSTRACT

**Background:** Glaucoma is a group of eye diseases which result in damage to the optic nerve and ultimately vision loss. Elevated intraocular pressure (IOP) remains as the one major known risk factor for both the development and progression of glaucoma. Metabolic syndrome (MS) have been found to relate to elevated IOP. The aim of the study is to examine the association between MS and IOP by comparing central corneal thicknesses (CCT).

**Methods:** The study was carried out with 169 subjects consists of 94 were clinically diagnosed MS patients and 75 are healthy controls. Serum fasting glucose, triglyceride and HDL cholesterol levels were measured, and waist circumference, body mass index and blood pressure of all patients were recorded. Ophthalmological examinations, including IOP and CCT measurements were done on everyone.

**Results:** Higher IOP was observed in subjects with MS than those without MS. There was significant difference in the CCT values between the groups with and without MS ( $p < 0.05$ ). Most of the MS components were associated with IOP and CCT ( $p < 0.05$ ).

**Conclusions:** The study concludes that components of MS have strong association with IOP and CCT. The prevalence of MS is increasing rapidly in developing countries and the main cause for MS is sedentary lifestyle. Since there is relationship between MS and IOP, lifestyle intervention might have therapeutic potential to reduce IOP. Further studies are warranted to bring about the possible underlying relationship between components of MS and IOP.

**Keywords:** Central corneal thicknesses, Glaucoma, Intraocular pressure, Metabolic syndrome

## INTRODUCTION

Glaucoma is a group of eye diseases which result in damage to the optic nerve and ultimately vision loss.<sup>1</sup> Primary open-angle glaucoma (POAG) is the most common form of the disease, accounting for about 60% to 70% of all glaucoma cases. Although glaucoma is a multifactorial disease, elevated intraocular pressure (IOP) remains as the one major known risk factor for both the development and progression of glaucoma.<sup>2,3</sup>

Metabolic syndrome (MS) is a constellation of physical conditions and metabolic abnormalities characterized by central obesity, insulin resistance, dyslipidemia, and hypertension.

Diabetes, hypertension and obesity have been found to be connected with elevated IOP.<sup>4-6</sup> Previous studies suggested that elevated IOP is an expected condition in metabolic disturbances that are associated with the components of MS.<sup>7-9</sup>

The association between central corneal thickness (CCT) and IOP is well known by reporting eyes with greater mean CCT tend to have higher IOP.<sup>10-12</sup> Hence, this study intended to compare the CCT of the patients to determine its association between MS and IOP.

As MS is an important social burden of this century and are risk factors for IOP, it is a great challenging task to examine the relationship between MS and IOP, and to compare the IOP levels in subjects with and without MS by comparing CCT.

## METHODS

In this cross-sectional study 169 subjects were employed who attended outpatient and in-patient department of Ophthalmology in collaboration with Dept. of Biochemistry, Sri Lakshmi Narayana Institute of Medical Sciences, Pondicherry, India. Of 169 subjects, 94 were clinically diagnosed MS patients and 75 healthy controls. Informed consent was obtained from the patients and the study was approved by institutional ethical committee. The patients were in the age group of 35 to 58 years were selected and the clinical information including sex were obtained from the medical records and patients personal interview.

Patients with Type 1 diabetes, secondary diabetes, gestational diabetes, past histories of glaucoma, surgery, use of steroid drugs or diabetic retinopathy were excluded were excluded based on history, clinical examination, routine blood investigations.

### Data collection

Blood pressure was measured for all the patients. Fasting blood glucose (FBS) and were estimated by GOD-POD method. Serum TG was measured by Glycerol 3 phosphate oxidase N-ethyl sulphopropyl anisidine method. Serum high density lipoprotein (HDL) was estimated by enzyme selective protection method. MS risk was defined according to the national cholesterol education program third adult treatment panel guidelines

(NCEP ATP III) (13) and the subjects have been developed to MS if they have scored at least three of the five components.

The components of metabolic syndrome included: waist circumference > 102 cm in men or > 88 cm in women, triglyceride  $\geq$  150 mg per 100 ml, HDL < 40 mg per 100 ml in men or < 50 mg per 100 ml in women, blood pressure  $\geq$  130/85 mmHg and fasting glucose  $\geq$  100 mg per 100 ml. Metabolic syndrome was defined as having at least three of the five components.<sup>13</sup>

### Evaluation of eye

Ophthalmological examinations were executed between 8:00 am and 11:00 am. The best-corrected visual acuity, refraction, IOP measurement by non-contact tonometry (canon auto tonometer TX-F, canon, USA) and dilated fundus examination were performed. Three consecutive measurements for each eye were taken, and the average IOP of the right eye was used for investigation. Ocular hypertension was defined as an IOP  $\geq$  21 mmHg in the right eye. Five CCT measurements were taken from each eye with a Zeiss humphrey, ultrasound biomicroscope (Zeiss humphrey, San leandro, USA), and the mean reading was taken for analysis.

### Statistical analysis

Data analysis was performed using SPSS statistical software (version 22, SPSS, Inc., Chicago, Illinois, USA). The results are presented as mean  $\pm$  SD. Chi-square was used to test statistical significant difference between the groups. Student's t-test was used to compare quantitative measurements between participants without and with the MS. A value of  $P < 0.05$  was considered statistically significant.

## RESULTS

The characteristics of the study subjects are in shown Table 1.

**Table 1: Clinical characteristic of subjects with and without MS.**

Parameters	n	Without MS	With MS	p-value	Reference values
Age (years)	169	45.34 $\pm$ 10.63	54.3 $\pm$ 10.89	0.04	
Male (%)	57	40.3	59.6	0.001	
BMI (Kg/m <sup>2</sup> )	169	22.5 $\pm$ 4.12	27.8 $\pm$ 10.2	0.0001	18.5-24
Waist circumference (cm)	169	99.12 $\pm$ 10.91	114 $\pm$ 9.73	0.001	Male<102 Female<88
Intraocular pressure (mmHg)	169	15.3 $\pm$ 3.9	17.8 $\pm$ 3.4	0.01	
Ocular hypertension (%)	169	2.47	7.85	0.05	

BMI-body mass index, MS-metabolic syndrome,  $p < 0.05$ -significant.

The mean age was 54.3 for the MS group and 45.34 for CON group. Of 169 patients, 94 patients (34 men and 60

women) were in the MS group and 75 (23 men and 52 women) in the control group. Significant statistical

difference was found in the age and gender between MS and CON groups. The mean IOP was 17.8 mmHg in the MS group and found highly significant when compared to

CON group having 15.3 mmHg. The incidence of ocular hypertension was 7.85% in those with MS and 2.47 % in those without MS.

**Table 2: Association between mean values of intraocular pressure and components of MS.**

Components of MS	Occurrence	n	Mean IOP	p-value
Abdominal obesity	Yes	77	17.13±4.18	0.004
	No	92	15.87±3.67	
Hyperglycemia	Yes	76	17.11±4.2	0.007
	No	93	15.91±3.86	
Triglyceride	Yes	79	17.54±5.12	0.003
	No	90	15.3±3.12	
Low HDL-C	Yes	80	16.82±4.32	0.05
	No	89	15.35±3.17	
Blood pressure	Yes	78	17.25±4.9	0.005
	No	91	15.64±3.87	

HDL-C high density lipoprotein cholesterol, P<0.05-Significant.

Association between IOP and components of MS are given in Tables 2 and 3. IOP was positively associated with participants showed, abdominal obesity, high fasting glucose, high triglycerides and high blood pressure when compared to subjects without MS (Table 2). Subjects with 3 or/and 4-5 MS characteristics have higher IOP than those without these risk factors (Table 3).

The mean values of CCT for subjects with and without MS are represented in Table 4. Patients with MS had 595.54 µm of mean values of CCT as compared to CON group (505.3 µm). There was significant difference in the CCT values between the two groups (p <0.05). From the data, it is found that components of MS were found to be associated with CCT.

**Table 3: Mean intraocular pressure according to numbers of positive MS component.**

No. of positive MS parameters	Occurrence	n	Mean IOP	p-value
0-2	Yes	83	15.12±3.12	0.712
	No	86	15.34±3.44	
Only 3	Yes	78	17.43±5.16	0.038
	No	91	15.52±4.1	
3-5	Yes	75	17.97±5.65	0.03
	No	94	15.66±4.42	

MS-metabolic syndrome, P<0.05-Significant.

**Table 4: Association between mean values of CCT and components of MS.**

Components of MS	Occurrence	n	Mean IOP	p-value
Abdominal obesity	Yes	77	589±44.1	0.02
	No	92	508.87±33.6	
Hyperglycemia	Yes	76	581.8±40.2	0.028
	No	93	510.91±32.86	
Triglyceride	Yes	79	595.54±39.92	0.036
	No	90	505.3±33.6	
Low HDL-C	Yes	80	592.6±45.3	0.042
	No	89	507.6±35.7	
Blood pressure	Yes	78	594.25±43.9	0.04
	No	91	504.64±34.87	

HDL-C high density lipoprotein cholesterol, P<0.05-Significant.

## DISCUSSION

In this study, we found that the metabolic syndrome and its components were associated with IOP. Consistent with our findings, previous studies also reported that subjects with metabolic syndrome had higher IOPs.

Age is also one important factor which predisposes MS and studies from Western populations have shown that ageing is positively correlated with IOP, and is a novel cardiometabolic risk factors.<sup>6,9</sup> In support of this, we found significance in age and gender of those with and without MS.

BMI is a valuable tool to assess MS. Many studies reported the significant correlation between BMI and IOP.<sup>14-17</sup> Studies suggested the mechanism behind this association is that the increase of intraorbital fat tissues raises the venous pressure and blood viscosity, leading to a reduction in aqueous outflow and an increased IOP.<sup>11,18</sup>

Our results support the findings of many studies that have demonstrated that blood pressure is one of the components of MS and is positively associated with IOP.<sup>7-9, 19</sup> Further they reported blood pressure is the one strongest predictor of elevated IOP. Several studies explained the relationship between systemic hypertension and rise in IOP. They have demonstrated that elevated blood pressure results in increased ciliary artery perfusion, resulting in increased aqueous production which is the main cause for increasing blood pressure.<sup>19-21</sup> Additionally, increased sympathetic tone and serum corticosteroids were found to be responsible for high IOP in patients having high blood pressure.<sup>22</sup>

Association between high plasma glucose levels and IOP were well reported however the mechanism is still not clear. Studies suggested that the osmotic gradient induced by elevated blood glucose, with a consequent fluid shift into the intraocular space, and autonomic dysfunction have been the proposed factors for explaining the relationship between high plasma glucose and IOP.<sup>23,24</sup>

Concerning serum lipids on IOP, some previous studies have shown positive relationship between serum triglyceride levels and IOP.<sup>5,11,25,26</sup> Comparable results were observed in the study and it suggests that hypertriglyceridemia may commonly associate with obesity. Several studies have established similar relationship between obesity and elevated IOP.<sup>11,16,26</sup> Further relationship between increased IOP and dyslipidemia was explained by an increase in blood viscosity and a decrease in aqueous outflow.<sup>11</sup>

The actual mechanism exists between MS and IOP is still not known. However, recent research has revealed some potential pathophysiological links. They explained sympathetic hyperactivation, the endocannabinoid pathway, and the aquaporins are possible links between the MS and IOP.<sup>25,27-34</sup>

The measurement of central corneal thickness has become a very exciting ocular parameter owing to its importance as an indicator of corneal health status. Extremes in the CCT can lead to errors in IOP measurement. Present study investigated the correlation between MS and IOP changes by analysing the CCT of patients. There was statistical significance found between the CCT of those with MS when compared to the control group. Hence, it can be concluded that there is a definite relationship between MS and elevated IOP. Multitude of studies reported that CCT was greater in individuals with diabetes and MS.<sup>12,35</sup> The reason for this association is unknown but is believed to be related to the dysfunction of the corneal endothelial physiology and increased corneal hydration.<sup>36-38</sup>

## CONCLUSION

Current study shows that components of MS have strong association with IOP. The prevalence of MS is increasing rapidly in developing countries and the main cause for MS is sedentary lifestyle. Since there is relationship between MS and IOP, lifestyle intervention might have therapeutic potential to reduce IOP. Further studies are warranted to bring about the possible underlying relationship between components of MS and IOP. Clinicians and researchers in this field are encouraged to perform similar studies to find out the casual link between MS and IOP. Pending confirmatory results in larger studies will help ophthalmologists for the early diagnosis and to reduce impact on the incidence of POAG.

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