·Investigation·

Metabolic syndrome: a risk factor for high intraocular pressure in the Israeli population

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Abstract

• AIM: To evaluate the association among elevated intraocular pressure (IOP), the metabolic syndrome (MetS), body mass index (BMI), and some of their components in the Israeli population.

• METHODS: We retrospectively reviewed the charts of 12 747 soldiers of the Israeli Defense Forces, aged 35y or older, who underwent a routine periodical medical examination between 1991 and 2004. None of the subjects received medical treatment for either glaucoma or ocular hypertension. High IOP (>21 mm Hg) was correlated with age, sex, arterial blood pressure, total blood cholesterol levels, triglyceride levels, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, smoking , BMI and MetS.

• RESULTS: A statistically significant difference was found between the IOP of subjects with a low risk and higher risk for the development of MetS (P<0.0001 for males, P=0.0026 for females). A statistically significant positive correlation was found in male subjects between high BMI and elevated IOP (r=0.11677, P<0.0001).

• CONCLUSION: MetS and BMI were significantly more prevalent in subjects with increased IOP levels. We suggest that both should be taken into consideration in the assessment of glaucoma suspects.

• **KEYWORDS:** glaucoma; body mass index; Metabollic syndrome
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INTRODUCTION

Intraocular pressure (IOP) is well established as the most significant risk factor for both the development and progression of glaucoma [1,2]. Several other independent, weaker risk factors have been identified. Of these, age and cup to disc (C/D) ratio are widely accepted by researchers, while family history, diabetes, myopia and blood pressure are subject to continuous debate regarding their effect on glaucoma risk and progression [3-6]. The success of risk factor-guided management in other fields, such as in the treatment of cardiovascular diseases, led glaucoma experts to suggest the adoption of this concept to glaucoma management [7]. The basis for this concept is identification of associated risk factors. Their presence and grade of severity may affect the main risk factors subsequently which, in the case of glaucoma, is the IOP. Accounting for these additional risk factors can supplement the decision on the aggressiveness of treatment.

One of the major risk factors for cardiovascular disease is dyslipidemia, which can be reduced by altering dietary intake, pursuing aerobic physical activity and other life style modifications, as well as medication use. Similarly, contributing risk factors to cardiovascular diseases can be diminished by lowering blood pressure, blood glucose level and obesity, or by encouraging physicalexercise, and can also be subject to therapy and behavioral changes [8]. In glaucoma, the main risk factor, IOP, can be altered both medically and surgically, yet some of the known additional risk factors cannot be subjected to change, such as age, central corneal thickness, family history, and C/D ratio at the time of diagnosis. Nevertheless, these risk factors can contribute to

Table 1 Distribution according to IOP and predisposing risk factors for MetS *n*(%)

No. of predisposing factors to MetS	IOP <20 mm Hg		IOP >21 mm Hg	
	M	F	M	F
0-2	7799 (88.4)	1008 (90.8)	1024 (11.6)	102 (9.2)
3-5	2196 (82.7)	133 (83.1)	458 (17.26)	27 (16.9)

IOP: Intraocular pressure; MetS: Metabolic syndrome; *P* value for males<0.0001, for females=0.0026. *n*=3809 of 11 477 males and 497 of 1270 females were excluded due to missing values.

Table 2 Univariant analysis of risk factors of BMI versus high IOP *n*=1552

Variable	% of IOP >21 mm Hg in subjects with normal BMI	% of IOP >21 mm Hg in subjects with abnormal BMI	*P*	*R*
Elevated diastolic blood pressure	17.3	26.3	0.01[a]	0.05154
Smoking	18.2	17.9	0.55	0.03141
Blood lipid level	17.6	18.3	0.73	0.04259
Ergometric stress testing	18.1	19.9	0.69	-0.0909

BMI: Body mass index; IOP: Intraocular pressure. [a]Statistically significant.

the decision as to how best to treat or prevent the disease. Central corneal thickness serves as an example of how a risk factor can play a major role in assessing the risk for glaucoma transformation from ocular hypertension[9].

We investigated the association between metabolic syndrome (MetS) [10-14], body mass index (BMI), obesity, insulin resistance[15], hyperglycemia, hypertriglyceridemia, hypertension, and the measured IOP, seeking to identify systemic risk factors for glaucoma[16-20].

SUBJECTS AND METHODS

Subjects We retrospectively collected data on 19 443 subjects, aged 35-55y, who underwent a compulsory routine health assessment in the Israel Defense Forces. We included for analysis the complete records of 12 747 subjects: 11 477 males and 1270 females with complete records for calculating MetS. We compared the percentage of examinees with IOP higher than 21 mm Hg with normal versus abnormal values of selected systemic health characteristics. IOP measurements reflected the average of three-puff tonometer readings (Reichert AT555, Depew measurements was taken). All measurements were taken between 9 a.m. and 1 p.m. For analysis purposes, we took into account the higher IOP reading of both eyes in each subject. The study and data collection conformed to all local laws and were compliant with the principles of the Declaration of Helsinki.

Methods The following parameters were recorded: systolic and diastolic blood pressure, blood level of total cholesterol, high density lipoprotein (HDL), low density lipoprotein (LDL) and triglycerides, ergometric stress testing results, and current and past history of cigarette packs smoked per day. MetS risk was calculated according to the International Diabetes Federation (IDF) protocols [15]. Subjects were deemed to have an increased risk for developing cardiovascular disease if they achieved a score of three or more detrimental factors. We calculated the BMI for a subgroup of 1552 male subjects and divided the subjects into three groups: those with a low BMI who had a score of 25 or less, those with a moderate BMI with a score between 25 and 30, and those with a high BMI with a score over 30.

Table 3 Univariant analysis of percentage of high IOP in each of the three BMI sub-groups *n*=1552

BMI	% of IOP >21 mm Hg
<25	14.0
25-30	19.2
>30	24.0

BMI: Body mass index; IOP: Intraocular pressure; *r*=0.11677, *P*<0.001.

Statistical Analysis Commercial software (SAS system ver.8; SAS, Cary, NC, USA) was used to analyze the data. Univariant & multivariant analysis was applied to all results utilizing Pearson correlation coefficients and multivariate linear regression to test for statistical significance. Chi-square was used to test the MetS groups for statistical significant difference.

RESULTS

Mean IOP was 17.3 mm Hg (standard deviation 3.9, range 9 to 32). All subjects with MetS were significantly more prone to have an elevated IOP greater than 21 mm Hg (*P*<0.0001) (Table 1). Univariant analysis of blood pressure, smoking habits, dyslipidemia and ergometric stress testing versus high IOP is illustrated in Table 2. High blood pressure was associated with a higher percentage of IOP>21 mm Hg. No association was found between the other variables and IOP. Table 3 summarizes the univariant analysis of the percentage of high IOP in each of the three sub-groups, divided according to BMI levels. Higher values of BMI were associated with a higher IOP.

Only BMI was positively correlated with IOP greater than 21 mm Hg in a multivariate analysis of BMI, elevated systolic and diastolic blood pressure, elevated cholesterol blood levels (HDL, LDL, triglycerides), a history of smoking, and abnormal ergometric stress testing.

DISCUSSION

MetS and BMI were positively correlated with increased IOP in our study as well as in the literature [10-21]. One study originating in Japan found that MetS was a risk factor for ocular hypertension, while another Japanese study found that obesity alone was a risk factor for increased IOP [16-17]. Chang *et al* [18] found that MetS and other insulin resistance-related features were strongly associated with IOP. In the largest study by Nauman-Casey *et al* [19], on the relationship between components of MetS and primary open angle glaucoma (POAG) in the United States, it was found that both hypertension and diabetes were independently but additively related to POAG, and that only obese women were found to be at increased risk for glaucoma. The latter report, which studied a large group, also found that hyperlipidemia increased the risk of POAG, but only when associated with diabetes and hypertension.

Some studies found no association between MetS and POAG but confounding factors were not completely controlled nor adjusted due in part to a small sample size[19].

BMI had a significant positive correlation with IOP in the multivariate analysis of risk factors in several previous reports [21-22]. Klein *et al* [23] and Wu and Leske [24] reported a positive correlation between BMI and glaucoma, but other reports failed to show this association. No association was observed between elevated BMI and glaucoma [9]. There was no statistical difference in BMI between glaucoma patients and controls. On the contrary, there was a tendency for glaucoma patients to have a lower BMI. In a study by Pasquale *et al* [25], a higher BMI in women was associated with a lower risk of POAG with an IOP of 21 mm Hg or less at diagnosis. In contrast, this was not true for men [25]. In a study by Asrani *et al* [26], normal tension glaucoma patients were more likely to have a lower BMI and lower systolic blood pressure when compared to POAG patients. In Singapore, it was reported that individuals with a lower BMI have a lower neuroretinal rim area and a larger optic C/D ratio[27].

People with MetS are more likely to have an elevated IOP as well as POAG, as seen both in our report and in others. In contrast, although our study supports the positive correlation between elevated BMI and increased IOP, the literature shows conflicting results to that effect[22-25,27].

Increase in fat in the orbital space may lead to increased venous pressure , diminishing the outflow facility, yet other insulin resistance related features might be involved in the pathogenesis of ocular hypertension[6,18].

The limitations of this study are its retrospective nature and the fact that the data was collected in 2004. This reduced the number of subjects that had all the relevant data for analysis as well as did not allow us to present detailed information on 2 variables used for calculating MetS.

Neither our study nor any other report included information about subjects with ocular hypertension who later developed glaucoma in relation to MetS or BMI. We might conclude at this stage that clinicians might use MetS and perhaps also elevated BMI to better predict if an individual is likely to have elevated IOP or to acquire POAG. This is of particular value as, due to the rising number of patients with MetS in the general population, this may result in an increased prevalence of POAG if the MetS is not addressed and controlled by timely public preventive health programs and an individualized approach to obesity.

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