Research Article

Comparison of visual field defect severity level between nonarteritic anterior ischemic optic neuropathy with and without metabolic syndrome

Seskoati Prayitnaningsih*, Devi Putri Swadayani

ABSTRACT

Background: Nonarteritic anterior ischemic optic neuropathy (NA-AION) is the second most common optic neuropathy in adults, with an incidence rate of 2.3–10.2/100,000 population/year in the US. Metabolic syndrome (MS) is known to be one systemic risk factor of NA-AION. This study aimed to determine the relationship between NA-AION and MS. **Methods:** This study use data from medical records from neuro-ophthalmology polyclinic in Dr. Saiful Anwar General Hospital from 2015 to 2017. Visual acuity (VA) established from Snellen chart examination, anterior segment from biomicroscopy examination, posterior segment from direct fundoscopy, and perimetry (geographic appearance of visual field defect and mean defect [MD]). Laboratory examination (MS component based on International Diabetes Federation 2006 consensus), waist circumference, blood pressure, height and weight, as well as patient with edema papil at neuro-ophthalmology outpatient clinic, in Dr. Saiful Anwar General Hospital, Malang. All data of NA-AION patients with and without MS were analyzed using SPSS 20.0 (Chi-square, Spearman correlation, and Mann–Whitney U-test). **Results:** This study involved 52 samples from medical record data where most subjects were in the age ranging of 41–60 years old, mean age 54 years, and no gender predominance. More than one-third (40.38%) of NA-AION patients experienced MS. The correlation between MS and perimetry MD value was weak (P = 0.322), Spearman correlation contingency coefficient of 0.251, and Mann–Whitney result sig. Z (0.612). The initial patient VA was 6/6–6/18. In this research, a mean waist circumference of 85.5 cm and body mass index of 26.5 (OW) were obtained. The bilateral attack, segmental edema of optic nerve hypoplasia, and altitudinal visual field defect with MD >12 dB were most dominant. **Conclusion:** About 40.38% of patient with NA-AON experienced MS, showing a weak correlation with no significant difference between the presence and absence of MS. No gender predominance was found. A multidisciplinary scientific approach is needed to identify the risk factors of NA-AION.

KEY WORDS: International Diabetes Federation 2006, Metabolic syndrome, Nonarteritic anterior ischemic optic neuropathy, Waist circumference

BACKGROUND

Anterior ischemic optic neuropathy (AION) represents an acute ischemic disruption of the optic nerve and could cause great vision lost.[1] Clinically, the disease is classified as arteritic AION (A-AION) and nonarteritic AION (NA-AION). NA-AION is the second most common optic neuropathy in adults above 50 years old.[2,3] Although clinical manifestations and history of the disease are known, not much about pathogenesis has been observed and there is no effective treatment proven to obtain significant results.[4,5] Epidemiologically, the incidence rate in the US is 2.3–10.2/100,000 populations and at least 6000 new cases emerge every year.[5] This disease occurs more frequently in Caucasian than African-American or Hispanic populations.

Metabolic syndrome (MS) or insulin resistance syndrome is a collection of risk factors responsible for increased morbidity in some diseases.[6] The main components of this syndrome are insulin resistance, central obesity, hyperglycemia, diabetes, hypertension, dyslipidemia, triglyceride (TG) increase, and high-density lipoprotein (HDL) cholesterol decrease.[7] International Diabetes Federation (IDF) states that

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Website: jprsolutions.info | ISSN: 0975-7619

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Received on: 10-03-2019; Revised on: 14-05-2019; Accepted on: 15-06-2019

approximately 20–25% of the adult population in the world experienced MS.[8] The Framingham Offspring Study found that 29.4% of males and 23.1% of females aged 26–82 years suffer from MS. The more MS components occur, the higher the chance of mortality.[7]

Until now, NA-AION pathogenesis is not yet fully understand due to multifactorial risk factors. Other than anatomic predisposition, systemic risk factors play an important role on its pathogenesis.[9] Systemic risk factor component of MS proved to have an impact on microcirculation and blood flow autoregulation of the papilla optic nerve; thus, it is said that both factors have a synergic effect. To obtain comparative data about severity level of visual field defects determined by mean defect (MD) of perimetry between patients of NA-AION with and without MS (based on IDF criteria), authors tried to determine by a cross-sectional approach using patient medical records of Dr. Saiful Anwar General Hospital, Malang.

METHODS

This was a descriptive observational research, where the data extracted from medical record of NA-AION in neuro-ophthalmology outpatients clinic were demographic data (age and gender), anterior segment examination, direct fundoscopy, Humphrey perimetry (the type of visual field defect and MD), and laboratory results (MS components based on 2006 IDF consensus). Measurement of abdominal circumference and body mass index calculation to diagnose central obesity was needed. To determine MS, the measurement of blood pressure and laboratory examinations (fasting blood sugar, HDL, and TG) was performed to the patients. All NA-AION patients, with or without MS, were included in statistical analysis with SPSS 20.0 (Chi-square, Spearman correlation, and Mann–Whitney U-test).

This research gained ethical clearance from Health Research Ethical Commission of Dr. Saiful Anwar Hospital, Malang (Registration number: 400/121/K.3/302/2017). Inclusion criteria were medical records with diagnosis of NA-AION or suspected NA-AION at ophthalmology clinic, neuro-ophthalmology subdivision, based on history taking, ophthalmic examination, fundoscopic and perimetry examinations, available data on MS components, no disorders in refractory media, and other disorders that might alter the optic neuron function. Incomplete data on metabolic components and supporting data in NA-AION diagnosis were the exclusion criteria. All NA-AION patients, with or without MS, were included in statistical analysis with SPSS 20.0 (Chi-square, Spearman correlation, and Mann–Whitney U-test).

RESULTS

Data were conducted from medical records since 2015–2017. There were 52 medical records fulfilled the inclusion criteria. Correlation between MS and mean deviation of perimetry using Chi-square test and Spearman correlation (P = 0.322) with the coefficient contingency of 0.251 ($P < 0.05$) was weak and insignificant. Mann–Whitney statistical analysis to test the difference of mean between NA-AION patients with or without MS resulted in sig. Z value of 0.612, indicated no significant difference of visual field defect severity level between patients NA-AION with and without MS.

From demographical data and eye examinations of 52 subjects (26 males and 26 females), most of them were at 41–50 years old and 17 people were 51–60 years old (average age was 54 years old). Waist circumference data were measured on 24 of 52 patients, and the largest waist size found was 107 cm in a male (average waist size was 85.8 cm). Body mass index (BMI) data were taken from 28 of 52 patients. Highest BMI number was 36.2 kg/m^2, with an average of 26.5 kg/m^2 (overweight). According to data from Central Pathology Clinic of 52 subjects (growth domestic product [GDP], TG, and HDL), there were 14 patients with GDP <100 mg/dL (26.92%) and 38 patients with GDP >100 mg/dL (73.08%) [Figure 1]. For blood pressure, systole was >130 mmHg in 38 subjects (73.08%), systole was <130 mmHg in 14 subjects (26.93%), diastole was >86 mmHg in 39 subjects (75.00%), and diastole <86 mmHg in 13 subjects (25.00%) [Table 1]. Average HDL of male subjects was 42.88 mg/dL, while in females, it was 46.85 mg/dL. TGs increased >150 mg/dL were found in 31 subjects (59.62%), while TGs were <150 mg/dL in 21 subjects (40.38%) with an average of 177 mg/dL. Diabetes

Table 1: Cross-tabulation between metabolic syndrome and mean deviation perimetry with Chi-square and Spearman-Pearson correlation test shows not significance result and weak correlation

Metabolic syndrome	Mean deviation perimetry								Total	%
	A	%	B	%	C	%	D	%		
MS	1	1.92	2	3.85	7	13.46	11	21.15	21	40.38
Non-MS	0	0.00	8	15.38	8	15.38	15	28.85	31	59.62
Total	1	1.92	10	19.23	15	28.85	26	50.00	52	100.00

P=0.322. *MD perimetry value A: 0 dB to −2 dB; B: −3 dB to −5 dB; C: −6 dB to −12 dB; D: <−12 dB

Table 2: Comparison of the severity level of mean deviation perimetry between nonarteritic anterior ischemic optic neuropathy patient with and without metabolic syndrome (no significant difference between two groups) – Mann–Whitney U-test

Test	Mean deviation perimetry
Mann–Whitney U	300.500
Wilcoxon W	531.500
Z	−0.507
Asymp. sig. (two tailed)	0.612

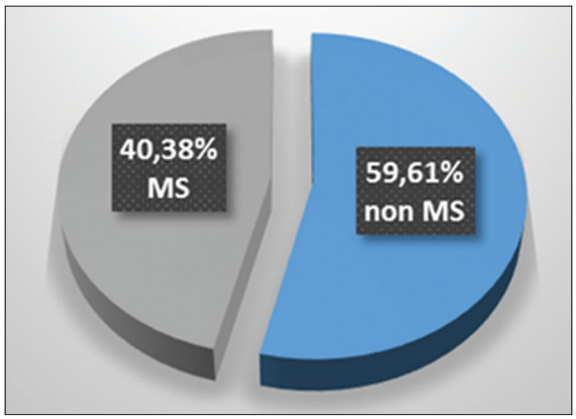

Figure 1: Nonarteritic anterior ischemic optic neuropathy patient diagram based on the presence of metabolic syndrome (MS) (40,38% have MS)

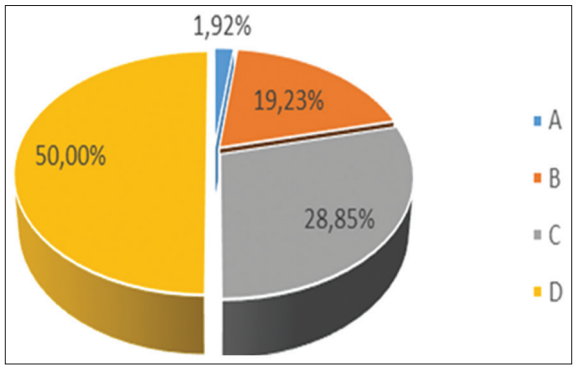

Figure 2: Nonarteritic anterior ischemic optic neuropathy patient diagram based on mean deviation perimetry, dominated mean deviation (MD) at <−12 dB (50%). *MD perimetry value A: 0 dB to −2 dB; B: −3 dB to −5 dB; C: −6 dB to −12 dB; D: <−12 dB

mellitus history was also recorded in 36 subjects (69.23%), hypertension in 46 subjects (88.46%), and dyslipidemia in 47 subjects (90.38%) [Figure 2]. The data of occurrence is on the right eye from 13 patients (25.00%), left eye from eight patients (15.38%) and both eyes from 31 patients (59.62%). Most of the VA recorded was from 6/6 to 6/18 in 20 subjects (38.46%). As many as, 25 patients were determined to have an altitudinal defect and 50.00% of them had MD perimetry <−12 dB. Segmental papilledema was observed in 31 NA-AION patients (40.38%) diagnosed with MS abnormalities [Tbale 2].

DISCUSSION

The descriptive analysis of gender and age of NA-AION patients showed that there was no gender predominance. Several studies have stated that there is no gender predilection of NA-AION disease. However, a retrospective study in Croatia revealed that gender predilection of NA-AION is higher in males at 2.9/100,000 male citizens and 2.5/100,000 for females every year.[1,2,4,10,11]

Based on age distribution, average age of NA-AION patients observed was 54 years old, which is in accordance with other studies that stated that the age of onset of patients diagnosed with NA-AION is above 57–67 years old, while the others stated an average age of onset from 55 to 67 years old.[3,4,10] NA-AION affects between 2.3 and 10.3 people per 100,000 individuals per year, making it the most common cause of acute optic neuropathy and also it presumed to result from vascular insufficiency in patient over the age of 50.[1,4,11]

From clinical pathology examination report, 38 subjects had fasting blood glucose >100 mg/dL (73.08%). HDL decreases were more likely to happen in female subjects and TG >150 mg/dL was found in 31 subjects (59.62%). These findings were similar to Lee *et al*. (2011), as more than 53% of NA-AION patients had diabetes mellitus history. Diabetes is estimated to play a role in vasculopathy and insulin resistance, and long-term exposure to hyperglycemia can cause blood vessel endothelium damage. This damage would lead to clogging and arteriosclerosis as well as obesity, which is included as a risk factor of NA-AION.[1,4,12,13] Insulin resistance would lead to endothelium dysfunction, related to oxidative stress, cardiovascular diseases including HDL cholesterol decrease, increased TGs, lipogenesis, elevated blood pressure, and other related conditions.[13-15]

In this research, most subjects naturally experienced blood pressure increases that were a little higher than a previous study, in which 35–50% of patients with NA-AION were diagnosed with systemic hypertension. Hypertension in NA-AION is expected to play a role through the activation of the renin-angiotensin system, causing blood vessel remodeling, endothelial dysfunction and leads to stiffness of blood vessels, tissue fibrosis, and increased plaque formation.[12,13,15]

Grouping analysis of MS was divided into categories A and B, A: Central obesity + two of four other MS factors or B: No central obesity and <2 of four other MS factors. Domination of category A in 21 subjects (40.38%) was most likely caused by unequal data of the central obesity determinant. Several studies and IDF 2006 stated that waist circumference is the

best determinant criteria (along with BMI) of central obesity because it has been distinguished based on ethnicity and gender.[8,15,16]

Most of the eye literalities were found to be bilateral (59.62%). There was no particular eye predilection of NA-AION patients. Repeated NA-AION attacks of the contralateral eye at that time were only 25%, while there were coincidence bilateral attacks in only 15% of cases.[1,3,4]

Initial VA ranged in most patients from 6/6 to 6/18, and NA-AION VA varied greatly from 6/6 to the absence of light perception.[17] Mostly, reduction of VA in NA-AION patients is fewer than in A-AION, where more than 50% of patients have VA >6/60. Color vision deficiency of NA-AION tends to parallel VA decreases.[3,4] The altitudinal defect with MD <−12 dB was commonly found in this research. The initial phase of the defect is generally in the form of arcuate and altitudinal. Then, after 6 months, 50% of patients would suffer from progressivity.[1,2,17] Perimetry MD has weak diagnostic significance but is able to describe patient visual deviation, with a lower value of MD indicating ischemic conditions.[1-3,17,18]

More than one-third (40.38%) of NA-AION subjects were diagnosed with MS. Factors related to optical disc structure have a role in NA-AION pathophysiology, patients with MS have a higher tendency to suffer from NA-AION due to the cluster effect and synergy of MS factors. The core of MS is hyperinsulinemia and oxidative stress, which lead to several abnormalities. Central obesity is the main component of MS occurrence, but the exact mechanism is not yet known. Obesity followed by increased lipid metabolism would lead to a rise in reactive oxygen species (ROS) production, both in circulation and in adipose cells. The rise in ROS production in adipose cells leads to an imbalance of oxidation-reduction reactions and reduced antioxidant enzymes in circulation (oxidative stress). More oxidative stress induces dysregulation of adipose tissue and this is the beginning of pathophysiology for MS. Diastolic dysfunction is also included with BMI increase and diabetes mellitus.[12,13]

Correlation analysis between MS and mean deviation perimetry using Chi-square test resulted in $P = 0.322$, with $P = 0.322 > 0.05$ ($\alpha = 5\%$), meaning that there is an insignificant correlation. The contingency coefficient value was 0.251, with $P = 0.322$ also showing weak correlation. Mann–Whitney U-test was used to measure the difference between groups, with the sig. $Z = 0.612$, which means that there was no significant difference between the two groups (MS and non-MS) for visual defect severity. MD is the patient's average deviation of all perimetric tests. Patients able to see darker stimulus than others in the same age and race would have a positive MD result, while patients who need brighter stimulus would have a negative MD result. MD had no significant or strong point for diagnosis but was able to describe patient visual deviation. Most NA-AION patients had a negative MD result because there is a need for the occurrence of ischemic conditions and perimetry examination to diagnose NA-AION.[17,18]

CONCLUSION

Most of NA-AION patients had abnormalities in MS components, which were fasting blood glucose, HDL, TG, and blood pressure, but not central obesity. Mean value of abdominal circumference was 85.5 cm and mean BMI was 26.5 kg/m^2 (overweight). Even so, the correlation between MS and mean deviation of perimetry was weak and statistically insignificant. There was also no difference in visual field defect severity between NA-AION patients with and without MS.

ACKNOWLEDGMENTS

The authors would like to thank the University of Brawijaya for facilitated this research.

AUTHORS' CONTRIBUTIONS

Seskoati Prayitnaningsih performed the study design and interpretation of data and Devi Putri Swadayani contributed to the drafting and final approval of the article.

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Source of support: Nil; Conflict of interest: None Declared