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Risk factors of anterior ischemic optic neuropathy among a sample of patients in Erbil City

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Abstract

Background and objectives: Although a lot of studies suggested the predisposition of many risk factors, non-arteritic anterior ischemic optic neuropathy was considered for a long time to be idiopathic. This study aimed to assess the relationship between different factors and anterior ischemic optic neuropathy among a sample of patients in Erbil city.

Methods: A case-control study was conducted in Erbil city, Iraq from 2008 to 2011. A total of 36 cases of non-arteritic anterior ischemic optic neuropathy and 36 controls with other visual problems were included.

Results: Eight percent of patients in this study had one or more risk factors (*P* = 0.001), in particular hypertension and diabetes were shown to have a significant relationship (*P* = 0.046 and 0.001, respectively). The absence of physiological cup over the optic disc has crucial importance both independently (*P* = 0.001) and in association with diabetes (*P* = 0.001). Old age and male gender were significant factors in relation to co-morbidities (*P* = 0.001 and 0.038, respectively).

Conclusion: The study had concluded that hypertension, diabetes, age, male gender and absent physiological cup over the optic disc were important risk factors for anterior ischemic optic neuropathy.

Keywords: Anterior ischemic optic neuropathy; Giant cell arteritis; Non arteritic anterior ischemic optic neuropathy.

Introduction

Field defects typical of ischemic optic neuropathy were probably first described by Knapp in 1875. Miller and Smith first used the term ischemic optic neuropathy in 1966, and Hayreh later added the term anterior. In 1924, Uhthoff first described the severe visual loss, with field defects and swollen optic discs.[1] Anterior ischemic optic neuropathy is caused by insufficient blood flow through the posterior ciliary arteries that supply the optic disc. It produces a painless monocular visual loss that is usually sudden, although some patients have progressive worsening.[2] It can be nonarteritic (nonarteritic anterior ischemic optic neuropathy [NA-ION]) or arteritic, the latter being associated with giant cell arteritis (GCA; often termed temporal arteritis).[2] The nonarteritic form of AION is more common (accounting for 90%–95% of AION cases) and occurs in a relatively younger age group (mean age, 60 years) than the arteritic form.[3-5] There are approximately 6000 new cases per year and Caucasians account for nearly 95% of cases.[5,6] Men and women are nearly equally affected, and the mean age at symptom onset varies between 57 and 65 years. Predispositions include structural crowding of the optic nerve head so that the physiological cup is either very small or absent, hypertension, diabetes mellitus, hyperlipidemia, collagen vascular disease, antiphospholipid antibody syndrome, hyperhomocysteinemia, sudden hypotensive events, cataract surgery, sleep apnea syndrome and erectile dysfunction.[4-8] Systemic hypertension has been documented in up to 47% of patients

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who have NA-AION and diabetes in up to 24%. Diabetics, in particular, show a predisposition to NA-AION at a young age.[5] Optic disc drusen might increase the risk of developing NA-AION by theoretically contributing to the "crowded" optic nerve in discs with a small cup to disc ratios. There are anecdotal reports of NA-AION occurring in patients with optic disc drusen, but a causal relationship has not been proved.[9-11] Since 1974, several studies have shown that in eyes with NA-AION there is a significantly higher prevalence of absent or small cup than in the general population.[12-14] No treatment is available; Prevention with aspirin has not been demonstrated to be effective, although it is recommended.[15] Many patients with NA-AION notice their symptoms in the morning.[16] This has prompted investigations into changes in the systemic blood pressure at night in patients with NA-AION[16,17] and raises the question of whether other nocturnal events may predispose patients to NA-AION. AION can occur without any obvious preliminary cause or predisposing factors, but it is more likely to occur in those people who are already having a risk or more for atherosclerosis and in one-quarter of patients it can affect the other eye. This study will increase the awareness of both doctors and patients about the role of different associated factors like diabetes, hypertension, hyperlipidemia, and smoking in increasing the susceptibility to optic nerve ischemia and disturbance of vision, and we tried to show to which extent these factors were important in our patients in Erbil city of Iraq.

Methods

This case-control study was carried out in our private neurology and ophthalmology clinics and outpatient clinics in Hawler and Rizgary Teaching Hospitals, Erbil, Iraq from July 2008 to May 2011. Patients were included in this study from different ages who developed an attack of sudden blurring or loss of vision in one eye. They were examined ophthalmologically and neurologically by direct patient interview, and their fundoscopy showed abnormalities in their optic disc +/- retina. Medical examination was done for vital signs, any tenderness over the temporal arteries and pulses (especially those above 50 of age). Magnetic resonance imaging (MRI) were done for all patients, thorough blood investigations were done for these patients, blood group was obtained for all, most of them did visual evoked potential (VEP) study and carotid Doppler was done for 27patients. Patients with optic neuritis and patients with AION due to giant cell arteritis were excluded from the study. Only 36 patients were included in this study who did not fit diagnosis other than NA-AION, A control group of 36 patients who came for other visual problems was chosen to participate in this study. A questionnaire designed by the researchers was used to collect information from the patients regarding general health and history of medical diseases, such as hypertension, diabetes mellitus (DM), coronary heart disease, smoking, and other vascular risk factors. Patients were investigated for dyslipidemia (serum cholesterol more than 200 mg/dl, and serum triglyceride more than 150 mg/dl were considered high). The MRI sequences T1, T2, and FLAIR were obtained. The MRI scanner was Siemens 1.5 Tesla (Siemens, Erlangen, Germany). VEP study was done with the advanced device (XAI- MEDICA neuro-com Ukraine). Verbal informed consent was taken from the patients after explaining the design and aims of the study, and all had no objection to participating in the study. The research committee from the College of Medicine, Hawler Medical University approved the study protocol. Chi-square test and Fisher exact test were used for association between AION and risk factors, and *a P* value of ≤0.05 was considered statistically significant.

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Results

Socio-demographic characteristics of the study population

A total of 72 respondents (36 patients and another 36 individuals as a control group) had participated in the current study, their age ranged from 30 to 88 year old, with a mean of 51.6 years ± 12.42 SD. One third (33.3%) of the control group were above 50 years old compared to 63.89% of the cases. Among the respondents, 21 (58.3%) were males from both study groups with a male to female ratio of 1.4: 1 (Table 1).

Risk factors and comorbidities among the study population

About 19% of the cases have no risk factors, compared to 55% of the control group, while half (50%) of the cases have more than one complication, with a significant statistical association (*P* = 0.001). Among these risk factors hypertension and diabetes were found to be significant (*P* = 0.046 and 0.000, respectively). Regarding other co-morbidities, smoking and hyperlipidemia, it was prevalent among both groups (cases and controls), with no significant statistical association (*P* = 0.759 and 0.772, respectively) as shown in Table 2.

Table 1: Socio-demographic characteristics of the study population.

Variables	Cases No. (%)	Controls No. (%)	*P* value
Age groups			
Less than 50 years	13 (36.1)	24 (66.6)	
51- 60 years	12 (33.3)	4 (11.1)	0.020
61 years and more	11 (30.5)	8 (22.2)	
Total	**36**	**36**	
Sex			
Male	21(58.3)	21(58.3)	
Female	15 (41.6)	15 (41.6)	1.00
Total	**36**	**36**	

Table 2: Risk factors and comorbidities among the study population.

Variables	Cases N = 36 No. (%)	Controls No = 36 No. (%)	*P* value
Risk factors			
No risk factor	7(19.4)	20(55.5)	0.001
One risk factor	11(30.5)	11(30.5)	
Two and more risk factors	18(50.0)	5(13.9)	
Co-Morbidities			
Hypertension	16 (44.4)	8 (22.2)	0.046
Diabetes mellitus	18(50.0)	3(8.3)	0.001*
Smoking	7(19.4)	6(16.6)	0.759
Hyperlipidemia	8(22.2)	7(19.4)	0.772

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Association of co-morbidities with age groups and gender of the study sample

Age is another important risk factor in relation to co-morbidities, majority of patients with age more than 60 year had one or more associated co-morbidities (36.8% and 57.8%, respectively) with significant statistical difference (*P* = 0.001), of these co-morbidities, hypertension and diabetes (50.0% and 52.4% respectively) were found to have significant statistical difference (*P* = 0.001 for each). Male gender is more associated with co-morbidities, where males had reported that 40.4% of them had one co-morbidity and 33.3% had more than two co-morbidities, with significant statistical association (*P* = 0.038), also smoking showed significant relation with male gender (*P* value = 0.006), while hypertension, diabetes, and hyperlipidemia were not statistically significant with gender of the patients (*P* = 1.0, 0.795 and 0.563, respectively) as shown in Table 3.

Table 3: Association of co-morbidities with age groups and gender of the study sample. N= 72

	Age groups (No. %)			
Variables	**Less than 50 years N= 37**	**51- 60 years N= 16**	**61 years & more N= 19**	***P* value**
No risk factor	23(62.1)	3 (18.7)	1 (5.2)	
One risk factor	8 (21.6)	7 (43.7)	7 (36.8)	
Two and more risk factors	6 (16.2)	6 (37.5)	11(57.8)	0.001*
Hypertension	4 (10.8)	8 (50.0)	12 (63.1)	0.001*
Diabetes mellitus	4 (10.8)	6 (37.5)	11 (57.8)	0.001*
Smoking	7(18.9)	1(6.2)	5 (26.3)	0.338*
Hyperlipidemia	4 (10.8)	4 (25.0)	7 (36.8)	0.070*
Gender, (No. & %)				
	Male N=42		**Female N=30**	
No risk factor	11(26.1)		16 (53.3)	
One risk factor	17 (40.4)		5 (16.6)	
Two and more risk factors	14 (33.3)		9 (30.0)	0.038
Hypertension	14 (33.3)		10 (33.3)	1.00
Diabetes mellitus	13 (30.9)		8 (26.6)	0.795
Smoking	12 (28.5)		1(3.3)	0.006 *
Hyperlipidemia	10 (23.8)		5 (16.6)	0.563

*: Fisher exact test

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Physical cup appearance between cases and controls

The absence of physiological cup over the optic disc was higher among cases compared to the control group (80% and 20%, respectively) with a highly significant statistical association (P = 0.001) as shown in Table 4.

Association between the absence of physical cup and risk factors

The physiological cup over the optic disc was absent among 26.6% of those patients with no risk factors, while 26.6 % of those with one risk factor and 46.6% of those with two and more risk factors, with no significant statistical association (*P* = 0.079). Co-morbidities like hypertension, smoking, and hyperlipidemia were not significantly associated with the absence of physical cup (*P* = 0.447, 0.537 and 1.0, respectively), only diabetes was significantly associated (*P* = 0.001) as shown in Table 5.

Table 4: Association of physical cup appearance between cases and controls.

Variables	Physical cup appearance		*P* value
	No No. (%)	Yes No. (%)	
Cases	24 (80.0)	12 (28.5)	0.001
Controls	6 (20.0)	30 (71.4)	
Total	30(41.7)	42(58.3)	

Table 5: Association between physical cup appearance and risk factors (n= 72).

Variables	Physical cup appearance		*P* value
	No (Total=30) No. (%)	Yes (Total=42) No. (%)	
Risk factors			
No risk factor	8 (26.6)	19 (45.2)	
One risk factor	8 (26.6)	14 (33.3)	0.079
Two and more risk factors	14 (46.6)	9 (21.4)	
Co- Morbidities			
Hypertension	12 (40.0)	12 (28.5)	0.447
Diabetes mellitus	15 (50.0)	6(14.2)	0.001
Smoking	4 (13.3)	9 (21.4)	0.537
Hyperlipidemia	6 (40.0)	9 (60.0)	1.00

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Blood group O+ve was most common among cases compared to controls (63.8% and 36.1%, respectively) with no significant statistical association (Table 6). Figure 1 shows the association between risk factors and blood group of the patients.

Discussion

Ischemic optic neuropathy is one of the major causes of blindness or seriously impaired vision, yet there is disagreement as to its pathogenesis, clinical features and especially its management. This is because ischemic optic neuropathy is not one disease but a spectrum of several different types, each with its etiology, pathogenesis, clinical features, and management. In our study, we had excluded cases other than non arteritc AION, searching for the possible relation with risk factors. The mean age in our cases was 51 year, which is relatively younger than what mentioned in other international studies like Lee et al.[3] and Atkins and colleagues[5](60 years). This may be related to poor adherence of our patients to their anti-hypertensive and anti-diabetes medications and low health education. Anyhow, age appeared to be a very important factor in association with other co-morbidities (*P* = 0.001) especially with hypertension and diabetes (*P* = 0.001 and 0.001, respectively). In our patients with NA-AION, aging was also shown to be significant in a study done by Monteiro[14] in Brazil. This finding may be explained by the fact that atherosclerosis and other associated risk factors are more frequent in late middle age and elderlies.

Table 6: Blood groups of cases and controls

Blood group	Cases N=36 No. (%)	Controls N=36 No. (%)	*P* value*
A-ve	0 (0.0)	2 (5.5)	0.058
A+ve	7(19.4)	5(13.8)	
AB+ve	3(8.3)	7 (19.4)	
B+ve	3(8.3)	8(22.2)	
O-ve	0(0.0)	1(2.7)	
O+ve	23(63.8)	13(36.1)	

*: Fisher exact test

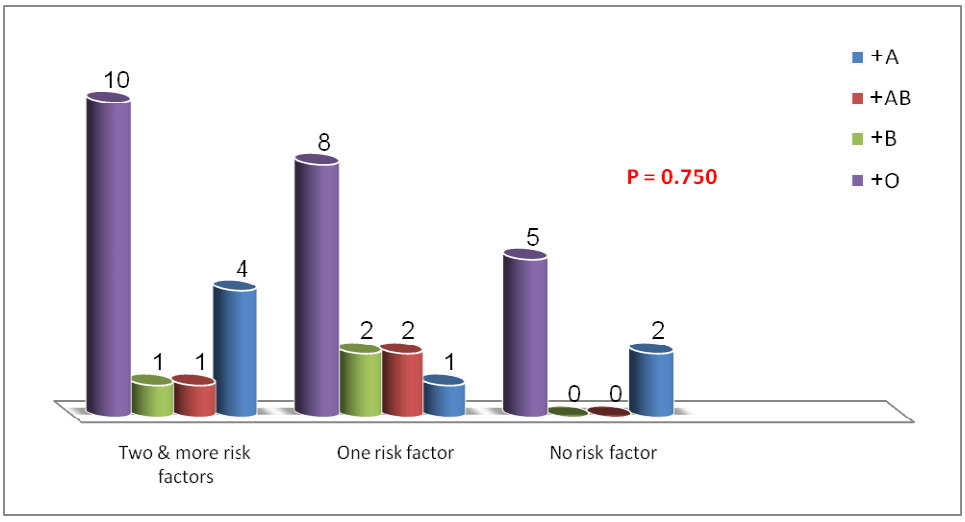

Figure1: Association between risk factors and blood group of the patients. n= 36.

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The presence of co-morbidities has special importance in our studied group and significant number of the cases have one or more risk factors (*P* = 0.001), of these risk factors diabetes and hypertension showed significant relation with anterior ischemic optic neuropathy (*P* = 0.001 and 0.046, respectively), which in turn highly agree with the findings of Lee et al.,[3] Atkins and colleagues,[5]and Hayreh.[7] On the other hand, smoking and hyperlipidemia appeared non-significant in our study, hyperlipidemia was found to be significant in the pre-mentioned studies, but smoking has no studied data, a larger study with a more included number of patients would give a better estimation of hyperlipidemia in our patients. In this sample, unlike other studies like Johnson and Arnold,[9] and Atkins and colleagues,[5] male patients were more than female to have an association with co-morbidities, and the relationship was statistically significant (*P* = 0.038). Smoking is the risk factor of importance in male group (*P* = 0.006), this may be attributed to the type of traditions and habits of the society in this area that considers smoking unacceptable for female. Physiological cup of the optic nerve disc has special importance in the relationship with the occurrence of anterior ischemic optic neuropathy as revealed by many studies done by Monteiro[14], Hayreh and Zimmerman[13] and Purvin et al.[12] that was attributed to the structural crowding over the optic nerve head with a small or absent cup. This is parallel with our finding in this study as a highly significant relationship as an independent factor with AION (*P* = 0.001) and when associated with diabetes (*P* = 0.001).

Conclusion

Hypertension, diabetes, age, male gender and absence of the physiological cup over the optic disc are significant risk factors for NA-AION in our sample of patients. It is recommended for future studies to further assess the other risk factors that may have important relation with the occurrence of NA-AION like hyperlipidemia, smoking, hematological diseases, sleep apnea, and uses of sildenafilt, which will be better estimated by a larger group of patients.

Competing interests

The authors declare that they have no competing interests.

References

1. Sethi H, Menon V, Saxena R. Anterior ischemic optic neuropathy (AION). DJO 2004; 10:4.
2. Hauser S, Josephson S, Harrison´s Neurology in Clinical Medicine. 3rd ed. USA: McGraw Hill Medical; 2013.
3. Lee MS, Grossman D, Arnold AC, Sloan FA. Incidence of nonarteritic anterior ischemic optic neuropathy: increased risk among diabetic patients. Ophthalmology 2011; 118:959–63.
4. Kanki J, Bowling B, Nischal K, Pearson A. Clinical Ophthalmology a Systematic Approach. 7th ed. UK: Elsevier; 2011.
5. Atkins E, Bruce B, Newman N, Biousse V. Treatment of Nonarteritic Anterior Ischemic Optic Neuropathy. Surv Ophthalmol 2010; 55(1):47–63.
6. Ropper A, Samuels M. Adams and Vector´s Principles of Neurology. 9th ed. USA McGraw Hill Medical; 2009.
7. Hayreh SS. Anterior ischemic Optic Neuropathy. Arch Neurol 1981; 38:675.
8. Yanoff M, Duker J. Ophthalmology. 4th ed. UK: Elsevier; 2013.
9. Johnson LN, Arnold AC. Incidence of nonarteritic and arteritic anterior ischemic optic neuropathy. Population-based study in the state of Missouri and Los Angeles County, California. J Neuroophthalmol 1994; 14(1):38–44.
10. Kerr NM, Chew SS, Danesh-Meyer HV. Non-arteritic anterior ischaemic optic neuropathy: a review and update. J Clin Neurosci 2009; 16(8):994–1000.
11. Liew SC, Mitchell P. Anterior ischaemic optic neuropathy in a patient with optic disc drusen. Aust N Z J Ophthalmol 1999; 27(2):157–60.
12. Purvin V, King R, Kawasaki A, Yee R. Anterior ischemic optic neuropathy in eyes with optic disc drusen. Arch Ophthalmol 2004; 122(1):48–53.
13. Hayreh SS, Zimmerman MB. Nonarteritic anterior ischemic optic neuropathy: refractive error and its relationship to cup/disc ratio. Ophthalmology 2008; 115(12):2275–81.
14. Monteiro M. Anterior ischemic optic neuropathy: a comparison of the optic disc area of patients with the arteritic and non-arteritic forms of the disease and that of normal controls. Arq Bras Oftalmol 2006; 69(6):805–10.
15. Kuppersmith MJ, Frohman L, Sanderson M. Aspirin reduces the incidence of second

https://doi.org/10.15218/zjms.2018.040

eye NAION: a retrospective study. J Neuroophthalmol 1997; 17(4):250–3.
16. Hayreh SS, Podhajsky PA, Zimmerman B. Nonarteritic anterior ischemic optic neuropathy: time of onset of visual loss. Am J Ophthalmol 1997; 124 (5):641–7.
17. Landau K, Winterkorn JM, Mailloux LU, Vetter W, Napolitano B. 24-Hour blood pressure monitoring in patients with anterior ischemic optic neuropathy. Arch Ophthalmol 1996; 114(5):570–5.