

A Hospital-Based Study on Aetiology of Third, Fourth and Sixth Cranial Nerve Palsies

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ABSTRACT

BACKGROUND

Neuro-ophthalmology deals with complex systemic diseases that affect the visual system and pose a challenge for ophthalmologists. Here the focus is on the diseases of the nervous system that affect vision, ocular motility, or pupillary reflexes. Diplopia, a common symptom of cranial nerve palsy, may result from ophthalmic, orbital, or neurologic disorders. Our study intended to determine the aetiology of ocular motor nerve palsies.

METHODS

A cross-sectional study was conducted for two years at a tertiary care centre in South India. We evaluated 30 patients who came to the Ophthalmology OPD or were admitted, after obtaining the approval of the Ethics committee.

RESULTS

A total number of 30 patients who fulfilled the inclusion criteria were studied. There were 14 male and 16 female patients. The age range was 12 - 87 years with a mean age of 45 years. The highest incidence noticed was isolated sixth nerve palsy in 13 (43.3 %) patients. 11 patients had isolated third nerve palsy (36.7 %), while mixed ocular motor nerve palsies (third, fourth and sixth) were seen in 6 patients (20 %). None of them had isolated fourth nerve palsy.

CONCLUSIONS

- The sixth nerve continued to be the most common among the ocular motor nerve palsies. Meningitis was the major cause.
- Diabetes and trauma, infections with CNS inflammation accounted for a majority of third nerve palsies.
- Multiple cranial nerve palsies had varied aetiology like HIV Infection, Tolosa Hunt Syndrome, aneurysm of intracavernous part of ICA, cavernous sinus thrombosis and trauma.
- The patient's age, associated symptoms, clinical features and types of palsy are of great importance to choose appropriate radiological methods to study and treat these isolated cranial nerve palsies.

KEY WORDS

Diabetes, Meningitis, Oculomotor Nerve, Trochlear Nerve, Abducent Nerve, Trauma

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BACKGROUND

Neuro-ophthalmology, an academically-oriented subspecialty, combines the fields of neurology and ophthalmology. It deals with complex systemic diseases that affect the visual system and pose a challenge for ophthalmologists. Here the focus is on the diseases of the nervous system that affect vision, ocular motility, or pupillary reflexes. Diplopia, a common symptom of cranial nerve palsy, may result from ophthalmic, orbital, or neurologic disorders. It can be congenital, traumatic, or due to vascular diseases like hypertension, diabetes, strokes, aneurysms etc. Microvascular ischemia is presumed to be one of the leading causes of acquired ocular motor cranial nerve palsy, particularly in older patients. It can also be due to infections, migraines, tumours, or elevated intracranial pressure. Palsies of the extraocular muscles commonly present as binocular diplopia because the images do not fall on corresponding points of each retina. It is important to identify associated signs and symptoms and determine in which gazes double vision occurs to identify which cranial nerves are affected.

The position of the globe in the orbit is maintained by the extraocular muscles which are innervated by the third, fourth and sixth cranial nerves. Extraocular movements are governed by higher centres like the motor cortex, midbrain, pons, cerebellum and vestibular apparatus interlinked to the visual system. Any disturbance to these vital structures can lead to ocular motility disorders. Paralysis of the extraocular muscle due to lesions in one or all of these cranial nerves results in restriction of one or both eye movements which causes loss of binocular single vision. Clinical manifestations of ocular motor nerve palsies may differ based on the cause and the location of the lesions involving the third, fourth and sixth cranial nerves. Symptoms may include diplopia, ptosis, facial anaesthesia and dysarthria, ataxia, dizziness, headache, nausea and vomiting, limb weakness etc.

Cranial nerve III supplies the superior, inferior, medial recti and inferior oblique muscles. It also supplies the levator palpebrae superioris and carries the parasympathetic innervations to the pupil. Involvement of this nerve will produce symptoms that involve one or more of these muscles and usually results in double vision. The trochlear nerve is the only cranial nerve to emerge from the dorsal aspect of the brain. Trochlear nerve palsy typically causes diplopia that worsens in downgaze. Hence, patients almost always report diplopia while reading. Cranial nerve VI is purely motor in function. It supplies the lateral rectus muscle and is responsible for the abduction of the eye.

The data showing the prevalence and causes of ocular nerve palsies in a selected population may help guide early diagnosis and evaluation. When evaluating a case with neurogenic diplopia, one must trace which ocular motor nerve is involved and locate the level of the lesion. Therefore careful evaluation of the patient is important to identify the type of diplopia (horizontal, vertical or oblique) and the deviation in which the two images are most widely separated. Associated features like ptosis, lid lag, facial asymmetry, anisocoria, vertigo and weakness help to localise the lesion and identify the cause.

Our study intended to determine the relative frequencies and aetiology of ocular motor nerve palsies.

METHODS

A cross-sectional study was conducted for two years at a tertiary care centre in South India. We evaluated 30 patients of both sexes who came to the Ophthalmology OPD or were admitted, after obtaining the approval of the Ethics committee.

All data collection and study adhered to the tenets of the Declaration of Helsinki and Good Clinical practice guidelines. The patient's particulars like age, sex, past medical history of hypertension, diabetes mellitus, vascular disorders, trauma and other systemic problems were documented. The duration from onset of symptom to presentation was noted. A detailed neuro-ophthalmic examination was done which included best-corrected visual acuity, colour vision, head posture, ptosis evaluation, extraocular movement, visual axis, diplopia charting, prism bar test for the degree of deviation of the eye, slit-lamp examination of the anterior segment, pupil size and reactions, lens profile and fundus examination (by direct, indirect ophthalmoscope and +78D lens with slit lamp). A complete neurological examination was done which included mental status, cognition, and examination of other cranial nerves, motor system, sensory system, cerebellar deficits, deep tendon reflexes, plantars and signs of meningeal irritation.

Routine investigations, CSF analysis, imaging of the skull, orbital fissures, optic foramina, paranasal sinus were done. CT scan and MRI scan were noted wherever indicated. The diagnosis of ocular motor nerve palsy was made based on the documented history and examination.

Inclusion Criteria

Patients with isolated or combined palsies of third, fourth and sixth cranial nerves were included in this study.

Exclusion Criteria

Patients with myasthenia gravis, myopathies and thyroid ophthalmopathy were excluded from the study.

Sample Size

The study population consisted of all 30 patients who presented within the study period with diplopia, headache, or restriction of ocular movements that met the inclusion and exclusion criteria.

Statistical analysis

Descriptive statistics including mean, standard deviation and frequency percentages were obtained and analysed using software SPSS version16.

RESULTS

A total of 30 patients in which there were 14 male and 16 female patients were studied. The age range was 12 - 87 years with a mean age of 45 years. [Table 1] The highest incidence was that of isolated sixth nerve palsy seen in 13 (43.3 %) patients. 11 patients had isolated third nerve palsy (36.7 %), while mixed ocular motor nerve palsies (third, fourth and sixth) were seen in 6 patients (20 %). None of the patients had isolated trochlear nerve palsy.

Nerve Palsy	III	IV	VI	Multiple
Total	11	0	13	6
Mean age	56.5	0	34.2	47.5
Age in years	23 - 87	0	12 - 63	32 - 68
Male	5	0	4	5
Female	6	0	9	1

Table 1. Age and Sex Distribution of Ocular Motor Nerve Palsies

Cranial Nerve	Rucker (1958) ³	Rucker (1966) ¹⁷	Rush and Young (1981) ²	Krishna and Mekhari (1973)	Rama et al. (1980) ¹	Present Study (2016)
III	33.5 % (335)	27.4 % (274)	29 % (290)	33.3 % (60)	31.1 % (28)	36.7 % (11)
IV	6.7 % (67)	8.4 % (84)	17.2 % (172)	0.5 % (1)	1.1 % (1)	0 %
VI	40.9 % (409)	51.5 % (515)	41.9 % (419)	41.5 % (74)	32.1 % (29)	43.3 % (13)
Multiple	18.9 % (189)	12.7 % (127)	1.9 % (19)	25 % (45)	35.5 % (32)	20 % (6)

Table 2. Distribution of Ocular Motor Nerve Palsies in Different Studies in Comparison with Our Study

Abducent Nerve

The sixth cranial nerve was the most affected in our study. Out of 13 patients (43.3 %) with sixth nerve palsy, seven patients had unilateral involvement and six patients had bilateral involvement. Figure 1: shows a case of bilateral sixth cranial nerve palsy.

The mean age in this group was 34.2 years with ages ranging between 12 and 63 years; nine (69 %) patients were females and four (31 %) patients were males. Female predominance was seen in patients with sixth nerve palsy. On fundus examination four patients (30.3 %) had papilloedema.

Out of the 13 patients with sixth nerve palsy, four patients (30.7 %) presented with meningitis, three (23.1 %) with a history of trauma, one patient each (7.7 % each) with basilar trunk aneurysm, idiopathic intracranial hypertension and diabetic neuropathy. The cause could not be identified in three patients (23.1 %).

All four meningitis patients with sixth nerve involvement had tubercular aetiology and two of them were positive for HIV antibodies by ELISA.

Third Cranial Nerve

There were 11 patients (36.7 %) with third cranial nerve palsy, five (44 %) were females and six (56 %) males. The mean age was 56.5 years with the age range between 23 and 87 years, 27.2 % were in the age group 50 - 59 years. The male-female ratio was 5:6. All the patients had unilateral involvement. The most common etiologic factors were diabetes mellitus and trauma in five patients each (45.5 %), followed by a case of HIV with toxoplasmosis of the central nervous system (one patient- 9 %). Out of five cases of diabetic third nerve palsy, three had diabetic retinopathy changes.

Multiple Cranial Nerve Palsy

There were six patients (20 %) with multiple cranial nerve palsies in our study, and all had total ophthalmoplegia. The mean age was 47.5 years, with an age range between 32 - 68 years.

There were five male patients and one female patient. Five had unilateral involvement and one had bilateral involvement.

The causative factors for multiple cranial nerve palsy were HIV infection in two patients (33.2 %), one with fulminating CMV retinitis, one (16.7 %) each with cavernous sinus thrombosis, trauma, Tolosa Hunt Syndrome, intracavernous right internal carotid artery (ICA) aneurysm.

DISCUSSION

In this study of 30 patients of ocular motor cranial nerve palsies, the majority of the sixth nerve palsy patients were in the 12 - 63 year age group and multiple nerve palsy patients were in the 30 - 60 years of age group, while third nerve palsies were equally distributed in the age range 23 - 87 years. (Table 1)

Earlier reports by Rama et al. 1980 and Rush and Younge, 1986 showed the incidence of cranial nerve palsies without specific reference to the nerves affected, age distribution or the underlying causes.^{1,2}

A comparison of nerve palsies in our study with earlier reports is shown. [Table 2]. As in our study, the 6th nerve was the most frequently affected in all these studies.

Sixth Cranial Nerve Palsy

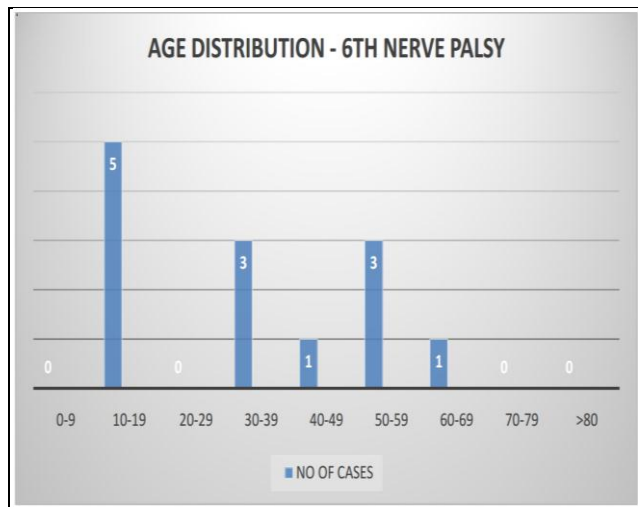
In our study, 13 (43.3 %) cases of 6th nerve palsy were noted. In seven patients (54 %) it was unilateral and in six (46 %) it was bilaterally affected. The commonest aetiology in our study was increased intracranial tension due to meningitis, unlike in the Rucker CW series where out of 409 patients 129 (31.54 %) had an undetermined cause.³ Similarly, Tiffin et al. and Menon V had reported unknown aetiology in 33 % and 36.2 % respectively.^{4,5} Majority of patients with 6th nerve palsy in our study were in the productive age group (Graph 1).

According to Mansour AM, 4 % of patients with AIDS developed ocular cranial nerve palsies.⁶ In AIDS, cranial nerve palsies can be multiple and bilateral. Brainstem toxoplasmosis was the commonest cause in AIDS patients.

Other causes found to be cryptococcosis, varicella-zoster, CMV, lymphomas, eosinophilic granuloma affecting cavernous sinus or apex of the orbit, and in our study two out of four tubercular meningitis patients had HIV infection.

The abducent nerve was affected by increased or decreased intracranial pressure. Due to its long course through the subarachnoid space, there is a chance of compression of the 6th nerve between the pons and the basilar artery, clivus or stretched at the apex of the petrous part of the temporal bone with intracranial pressure changes. As in the Rucker CW study we also noticed that trauma was the second leading cause of 6th nerve palsy (three patients, 23 %).³ 26 (19.5 %) out of 133 cases of 6th nerve palsies were traumatic in origin as shown by Robertson, Hines and

Rucker.⁷ 12 % of traumatic abducent nerve palsies were reported in Patel SV study also.⁸ Contusion or severance of the 6th nerve is the most common reason for paralysis after closed cranioencephalic trauma.



Graph 1. Sixth Cranial Nerve Palsy – Age Distribution



Figure 1. Bilateral 6th Nerve Palsy. A - Primary Position. B - Right Gaze. C - Left Gaze.

Oculomotor Nerve Palsy

11 patients had isolated third cranial nerve palsy and the incidence was more in the older age group. 27.3 % was in the mean age of 56.5 years.

As in Green WR, Hackett ER, and Schlezinger NS, the male: female ratio was 5:6 in our study also. All eleven patients (100 %) had drooping of the upper eyelid.⁹ This was in sharp contrast to a study conducted by Green WR and associates in which only 29.23 % of patients had ptosis.⁹

Solomons DJ and associates suggested that traumatic 3rd nerve palsy can be due to direct injury or secondary to progressing extradural or subdural hematoma.¹⁰ According to Heinz J high-speed closed head injury can lead to avulsion, contusion or intraneural or perineural hematoma.¹¹ In our study, fractures of orbital walls were seen in two. The incidence of traumatic third nerve palsy was 10.8 % in the Green WR study, 15.2 % out of the 335 cases by Rucker and 36.7% in our study.^{3,9}

One of the major causes of third nerve palsy in our study was diabetes mellitus (45.5 %), whereas Rush JA and associates found 8.60 % and 6.26 % in Rucker’s series.^{2,3}

Goldstein JE, Cogan DG noted that pupil sparing 3rd nerve palsy most commonly resulted from an intrinsic vascular lesion.¹² Asbury A, et al. felt that presumably there was a central ischemic infarct that spared the more peripherally placed parasympathetic fibres.¹³ Autopsy study by Dreyfus PM and associates demonstrated that diabetic 3rd nerve palsy was the result of occlusion of vasa nervosum leading to ischemic infarcts of the nerve.¹⁴ In contrast Hopf HC, Gutman L. concluded that mesencephalic infarct and not peripheral nerve lesion as the pathology under diabetic 3rd nerve palsy.¹⁵

Cerebral toxoplasmosis secondary to HIV accounted for oculomotor nerve palsy in one patient (9 %) in our study. Antworth AN, Beck RW also reported a 29-year-old parenteral drug abuser with toxoplasmosis and HIV.¹⁶

Multiple Cranial Nerve Palsy

Six (20 %) out of 30 patients had all three ocular nerves (third, fourth and sixth) affected with total ophthalmoplegia, matches with Rucker study (1958) (18.9 %).³ 100 % had total ophthalmoplegia. Five patients had unilateral involvement and one patient had bilateral involvement.

The common etiologic factor for multiple nerve palsy was HIV infection in 2 (33.2 %). Cavernous sinus thrombosis, trauma, aneurysm of intracavernous part of the internal carotid artery and Tolosa hunt syndrome seen in one (16.7 %) patient each. Six (5 %) out of 121 patients had aneurysms and one patient had multiple cranial nerve palsies in the Nolon study.¹⁶

The anatomic localization of lesions of the majority of sixth nerve palsy and isolated third nerve palsy was in the subarachnoid space. Subarachnoid space & intracavernous location were seen for the majority of multiple nerve palsies.

CONCLUSIONS

The following conclusions were drawn from this study.

- The sixth nerve continues to be the most common among the ocular motor nerve palsies. Meningitis was the major causative factor followed by trauma, basilar trunk aneurysm, diabetic neuropathy, intracranial hypertension and some were idiopathic.
- Diabetes, trauma and meningitis accounted for a majority of third nerve palsies.
- Multiple cranial nerve palsies had varied aetiology like opportunistic infections in HIV, cavernous sinus thrombosis, trauma, aneurysm of intracavernous part of ICA and Tolosa Hunt Syndrome.
- The patient’s age, associated symptoms, clinical features and types of palsy are of great importance to choose appropriate radiological methods to study and treat these isolated cranial nerve palsies.

Data sharing statement provided by the authors is available with the full text of this article at jemds.com.

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REFERENCES

- [1] Rama V, Vimala J, Chandershekhar M, et al. Ophthalmoplegia. (A study of ninety cases). *Indian J Ophthalmol* 1980;28(1):13-6.
- [2] Rush JA, Younge BR. Paralysis of cranial nerves III, IV and VI. Causes and Prognosis in 1,000 cases. *Arch Ophthalmol* 1981;99(1):76-9.
- [3] Rucker CW. Paralysis of the third, fourth and sixth cranial nerves. *Am J Ophthalmol* 1958;46(6):787-94.
- [4] Tiffin PA, MacEwen CJ, Craig EA, et al. Acquired palsy of the oculomotor, trochlear and abducens nerves. *Eye* 1996;10(Pt 3):377-84.
- [5] Menon V, Singh J, Prakash P. Aetiological patterns of ocular motor nerve palsies. *Indian J Ophthalmol* 1984;32(5):447-53.
- [6] Mansour AM. Neuro-ophthalmic findings in acquired immunodeficiency syndrome. *J Clin Neuro Ophthalmol* 1990;10(3):167-74.
- [7] Robertson DM, Hines JD, Rucker CW. Acquired sixth nerve palsies in children. *Arch Ophthalmol* 1970;83(5):574-79.
- [8] Patel SV, Mutyala S, Leske DA, et al. Incidence, association and evaluation of sixth nerve palsy using a population-based method. *Ophthalmology* 2004;111(2):369-75.
- [9] Green WR, Hackett ER, Schlezinger NS. Neuro ophthalmologic evaluation of oculomotor nerve paralysis. *Arch Ophthalmol* 1964;72:154-67.
- [10] Solomons NB, Solomon DJ, de Villiers JC. Direct traumatic third nerve palsy. *S Afr Med J* 1980;58(3):109-11.
- [11] Heinz J. Cranial nerve avulsion and other neural injuries in road accidents. *Med J Aust* 1969;2(25):1246-9.
- [12] Goldstein JE, Cogan DG. Diabetic ophthalmoplegia with special reference to the pupil. *Arch Ophthalmol* 1960;64:592-600.
- [13] Asbury AK, Aldredge H, Hershberg R, et al. Oculomotor palsy in diabetes mellitus: a clinical pathological study. *Brain* 1970;93(3):555-66.
- [14] Dreyfus PM, Hakim S, Adams RD. Diabetic ophthalmoplegia; report of case, with postmortem study and comments on vascular supply of human oculomotor nerve. *Arch Neurol and Psychiat* 1957;77(4):337-49.
- [15] Hopf HC, Gutmann L. Diabetic third nerve palsy: evidence for a mesencephalic lesion. *Neurology* 1990;40(7):1041-5.
- [16] Nolon J. Diplopia. *Br J Ophthalmol* 1968;52(2):166-71.
- [17] Rucker CW. The causes of paralysis of the third, fourth and sixth cranial nerves. *Am J Ophthalmol* 1966;61(5 Pt 2):1293-8.