# A clinical study of etiological factors contributing to third, fourth and sixth cranial nerve palsies

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#### ABSTRACT

**Aim:** To determine etiological factors contributing to third, fourth and sixth cranial nerve palsies. **Objectives:** To know the distribution of nerve palsies according to age. To determine distribution patterns of various etiologies of third, fourth and sixth cranial nerve palsies in different age groups. **Materials and Methods:** This is a prospective study of etiological factors contributing to ocular nerve palsies , 50 cases from outpatient department were selected for the purpose of study. **Results:** 50 Cases of ophthalmoplegia had been analysed which included both isolated and combined palsies. Isolated sixth nerve palsy was observed in 18 cases (36%), isolated third nerve palsy in 15 cases (30%). There was no single cases of isolated fourth nerve palsy in this study. The

remaining 17 cases (34%) had involvement of 3<sup>rd</sup>,4<sup>th</sup> and 6<sup>th</sup> nerves in various combinations. In 4 out of 15 cases of isolated III nerve palsy (26.66%)there was pupil sparing. Of these 3 were cases of micro vascular ischemia and 1 case of meningioma with partial III nerve palsy. Out of the total cases in 5 cases (33.33%) there was bilateral involvement .Most of the cases of undetermined aetiology were of sixth nerve palsy(40%). Most common cause of third nerve palsy was inflammatory aetiology and sixth nerve palsy was trauma and tuberculosis. Third nerve was most commonly involved in the age group of 41-50 years (27.77%) and sixth nerve in the age group of 21-30 years and 41-50 years(22.72%). Inflammatory diseases (48%) were the most common aetiology in this study followed by trauma (14%) and undetermined aetiology(16%).Vascular aetiology was more common in elderly, trauma in middle age, tuberculosis in younger age group. Most of the patients showed (76.59%) showed either complete or partial recovery. Cases of vascular diseases and tuberculosis had more no. of cases with complete recovery (66.67% and 55.56%). All the cases of undetermined aetiology had complete recovery. In trauma and tumours, there was variable pattern of recovery. **Conclusion:** Isolated nerve palsies are more common than multiple ocular motor nerve palsies. Sixth nerve palsy is found to be more commonly involved followed by third nerve and multiple nerve palsies.

Key words: Cranial,ocular,muscles

#### Introduction

Third,Fourth and Sixth Cranial nerves supply extra ocular muscles, Levator palpebrae superioris, sphincter pupillae and ciliary muscle. Third, Fourth and Sixth cranial nerves are commonly encountered in

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clinical practice and usually express an underlying local, regional or general disease. Ocular motor nerve palsy can be caused by disorders or lesions that affect the nerve at any location, from their nuclear origin to their termination on the extra ocular muscles. They may be unilateral or bilateral, may involve one or more nerves at the same time. Clinical manifestations of ocular motor nerve palsies may differ according to the type and localisation of the lesions involving the third, fourth and sixth cranial nerves. They usually present with diplopia, defective vision, restriction of

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ocular movements and ptosis[1,2]. They may have other findings like brain stem neurological deficits, meningeal signs, involvement of other cranial nerves and orbital signs which can be clues to the underlying etiologies[1]. The basic patterns regarding the frequency of nerve palsies have remained fairly consistent but there is a changing etiological pattern. In order to find out etiology it is important to carry out a detailed examination and complementary investigations. No cause is found often despite a battery of investigations. A colloborative approach with other specialities is essential to enhance the diagnostic accuracy. This study is to find out etiologies which are emerging as frequent causes of Third, Fourth and Sixth cranial nerve palsies. Very few reports are available on this subject from our country. Data on the causes of ocular motor nerve palsies in a defined population may be useful in guiding diagnosis and evaluation, especially when colloborative work up and sophisticated complementary investigations are not available. In recent years, the twin developments of advancing technology and proliferating subspecialities have made accurate neuro-ophthalmic diagnosis a widespread reality[5].

Importance of ocular motor nerve palsies to ophthalmologist: Acquired palsies of ocular motor nerves are commonly initially referred to the ophthalmology emergency department and are often perceived as a sign of serious underlying pathology. instance, one of the true For neuroophthalmologic emergencies occur when there is compression of the third nerve resulting from an expanding aneurysm at the junction of internal carotid and posterior communicating arteries[3]. Such compressions most often, but not always are painful and in almost all instances involve the pupil. This is one of the few life threatening situation presentation[4] in neuro-ophthalmology and one in which appropriate diagnosis and treatment is life saving.

## Materials and Methods

This is a prospective study of etiological factors contributing to ocular nerve palsies which was carried out in the Regional Eye Hospital, Warangal during the period December 2014 to November 2015. 50 cases from outpatient department were selected for the purpose of study. 50 patients coming to Regional eye hospital were examined as per protocol.

**Inclusion Criteria**: All age groups and both sexes are being included.

**Exclusion Criteria:** Ocular nerve palsy secondary to neurosurgery.

In history taking much importance was given to the present illness, mode of onset, whether there were any attacks of headache, fever, trauma, vomitings, convulsions, history of exposure etc. In past history importance was given to diseases such as diabetes mellitus, hypertension and tuberculosis. In personal history patient was questioned regarding his dietary habits, appetite, bowel habits and frequency of micturition and addictions. In general examination detailed examination was made to find any septic foci, lymphadenopathies. primaries and secondaries. Nutritional condition of the patient was also considered. Routine complete ophthalmological examination was done. More stress was given to orthoptic and neurological examinations. Visual fields and tension were recorded if their involvement was suspected. Besides routine investigations like urine analysis, complete blood picture, VDRL, Mantoux test etc. some special investigations like blood sugar levels (fasting and post lunch), CSF analysis, angiogram, and X-ray of paranasal sinuses were taken and X-ray chest was taken when required. Radioimaging like CT Brain and Orbits-plain / contrast and MRI of brain,CT angiogram was done in all cases.Whenever required patient was advised Vascular imaging techniques like Contrast Angiography, MRA (Magnetic Resonance Angiography), Metabolic and Functional imaging like MRS(Magnetic resonance spectroscopy) and fMRI(Functional MRI).<sup>31</sup> All these cases were examined at frequent intervals to assess the prognosis of the patients. The cases were referred whenever required to Neurosurgeon, Gynaecologist, E.N.T. Surgeon for their opinions and to exclude the possibility of any septic foci. The aetiological factors in these cases were confirmed on the basis of history, clinical signs, laboratory investigations, opinion of the specialists to whom they were referred and response to the treatment given. The patients were treated in general with parenteral injections of vitamin B1, B6, B12. In special cases antibiotics like streptomycin, Ampicillin, Taxim, Cifran Gentamycin were given. Steroids were given when they were indicated.

## Results

50 patients attending Regional eye hospital, Warangal clinically diagnosed as ocular motor nerve paralysis are studied. Results of the study are presented below

Age in years	Males	Females	Total	Percentage
0-10	4	1	5	10%
11-20	3	5	8	16%
21-30	6	5	11	22%
31-40	4	-	4	8%
41-50	9	3	12	24%
51-above Total	6 32	4 18	10 50	20% 100%
Nerves involved				
VI nerve	10	8	18	36%
III nerve	11	4	15	30%
III, IV, VI nerves	3	5	8	16%
III, VI nerves	5		5	10%
Combination of III, IV, VI, V	3	1	4	8%
III, IV nerves				
IV nerve				

Table 1: shows age incidence of ocular motor nerve palsies, combinations of nerves involved in relation to
sex, sex distribution

The mean age is 36 years. Age distribution showed that most of the patients are in the age group of 41-50 years followed by 21-30 years. In this study Males are affected more commonly than females. Contributing 64% of total and females constitute 36% of the total.

 Table 2: shows laterality, distribution of nerve palsies, cause of third nerve palsy, cause of sixth nerve palsy, etiological factors.

Laterality	Number of patients	Percentage
Right eye	24	48%
Left eye	26	52%
Type of nerve palsy	Number of cases	Percentage
III	15	30%
IV	0	0%
VI	18	36%
III+IV	4	8%
III+VI	5	10%
III+IV+VI	8	16%
Total	50	100%
Etiology	Number of cases	Percentage
Inflammatory	7	46.66%
Vascular Diseases	4	26.66%
Trauma	2	13.33%
Tumour	1	6.66%
Undetermined	1	6.66%
Total	15	100.00%
Etiology	Number of cases	Percentage
Vascular	3	16.66%
Trauma	5	27.77%
Tumor	2	11.11%
ТВ	4	22.22%
Undetermined	4	22.22%
Total	18	100.00%
Etiological Factor	Number of patients	Percentage

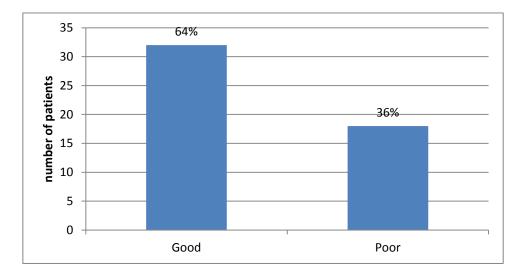
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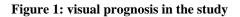
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Inflammatory	24	48%
Traumatic	7	14%
Diabetes	6	12%
Undetermined	8	16%
Neoplasms	5	10%

In this study out of total 50 cases Left eye involvement is more commonly seen accounting for 52% of the total and Right eye is of 48% of the total. In this study sixth cranial nerve is most commonly affected (36%) followed by third cranial nerve (30%) and multiple ocular motor nerves (16%) involvement. No single case of isolated fourth nerve palsy had been noted. Total no of cases of third nerve palsy were 15.Out of these inflammatory etiology was seen in 7 cases (46.6%) and Vascular etiology in 4 cases (26.6%). Trauma was the cause in 2 cases (13.3%) and undetermined in 1 case (6.6%). Total no of cases of sixth nerve palsy were 18.0f these vascular etiology is seen in 3 cases (16.6%). Trauma was the cause in 5 cases (27.7%), tuberculosis in 4 cases (22.2%) and undetermined in 4 cases (22.2%). In this study out of all the etiological factors, inflammatory is the most common cause constituting 48% of the total followed by undetermined etiology inspite of all the investigations done.

Cranial nerve	III	IV	VI	III,IV	III,VI	III,IV, VI	Other Combinations	TOTAL
No. of cases	15	0	18	0	5	8	4	50
Inflammatory	5	0	12	0	2	4	1	24
Neoplasms	0	0	1	0	1	2	1	5
Trauma	2	0	3	0	1	1	0	14
Diabetes	4	0	1	0	1	0	0	6
Undetermined	4	0	1	0	0	0	3	8





Following early recognition and prompt treatment the prognosis is usually good. 64% of cases have shown good visual improvement. Multiple ocular motor nerve palsies were seen in 17 cases. Of these

III+IV nerves were involved in 4 cases, III+VI nerves in 5 cases and III+IV+VI nerves in 8 cases. Most of these patients are in age group of 31-40 years.

## Discussion

**Age Distribution:** In this study of 50 patients of ocular motor cranial nerve palsies, sixth cranial nerve is most commonly affected (44%) followed by third cranial nerve (36%) and multiple ocular motor nerves (20%) involvement. Most of the patients were in the

age group of 41-50 years. Majority of third nerve palsy patients were in the age group of 41-50 years, sixth nerve palsy patients were in age group of 21-30 years and multiple nerve palsy patients were in the 31-40 years of age group.

## Table 4: shows comparison of distribution of nerve palsies with other studies.

Cranial nerve palsy III	<b>Rucker</b> ( <b>1958</b> ) 33.5	<b>Rucker</b> (1966) 27.4	<b>Rush and Young</b> ( <b>1981</b> ) 29.0	Krishna and Mehkari (1972) 33.3	<b>Rama et</b> <b>al (1980)</b> 31.1	<b>PS Reddy</b> <i>et al</i> (1972) 43
IV	6.7	8.4	17.2	0.5	1.1	1
VI	40.9	51.5	41.9	41.5	32.2	30
Multiple	18.9	12.7	1.9	25	35.5	26

Distribution of nerve palsies: In the earlier reports (Rucker series) [6,7] (Rush and Younge,1981)[8] all the cases were analysed together, irrespective of the nerve involved for determining the peak incidence, the drawback in this approach being that various nerve palsies have different etiological patterns and occurrence of these causative factors has some relation to the various

age groups. Table 4 shows the comparison of frequency of nerve palsies between earlier reports and present series. Like in earlier series, sixth nerve was affected more frequently in our series (60%). Comparison of etiologies with other studies: In this study inflammatory aetiology was found to be the most common cause. It was followed by undetermined (16%) and trauma (14%).

Table 5: shows	comparison	of etiologies	with oth	er studies

Etiology	<b>Rucker</b> (1966)	MenonV et al	Rama et al	PS Reddy et al	Present series
Inflammatory	2	21.1	14.3	26	48
Vascular	1	6.1	13.33	12	12
Traumatic	1	28.7	17.78	15	14
Aneurysms	1	1.0	1.11	4	2
Neoplasms	1	12.2	29.8	27	8
Undetermined	2	30.5	6.67	22	16

In comparison with earlier studies , In Rucker study(1996), Rush & Younge study (1981) more no. of cases were of undetermined aetiology (28.2 and 30.4). In south Indian studies like Rama et al (1980) ,PS Reddy et al (1971) tuberculosis was the most common aetiology (21.11% and 26%) respectively. In this study there is a decline in the no. of cases of tuberculosis which could be due to prompt and appropriate treatment of TB leading to decreased rate of complications[9]. In comparison with other Indian studies like Menon V et al (6.1%), Rama et al (13.34%) and PS Reddy et al study (12%) there is an increase in vascular aetiology (24%). These could be because all the cases of the cerebro vascular stroke and micro vascular ischemia were included under vascular aetiology

and due to an increase in prevalence of systemic diseases like Diabetes and Hypertension. Trauma was seen in 14% cases which is in accordance with earlier studies like Rucker study(1966- 11.8%) Menon V et al study (18.7%) Rama et al study(15.1%). There were 8 cases of undetermined aetiology. In these cases a definitive aetiology causing ophthalmoplegia could not be made in spite of getting the above investigations done. But all the cases recovered completely either spontaneously or with oral steroids presuming a micro vascular or inflammatory aetiology. In earlier studies, the no. of cases with undetermined aetiology were more. In Rucker (1996) study it was 28.8% & Menon V et al study(1984) it was 30.5%. In PS Reddy et al study it was 22% but in Rama et al study it was only 6.67%

## for which no definite explanation was offered[10] **Third Cranial Nerve Palsy**

There were 15 cases who had isolated third cranial nerve palsy. A study of the age distribution reveals that the incidence of isolated oculomotor nerve paralysis is more in the older age group(41-50 years). The greatest incidence of isolated third nerve palsy was in fifth decade. The right oculomotor nerve was involved in 9 cases and left oculomotor nerve in 6 cases. The male: female ratio was 5:4. This was similar to the study conducted by Green WR et al who had sex incidence approximately equal on both sides. Vascular disease was the cause in 4 out of 15 cases(26.66%) of isolated third nerve palsy. The incidence of diabetic third nerve palsy in this study was 16.66%. Rush JA and associates had found the incidence of diabetic third nerve palsy to be 8.60%, whereas in Rucker's series, it was 6.26%[11]. In 2 cases, (13.34%) trauma to the head sustained in road traffic accidents was the cause. This was comparable to Richards & Young series (14.3%), Rush and Young series (16.1%), Rucker series (11.5%), Rama et al study (18.3%) and Menon V et al study (15.6%). Green WR and associates had found incidence of traumatic third nerve palsy as10.8% .HoopeR [12] reported third nerve involvement in 12 of 58 patients with trauma to head. Of the 335 cases of third nerve paralysis reported by Rucker, 15.2% were due to trauma. Rush JA and associates reported incidence of traumatic third nerve palsy as 16.2%. Elston JS[13] studied 20 patients with traumatic third nerve palsy. Of these 16 were males and average age was 25 yrs. In trauma as suggested by Solomons DJ[14] and associates, third nerve may be damaged either directly as a result of injury or indirectly due to compression from an expanding extradural or subdural hematoma. Heinz J [15] disclosed that third nerve is damaged in fatal, high speed closed head injury by either avulsion from mesencephalon, primary contusion necrosis or intra and perineural haemorrhage in subarachnoid space. In 3 cases tuberculosis was the etiological factor. In 2 it was tuberculous meningitis and in 1 was tuberculoma. This was comparable to south Indian studies like Rama et al study and PS Reddy study. In 1 case (6.66%) ,the cause could not be determined in spite of all investigations done. This much less than earlier studies. No was definitive explanation could be offered for this.

Etiologies of III cranial nerve palsy in other studies: In comparison of etiologies of III nerve palsy with other studies, In both the Rucker

series (1958 & 1996) more no.of cases were of undetermined etiology. In PS Reddy et al study (1972) most common cause of III nerve palsy was tuberculosis and vascular disease. In Rama et al study(1980) trauma was the most common cause of isolated III nerve palsy followed by vascular causes.In Menon V et al study more no of cases(30.15%) were of undetermined aetiology.<sup>16</sup> In Green et el study(1964), Richard & Younge study (1992), Rush & Younge(1981) study, more no. of cases of isolated III nerve palsy were of undetermined aetiology. Sixth Cranial Nerve Palsy: Isolated VI nerve palsy was the most common(36%) nerve palsy in this study. More no of patients of sixth nerve palsy were in the age group of 21-30 years. Trauma was the most common definitive etiology (27.77%) of sixth nerve palsy. Head injury was responsible for 5 cases(27.77%) of VI nerve palsy. This closely matches the incidence of traumatic sixth nerve palsy reported Rucker CW [8]. Also Patel SV reported by incidence of traumatic VI nerve palsy as 12%.Tuberculosis was the etiological factor in 4 cases (22.22%). Tuberculous meningitis was seen in 2 cases and tuberculoma in 2 cases. The paralysis of sixth nerve in 3 patients was attributed to vascular diseases. Uncontrolled diabetes was present in three cases. Neoplasm accounted for 2 cases (11.11%) of sixth nerve palsy. 4 patients (22.22%) of sixth nerve palsy did not have any identifiable cause. Out of 409 patients, Rucker had found that majority of them had undetermined cause i.e.,129 patients(31.54%).Similarly Tiffin et al, Menon V et al had reported that in majority of cases, aetiology was unknown (33% and 36.2% respectively). The sixth nerve is injured by alteration in intracranial pressure as a result of its unique course through subarachnoid space, With changes in intracranial pressure ,the nerve may be pressed between pons and basilar artery or clivus, orbit may be stretched along the edge of temporal bone[1718]. In PS Reddy et al study (1972) most common cause of VI nerve palsy was tuberculosis (26.66%).In Menon V et al study more no of cases of isolated sixth nerve palsy were of undetermined aetiology. Fourth Cranial Nerve Palsy: There was no single case of isolated IV nerve palsy in this study. This could be because of the rarity of the condition or due to difficulty in diagnosing a case of isolated IV nerve palsy. In Rama et al study there is 1 case of isolated IV nerve palsy(1.1%) out of 90 cases. In Rucker(1958) series & (1966) series it was 6.7% and 8.4% respectively.

In PS Reddy et al study it was 1 out of 100 cases. In Menon V et al study IV nerve palsy was observed in 6.1% of cases. This was much higher than that reported in other indian series. Multiple Ocular Motor Nerve Palsies: Out of 50 cases, 17 (34%) were of multiple ocular motor nerves involvement. This was much higher compared to that reported by Rucker (1958) (18.9%). More no of cases were in the age group of 31-40 years. III +IV nerves palsy: In 4 cases of III + IV nerve involvement, 2 cases were due to vascular diseases. On investigating both cases showed multiple infarcts in areas of midbrain and thalamus. Trauma was the aetiology in other 2 cases. They presented with seizures and defective vision. III + VI nerves palsy: There were 5 cases of III + VI nerves palsy. Of these 3 cases were due to tuberculous meningitis and 2 cases due to trauma. III + IV + VI nerves palsy: There were 8 cases in which all the three nerves were involved. In 2 cases vascular aetiology was the cause and tuberculosis in 2 cases. In 4 cases the cause could not be determined. Complete recovery after steroid therapy could suggest the possibility of an inflammatory process but the diagnosis could not be confirmed. In Menon V et al study most common cause of multiple cranial nerve palsies was head trauma 26.4%. In PS Reddy et al study (1972) most common cause was tuberculosis followed by cases of undetermined aetiology [19]. In Rama et al study (1980) tuberculosis was the most common cause of multiple cranial nerve involvement followed by vascular diseases.

Conclusion: Isolated nerve palsies are more common than multiple ocular motor nerve palsies. Sixth nerve palsy is found to be more commonly involved followed by third nerve and multiple nerve palsies. Data on the causes of ocular motor nerve palsies in a defined population may be useful in guiding diagnosis and evaluation; especially when collaborative work up and sophisticated complementary investigations are not available. There is a change in the pattern of aetiologies when compared with previous studies. There is an increase in no. of cases with vascular diseases. This could be due to an increase in the incidence of systemic diseases like diabetes and hypertension. There was a decline in the no. of cases of tuberculosis that lead to ophthalmoplegia. This could be due to prompt and appropriate treatment of the disease. But still the no. of cases of Tb leading to ophthalmoplegia were more indicating the need for proper management of the condition. Tuberculosis was the most common aetiology in younger age group (p value-0.008), trauma in middle age (p value-0.02) and inflammatory diseases in elderly age group (p value-0.03). All the cases of undetermined aetiology had complete recovery. Most of the cases might be of inflammatory aetiology or micro vascular ischemia which resulted in complete recovery.

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