ISSN: 2573-9573

Research Article

Journal of Ophthalmology & Clinical Research

The Incidence and Etiology of 3rd, 4th, 6th, and Multiple Cranial Nerve Palsies in South India: A 6-Month Retrospective Prevalence Study

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Submitted: 07 Jun 2022; **Accepted:** 13 Jun 2022; **Published:** 29 Jun 2022

Citation: *Samer Habeel, Karthik Kumar, Peter W MacIntosh and Virna M Shah (2022) The Incidence and Etiology of 3rd, 4th, 6th, nd Multiple Cranial Nerve Palsies in South India: A 6-Month Retrospective Prevalence Study. J Ophthalmol Clin Res 6(2): 133-138.*

Introduction

Cranial nerve palsies may occur secondary to various etiologies including vasculopathic risk factors, trauma, cerebrovascular accident, neoplasms, inflammation, pituitary apoplexy, aneurysm and giant cell arteritis [1-6]. Studies have compared various etiologies in the West, Korea, and North India but data aimed at the South Indian population is limited. Geographic specific data can help in better understanding region specific risk factors.

In our study, we evaluated the incidence and causes of cranial nerve (CN) palsies affecting the oculomotor (CN3), trochlear (CN4), and abducens (CN6) nerves in a South Indian population.

Subjects and Methods

A retrospective observational study was conducted at Aravind Eye Hospital, Coimbatore, Tamil Nadu, India of 391 patients evaluated at the tertiary eye care center between September 2019 and February of 2020. Details and clinical information including patient age, gender, diagnosis, symptoms, etiology, systemic history, imaging, and treatment were recorded.

Statistical analysis was done using Microsoft Excel. Comparisons between age and CN palsy prevalence, age and male to female ratio, as well as age and etiologies were also made. Statistics were presented as percentages, means, and standard deviations.

Study approval was obtained from the Institutional Human Ethics Committee at Aravind Eye Hospital in Coimbatore, India.

Results

A total of 391 outpatients were seen with CN3, CN4 and CN6 palsies. Of these 391 patients, 88 were CN3 palsies, 58 were CN4 palsies, 213 were CN6 palsies, and 32 presented with multiple cranial nerve palsies. Of the CN3 palsies, 23 were pupil involving and of these, 14 were traumatic, 3 neoplasm, 4 inflammatory and 2 microvascular ischemic.

Note: 42 etiologies were lost to follow up and listed as "incomplete evaluation."

The average age of patients with CN3, CN4, CN6, and multiple palsies were 55.6, 52.4, 54.9, and 47.4 years, respectively. The prevalence of CN3, CN4, CN6, and multiple palsies were 22.5%, 14.5%, 54.5%, and 8.2%, respectively, showing CN6 palsy to be the most prevalent of these palsies and representing over half of all palsies studied. Overall, males were more commonly afflicted by these cranial nerve palsies than females at a ratio of 2.69:1 (Table 1).

Table 1: General Demographics

	CN3	CN4	CN6	Multiple	All
Age of Onset (years)	55.6	52.4	54.9	47.4	54.1
Male:Female	63:25	42:16	158:55	22:10	286:107
Prevalence %	22.5	14.5	54.5	8.2	-
OD:OS*	40:44	28:27	111:96	11:14	190:180
*OD: Right Eye OS: Left Eye					

Our analysis showed that 194 of the 391 patients (50%) received some form of neuroimaging, either an MRI or CT scan. Sixty-four percent of CN3 palsies, 48% of CN4 palsies, 44% of CN6 palsies and 53% of patients with multiple cranial nerve palsies were imaged. One hundred and forty-three patients were imagined with MRI only, 31 with CT only, and 20 with both modalities.

Etiologies, Medical Histories, and Symptoms

The breakdown of the 391 patients by etiology is shown in Table 2 and Figure 1. Etiologies were categorized as microvascular ischemic, traumatic, inflammatory, idiopathic, neoplasm, cerebrovascular accident (CVA, including brainstem CVA), elevated intracranial pressure, neurovascular conflict, congenital, myositis, infectious, or carotid cavernous fistula (CCF).

Table 2: Etiologies present in CN 3, 4, 6 and multiple palsies (total number)

Etiology	CN3	CN4	CN6	CN Multiple	Total
Microvascular ischemic	38	28	154	7	227
Trauma	17	15	10	6	48
Inflammatory	8	2	7	3	20
Idiopathic	1	3	14	0	18
Neoplasm	3	0	6	2	11
CVA	8	2	4	0	14
Elevated Intracranial Pressure	0	0	3	0	3
Neurovascular Conflict	1	0	0	0	1
Congenital	0	2	0	0	2
Myositis	0	0	1	0	1
Infection	0	0	1	2	3
CCF	0	0	1	0	1
Lost to Follow Up	12	6	12	12	42
Total	88	58	213	32	391
CVA – Cerebrovascular accident CCF – Carotid-cavernous fistula					

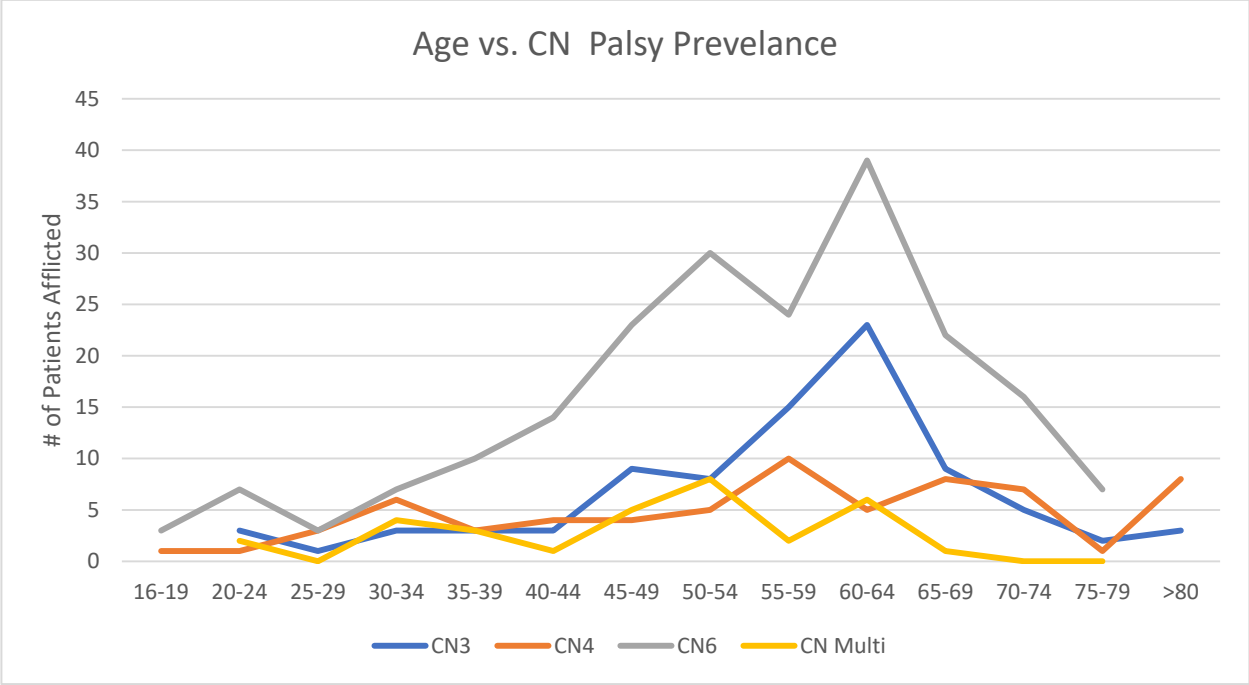

Figure 1: CN prevalence across age groups

The most common etiology regardless of cranial nerve affected was microvascular ischemic at 227 patients (58%). The second most common etiology was trauma at 48 patients (12.3%), followed by inflammatory at 20 patients (5.1%), idiopathic at 18 patients (4.6%), and neoplasm at 11 patients (2.8%) (Figure 1). Figure 2 compares patient history with CN3, CN4, CN6 and multiple cranial nerve palsies.

Patient histories included diabetes mellitus, hypertension, hypercholesterolemia, and other. The most common patient histories within the microvascular ischemic group were diabetes mellitus at 210 patients (53.7%), hypertension at 132 patients (33.8%), and hypercholesterolemia at 38 patients (9.7%).

The most common presenting symptom was diplopia, present in all 391 patients, followed by ptosis present in 67 patients (17.1%), pain in 29 patients (7.4%), and blurry vision in 25 patients (6.4%).

Incidence and Sex Ratio of CN Palsies across Age Groups

Cranial nerve palsy prevalence increases in direct proportion to age with peaks of all palsies occurring between 55-64 years (Figure 1). Multiple CN palsies peaked at 50-54 years, CN 4 at 55-59 years, and CN 3 and 6 at 60-64 years of age. In most cases, CN palsies were more prevalent in males than females. This ratio is greatest for CN6 palsy at 35-39 years and greatest in CN4 palsy at 70-74 years. Exceptions included CN3 patients between 25-29, CN4 patients between ages 16-19 and 25-29, and patients with multiple CN palsies between 65-69 which had ratios of 1:1. Male-to-female ratios of 3:0, 2:0, and 1:0 were changed to 3:1, 2:1, and 1:1 to make a ratio calculation possible.

Etiologies of CN Palsies Compared across Age Groups

The four most common etiologies of cranial nerve palsies (microvascular ischemic, traumatic, inflammatory, idiopathic) show a variable incidence relative to age (Figure 2). Trauma is the most prevalent etiology between ages 20-39, while ischemia is the most common amongst ages 40 and up.

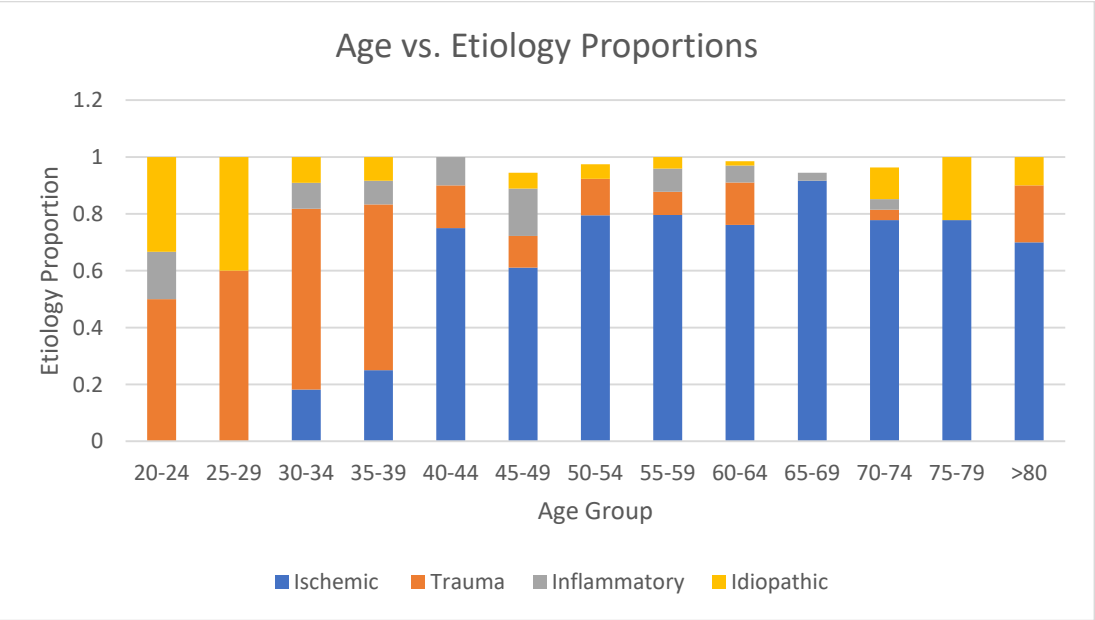

Figure 2: Proportions of etiology as they change with age (CN3, CN4, CN6, and multiple)

Discussion

In our study of cranial nerve palsies in a South Indian population, we found the most common etiologies for CN3, CN4 and CN6 to be microvascular ischemic, traumatic, inflammatory, and idiopathic. Microvascular ischemic causes were the most frequent but when patients presented with multiple cranial nerve palsies, traumatic causes were almost as frequent. Head trauma has been reported to be more associated with multiple cranial nerve injuries than singular palsies, as trauma is more likely to injure multiple nearby cranial nerves than the localized effects of ischemia and the confined susceptible areas of inflammation [7,8].

Three Western and Korean studies found trauma to represent 5% to 12% of cranial nerve palsies [1,4,5]. Our study, however, found trauma to be greater than all three of these studies at 12.3% prevalence of cranial nerve palsies. Road traffic accidents are more prevalent in India than in the West and Korea, possibly leading to increased traumatic etiology [9,10]. This connection was also made by a study recently published in North India, listing road traffic accidents as 68% of their traumatic cases [11].

In our study we found that neuroimaging rates were lower than in studies from the West, with 50% of patients receiving neuroimaging of MRI or CT scans in our study. This is compared to one US study in which 64% already had neuroimaging done before presentation and a further 36% had imaging ordered if it was not already done [2]. A second western study showed an 84.5% MRI referral rate for patients referred to the neuro-ophthalmology service [12]. Neuroimaging findings in a North India study were also found to be lower than Western studies, at a 32% rate for cases with diagnostic dilemma [11]. Studies have shown findings favoring neuroimaging at the time of diagnosis, but this tends to happen less in India to reduce health care costs that are often paid directly by the patient rather than insurance [13].

Diabetes mellitus, hypertension, and hypercholesterolemia were the top 3 most frequent reported patient histories in patients with CN3, CN4 and CN6 palsies, like findings in other studies [4,5]. This study differs, however, with diabetes having a higher prevalence with these cranial nerve palsies while western studies found hypertension to be more prevalent [4,14]. A similar trend to our study was also seen in a North Indian study [11]. As for symptoms, diplopia was the most common, followed by ptosis, blurry vision, then pain. Similar associations have been made by other studies [4,5].

In this study of south Indian population we found an age of onset of cranial nerve palsies about 15 years older than in the North Indian population study. Microvascular ischemic and traumatic etiologies were most common in both studies, but traumatic causes contributed half as many patients (12.3% vs 23.5%) in our study compared to the North Indian one, likely reflecting higher trauma rates there [11]. Diabetes, hypertension, and hypercholesterolemia were major comorbid diseases in both studies, but our study showed 15% fewer cases of hypertension (33.5% vs 48.5%) compared to the North Indian study [11].

Cranial nerve palsies were more prevalent in older patients, with CN3 and CN6 palsies highest amongst 60-64 year-olds and CN4 highest between 55-59 year-olds. Multiple cranial nerve palsies were most prevalent in the slightly younger 50-54 age group. This could be explained because of multiple cranial nerve palsies' higher association with traumatic etiologies which are more common in younger patients. In another study it was found that hospitaliza-

tions due to traumatic brain injuries were more prevalent in younger individuals [15,16]. It was also found in a study within India that 83% of victims of two-wheeler accidents were male, and they make up a large portion of traumatic injuries in India [17]. These findings can help in explaining the overall lower age range of multiple cranial nerve palsies as compared to the rest.

Our study also showed a high male-to-female ratio of 2.69:1. This was a trend seen in other studies, with ratios ranging from 1.2:1 to 2.5:1 [1,5,18]. This male preponderance is likely related to the higher prevalence of trauma, diabetes, and hypertension in males versus females and is much higher than the presenting male to female ratio of patients to this institution of 1.22:1 [19,20].

We also saw a change in the etiologies of cranial nerve palsy as a whole with age. Between ages 20-39, trauma is the most common etiology but this changes to ischemia at ages 40 and up. Traumatic brain injuries tend to be more prevalent in younger populations, according to a study that found 954 of 1,561 traumatic brain injury hospital visits to be between the ages of 0-34 [15]. Two-wheeler accidents also factor into this as they are more prevalent in India, with a large part of the affected demographic being males between the ages of 18-44 [17].

Limitations of our study include its retrospective nature, reliance on patient report for history details and low rates of neuroimaging due to financial constraints. This study also had referral bias of a tertiary eye care center, leading to etiological data that may not be as representative of the overall population.

Conclusion

In our study the most common cranial nerve palsy in this South Indian populations was the CN6 palsy with a male preponderance. Analysis also showed that 50% of patients received neuroimaging of either CT or MRI scans. The most common etiology was microvascular ischemia, followed by trauma, inflammation, and neoplasm. These etiologies also changed with age, with trauma being more prevalent at younger ages (20-39) and ischemia at older (40+). Of microvascular ischemic causes, diabetes was the most common underlying etiology followed by hypertension and hypercholesterolemia differing from Western findings of hypertension as the most common [1,14]. The most common presenting symptom was diplopia followed by ptosis, pain, and blurry vision. As compared to a North Indian study, age of onset in our South Indian study was 15 years older and traumatic causes contributed half as many patients (12.3% vs 23.5%). This likely reflects the higher incidence of traumatic cases with younger age in North India compared to our population. Hypertension made up 15% fewer cases (33.5% vs 48.5%) [11]. Understanding the different types of cranial nerve palsies in different geographic locales will help in better understanding a populations' risk in hopes of enhanced treatment and prevention techniques. From our data we propose that public health strategies focusing on diabetes care and motor vehicle safety might have an impact on overall cranial nerve palsies in this South Indian population.

Acknowledgements

P. W MacIntosh support: Core grant for vision research NEI P30 EY001792
Unrestricted RPB departmental grant

The authors have no conflicts of interest to disclose.

Conflicts of Interest

None.

Method of Literature Search

Google Scholar and PubMed were the main search engines used for the literature search. Search terms were based on combinations of "cranial nerve palsy," "Etiology," "Prevalence," "Symptoms," "Imaging CT MRI," and terms containing different demographics. Inclusion criteria entailed articles contributing either new perspectives and point of discussion or data and points of comparison to what we have collected. Most articles cited were published within the last 5 years and articles published greater than 10 years ago were kept to a minimum.

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