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Acquired Sixth Nerve Palsy : A Study Of Demographic And Etiologic Profile In A Tertiary Teaching Hospital

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Abstract

Abducent nerve palsy is the most common mononeuropathy . Ischaemic mononeuropathy secondary to Diabetes Mellitus, Hypertension is the most common cause .The other causes that have been cited are trauma , infections, demyelination, tumours and as a false localising sign secondary to raised intracranial pressure .

We analysed 25 consecutive patients prospectively who presented with binocular diplopia and were diagnosed as sixth nerve palsy after complete evaluation during a period of 6 months (nov 2019- April 2020).

We found that ischaemic mononeuropathy was the most common cause (44%) among our patients . Idiopathic intracranial hypertension(8 %), multiple sclerosis , Wernickes encephalopathy , Tolosa Hunt syndrome , obstructive hydrocephalus , post viral infection, subdural hygroma , superior orbital fissure syndrome , birth asphyxia each in 4 % cases was noted.

Keywords: NIL

Introduction

Lateral Rectus Nerve Palsy is caused by abducens nerve malfunction, which can occur anywhere along the nerve's path from the pons to the lateral rectus muscle, resulting in sixth nerve palsy.

The abducens nerve originates in the pons of the brainstem, from the abducens nucleus. At the intersection of the pons and the medulla, it leaves the brainstem .It then travels through Dorello's canal,piercing the dura mater and entering the subarachnoid region. The abducens nerve exits Dorello's canal and enters the cavernous sinus at the tip of the petrous temporal bone . It reaches the bony orbit via the superior orbital fissure after passing through the cavernous sinus to supply the lateral rectus

Material And Methods

A total of 25 patients who presented to the outpatient department of Dr D Y Patil Medical College during a period of 6 months with binocular diplopia with a diagnosis of sixth nerve palsy after detailed complete evaluation were enrolled in the study . Institutional clearance was obtained .

We noted demographic details like age at presentation, sex, presenting complaint, duration , associated systemic or neurological disorders, and any prior investigation or treatment .

Ophthalmic evaluation included visual acuity, anterior and posterior segment examination . Squint workup consisted of alternate cover test for distance and near , lateral incomitance , quantification with prism bar cover test or modified krimsky test depending on the vision . Ocular motility deficit was graded from -1 to -4 . Hess charting was not done as most were acute cases .Forced duction test was done

in one patient with long standing bilateral sixth nerve paresis post trauma . Colour vision assessment and pupillary evaluation were done . Examination of the cranial nerves was also undertaken. Additional fundus findings like presence of papilloedema , diabetic or hypertensive retinopathy changes or nystagmus were also noted .

A detailed systemic neurological examination was carried out in all patients .

We classified the patients according to the etiology .

Etiology was identified as ischemic, traumatic, compressive, iatrogenic, inflammatory, others, and idiopathic. Cases with vascular risk factors (like diabetes, hypertension, deranged lipid profile, and coronary artery disease) were identified as ischemic. In the absence of any underlying cause, it was designated as idiopathic.

Patients were subjected to blood tests fasting and post prandial blood sugar , gylcosylated hemoglobin , lipid profile , blood pressure assessment and other relevant tests like Mantoux test , RT PCR for covid in one patient , serum angiotensin converting enzyme for sarcoid .

Complete recovery was defined as complete resolution of diplopia and angle of squint. Partial recovery was defined as partial improvement or nil improvement

Data Analysis And Interpretation

Data was entered into Microsoft Excel (Windows 7; Version 2007) and analyses were done using the Statistical Package for Social Sciences (SPSS) for Windows software (version 22.0; SPSS Inc, Chicago). Descriptive statistics such as mean and standard deviation (SD) for continuous variables, frequencies and percentages were calculated for categorical Variables were determined. Bar charts and Pie charts were used for visual representation of the analyzed data. Level of significance was set at 0.05.

Results

We had 25 patients during the study period who presented to the ophthalmology outpatient department or were referred from other departments with complaints of binocular diplopia

Our analysis found that 44 % patients were in the age group of 40- 60 years , 28 %of patients were less than 30 years old ,.The mean age at presentation was 42.52 (SD 17.34)(graph 1)

The percentage of males involved were 56 % as against females who contributed to 44 % of the total .(graph 2)

The mean duration of presentation from onset was 7.80 days (SD 6.22).(Table 1)The sixth nerve palsy was involving left eye in 52 % , right eye in 32 % and bilateral in 8 % .The other associated ocular findings noted were as follows . Clinically signifyicant macular oedema was noted in 1 patient , moderate NPDR in 2 patients , external ophthalmoplegia in 1 patient , vertical nystagmus in 1 patient, horizontal gaze palsy in 1 patient , papilloedema in 2 patients and hypertensive retinopathy in 1 patient (graph 3)

The associated systemic conditions were as follows in (Table 2)

HBA1C was elevated in all patients with DM(44%) .

Elevated BP was noted in 12 % .

There was deranged lipid profile in 8 % of patients .

Magnetic resonance imaging of brain with orbit showed positive findings in ten patients . (Table 3)

According to the etiologic diagnosis we have the following results as in (Table 4)

We reviewed the patients at 2 months again to look for resolution of symptoms with improvement in ocular motility .We have follow up of

22 patients . 3 were lost to follow up. (graph 4)

All patients with ischaemic mononeuropathy had complete resolution . Patients (n = 2)with superior orbital fissure/ Tolosa Hunt syndrome too showed complete recovery following administration of steroids . The patient with post traumatic bilateral sixth nerve palsy was advised to undergo squint surgery as there was persistent abduction deficit .

Patients with Idiopathic intracranial hyper tension also showed complete normalisation with decrease in intracranial pressure following treatment with oral acetazolamide . Patient (n=1) with multiple sclerosis also had total resolution .There was one young female with mixed connective tissue disease and

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Wernickes encephalopathy secondary to chronic vomiting also had complete reversal following administration of intravenous thiamine .

Two cases of sixth nerve palsy with presumed viral infection all resolved completely.Only one patient we had following covid infection early in the first wave who also showed complete resolution .

The patient with cerebral palsy had partial improvement mostly requiring surgical intervention .

We do not have follow ups of patients with osteoma orbit, obstructive hydrocephalus and metabolic encephalopathy probably as they were referred to other specialised centres for surgeries .

Discussion

Cranial nerve 6 palsy, also known as Abducens nerve palsy or Lateral rectus palsy is the most common ocular motor palsy observed [1-3] . There are numerous causes of cranial nerve 6 palsy, with most common being trauma, inflammation, tumour & vasculopathic diseases some of which can be life threatening and need urgent treatment [4-6]. So its very important to know the demographic and etiologic profile in patients presenting with acquired sixth nerve palsy so that potentially fatal conditions are not missed . There are many retrospective studies available but ours is one of the few prospective study on this topic carried out in a tertiary care medical college .

Recovery can occur spontaneously within weeks to several months & occurs most frequently in patients whose palsies have an unknown/vascular etiology .

The aim of our study was to assess the demographic and etiological profile in a tertiary care teaching hospital . Our data provides the most common systemic associations , the various underlying aetiologies and highlights the need to do neuroimaging in cases associated with neurological signs and symptoms .

The most common systemic associations we noted were Diabetes mellitus alone , hypertension with concurrent Diabetes , hyper triglyceridemia . All patients with Diabetes mellitus had elevated HBA1c when tested at presentation. All patients with hypertension had high blood pressure at presentation . Elevated HBA1c and blood pressure were the two important factors causing ischaemic mononeuropathy .The etiological profile in our study remains somewhat similar to these studies where schema constitutes the commonest cause of acquired paralytic strabismus[7-10]

A major study at RP centre showed that etiology was as follows Ischemic 69.8 %, traumatic (17 %), compressive (3.8%), inflammatory /infectious (0) , idiopathic (7.5%) [18] . We did not have any cases of neoplasm probably as all our patients were adults and neoplasms are more common in paediatric age group . In the last few decades the prevalence of coronary artery disease and associated vascular co morbidities have been reported in young Indians[11,12] .

With modernisation , there has been increased stress, sedentary life style , lack of exercise are considered as the major risk factors contributing to the same 13-15. Our study has identified diabetes as the major risk factor as was also reported in a study from Korea.16 A population-based study of acquired sixth nerve palsy also reported an 8-fold increase in odds of having both diabetes and hypertension in cases over controls.17

Isolated sixth nerve palsy as presenting feature of multiple sclerosis is very rare . While brain stem involvement in multiple sclerosis (MS) is relatively common, isolated cranial nerve palsies are rare, especially when they represent the initial presenting sign of a new diagnosis of MS [24] . Our patient was young female who had isolated sixth nerve palsy . She had periventricular plaques on MRI suggestive of MS.

In our study a comparatively younger age at presentation in ischaemic group . A Nepal study also reported age of onset as 37 [20] . Compared to other studies [21-23] we had younger age of onset . This could be attributed to the early onset of Diabetes Mellitus mad Hypertension in India at present and hence diabetic related ischaemic complications.

Unlike other studies we had 56 % of patients belonging to the non ischaemic type with varied aetiologies . This could be explained because of the increasing referrals from various other departments in a medical college and the possibility that ischaemic ones presented to private practitioners rather than a medical college .

Males were affected more than the female our study which matches the study done by Park et al.[23] .Some studies reported no sex predilection for CN6 palsy[25] .

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The possible explanation could be that male gender is a risk factor for diabetes or hypertension in [26,27]

Neuroimaging was advised in 52% cases in our study and we found 40 % to have findings . The indications for neuroimaging in our patients were early onset cases , associated neurological signs , absence of any systemic risk factors and investigations , post traumatic , multiple cranial neuropathy . One study detected positive findings in 32 % of their patients in whom neuroimaging was done [18]

The high diagnostic yield in our study could be due to more number of younger patients and presence of neurologic signs .In the absence of risk factors, a suggestive history, or positive laboratory and clinical findings, neuroimaging can serve as a useful diagnostic tool in identifying the exact cause of sixth nerve palsy[19]

Various studies have quoted different recovery rates in sixth nerve palsy .It varies from 60.0 to 87.3%28 ,29,30. Higher recovery rates have been observed in vascular etiology compared to others 28, 31 . Sanders *et al*. reported that 51 of 59 patients (86%) experienced resolution of CN6 palsy, and only 3 patients required strabismus surgery32 . In our study we lost follow up of 3 patients (12%), rest of the 20 (90.9%) had complete resolution while two(9 %) had persistent squint and abduction deficit . Higher recovery rates could be due to better treatment of vasculopathic risk factors by admission and proper monitoring in the hospital . The various aetiologies like IIH , inflammatory neuropathy responded well to appropriate therapies .

Limitations of this study could be that it cannot be extrapolated to the general population because of low sample size and some referral bias in a medical college where more patients with coexisting systemic conditions visit.

Conclusion

Our study highlights the younger age of onset compared to previous studies in ischaemic mononeuropathies and a herculean task ahead to limit the vascular complications of DM, HTN by a multifaceted approach like improved active life style etc .The utilisation of neuroimaging could be limited to a cohort of patients based on individual case basis . Recovery in general is commendable with shorter duration of the disease and better glycemic and hyper tension control in ischaemic cases.

References

1. Elder, C., Hainline, C., Galetta, S. L., Balcer, L. J. & Rucker, J. C. Isolated Abducens Nerve Palsy: Update on Evaluation and Diagnosis. Current neurology and neuroscience reports 16, 69, https://doi.org/10.1007/s11910-016-0671-4 (2016).
2. Tamhankar, M. A. et al. Isolated third, fourth, and sixth cranial nerve palsies from presumed microvascular versus other causes: a prospective study. Ophthalmology 120, 2264–2269, https://doi.org/10.1016/j.ophtha.2013.04.009 (2013).
3. Park, U. C., Kim, S. J., Hwang, J. M. & Yu, Y. S. Clinical features and natural history of acquired third, fourth, and sixth cranial nerve palsy. Eye (London, England) 22, 691–696, https://doi.org/10.1038/sj.eye.6702720 (2008).
4. Rush, J. A. & Younge, B. R. Paralysis of cranial nerves III, IV, and VI. Cause and prognosis in 1,000 cases. Archives of ophthalmology (Chicago, Ill.: 1960) 99, 76–79 (1981).
5. Patel, S. V., Mutyala, S., Leske, D. A., Hodge, D. O. & Holmes, J. M. Incidence, associations, and evaluation of sixth nerve palsy using a population-based method. Ophthalmology 111, 369–375, https://doi.org/10.1016/j.ophtha.2003.05.024 (2004).
6. Choi, K. D. et al. Acquired Ocular Motor Nerve Palsy in Neurology Clinics: A Prospective Multicenter Study. Journal of clinical neurology (Seoul, Korea) 15, 221–227, https://doi.org/10.3988/jcn.2019.15.2.221 (2019).
7. Park UC, Kim SJ, Hwang JM, et al. Clinical features and natural history of acquired third, fourth and sixth nerve palsy. Eye (Lond). 2008;22:691–696.
8. Akagi T, Miyamoto K, Kashii S, et al. Cause and prognosis of neurologically isolated third, fourth, or sixth cranial nerve dysfunction in cases of oculomotor palsy. Jpn J Ophthalmol. 2008;52:32–35.
9. Ho TS, Lin HS, Lin MC, et al. Acquired paralytic strabismus in Southern Taiwan. J Chin Med Assoc. 2013;76:340–343.

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10. Berlit P. Isolated and combined pareses of cranial nerves III, IV, and VI. A retrospective study of 412 patients. J Neurol Sci. 1991;103:10 – 15.
11. Dalal J, Hiremath MS, Das MK, et al. Vascular disease in young Indians (20–40 years): role of ischemic heart disease. J Clin Diagn Res. 2016;10. OE08-OE12.
12. Kaveeshwar SA, Cornwall J. The current state of diabetes mellitus in India. Australas Med J. 2014;7:45 – 48.
13. Enas EA, Garg A, Davidson MA, et al. Coronary heart disease and its risk factors in first-generation immigrant Asian Indians to the United States of America. Indian Heart J. 1996;48:343–353.
14. Joshi P, Islam S, Pais P, et al. Risk factors for early myocardial infarction in South Asians compared with individuals in other countries. JAMA. 2007;297:286 – 294.
15. Hasan A, Agarwal A, Parvez A, et al. Premature coronary artery disease and risk factors in India. Indian J Cardiol. 2013;16:5–11.
16. Jung JS, Kim DH. Risk Factors and prognosis of isolated ischemic third, fourth, or sixth cranial nerve palsies in the Korean population. J Neuroophthalmol. 2015;35:37–40.
17. Patel SV, Holmes JM, Hodge DO, et al. Diabetes and hypertension in isolated sixth nerve palsy: a population-based study. Ophthalmology. 2005;112:760 – 763.
18. Swati Phuljhele, MD, Rebika Dhiman, MD, Medha Sharma, MD, Sanjay Kumar Kusiyait, BSc Rohit Saxena, MD, Karthikeyan Mahalingam, MD, and Pradeep Sharma, MD
19. Acquired Ocular Motor Palsy: Current Demographic and Etiological Profile ,Asia-Pacific Journal of Ophthalmology Volume 9, Number 1, January/February 2020
20. Nair AG, Ambika S, Noronha VO, Gandhi RA. The diagnostic yield of neuroimaging in sixth nerve palsy - Sankara Nethralaya Abducens Palsy Study (SNAPS): Report 1. Indian J Ophthalmol 2014;62:1008-12.
21. Suman Adhikari et al : Clinical Profile of Extraocular Muscle Palsy: A Retrospective Study Optometry & Visual Performance Volume 1 | Issue 6
22. Tiffin PA, MacEwen CJ, Craig EA, Clayton G. Acquired palsy of the oculomotor, trochlear and abducens nerves. Eye 1996;10:377-84.
23. Berlit P. Isolated and combined pareses of cranial nerves III, IV, and VI. A retrospective study of 412 patients. J Neurol Sci 1991;103:10-5.
24. Park U-C, Kim S-J, Hwang J-M, Yu YS. Clinical features and natural history of acquired third, fourth, and sixth cranial nerve palsy. Eye 2008;22:691-6.
25. Sargon Bet-Shlimon Mill Etienne New York Medical College, Isolated Abducens Palsy as the First Presenting Sign of Multiple Sclerosis New York, NY, USA Case Rep Neurol 2016;8:272–275
26. Shrader, E. C. & Schlezinger, N. S. Neuro-ophthalmologic evaluation of abducens nerve paralysis. Archives of ophthalmology (Chicago, Ill.: 1960) 63, 84–91 (1960).
27. Choi, K. M. et al. Prevalence of prehypertension and hypertension in a Korean population: Korean National Health and Nutrition Survey 2001. Journal of hypertension 24, 1515–1521, https://doi.org/10.1097/01.hjh.0000239286.02389.0f (2006).
28. Kim, D. J. The epidemiology of diabetes in Korea. Diabetes & metabolism journal 35, 303–308, https://doi.org/10.4093/ dmj.2011.35.4.303 (2011).
29. Park, U. C., Kim, S. J., Hwang, J. M. & Yu, Y. S. Clinical features and natural history of acquired third, fourth, and sixth cranial nerve palsy. Eye (London, England) 22, 691–696, https://doi.org/10.1038/sj.eye.6702720 (2008).
30. Kim, K., Noh, S. R., Kang, M. S. & Jin, K. H. Clinical Course and Prognostic Factors of Acquired Third, Fourth, and Sixth Cranial Nerve Palsy in Korean Patients. Korean J Ophthalmol 32, 221–227, https://doi.org/10.3341/kjo.2017.0051 (2018).
31. Akagi, T., Miyamoto, K., Kashii, S. & Yoshimura, N. Cause and prognosis of neurologically isolated third, fourth, or sixth cranial nerve dysfunction in cases of oculomotor palsy. Japanese journal of ophthalmology 52, 32–35, https://doi.org/10.1007/s10384-007-0489-3 (2008).

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32. Richards, B. W., Jones, F. R. Jr. & Younge, B. R. Causes and prognosis in 4,278 cases of paralysis of the oculomotor, trochlear, and abducens cranial nerves. American journal of ophthalmology 113, 489–496 (1992).

33. Sanders, S. K., Kawasaki, A. & Purvin, V. A. Long-term prognosis in patients with vasculopathic sixth nerve palsy. American journal of ophthalmology 134, 81–84 (2002).

Tables

Table 1: Distribution of Study Subjects according to the Onset (N=25)

Onset	**No.**	**Percent**
3-5	12	48.0
6-10	7	28.0
>10	6	24.0
Mean (SD)	7.80 (6.22)	
Median	6.00	

Table 2: Distribution of Study Subjects according to the Systemic Conditions (N=25)

Systemic Conditions	**No.**	**Percent**
DM	9	36.0
DM & HTN	3	12.0
Hypertriglyceridemia	2	8.0
RTA	1	4.0
Pharyngitis	1	4.0
Connective Tissue Disease	1	4.0
Cerebral Palsy	1	4.0
Covid Infection	1	4.0
None	7	28.0

Table 3: Distribution of Study Subjects according to the MRI Findings (N=25)

MRI Findings	**No.**	**Percent**
Osteoma Orbit	1	4.0
Chronic Ischaemia	1	4.0
Chronic Subdural Hygroma	1	4.0
Hyperintense T1 on Basal	1	4.0

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Ganglia		
IIH	1	4.0
Lacunar Infarct Thalamus	1	4.0
Multiple Sclerosis	1	4.0
Stenosis Foramen Munroe	1	4.0
Wernickes Encephalopathy	1	4.0
Tortuosity Optic Nerves	1	4.0

Table 4: Distribution of Study Subjects according to the Diagnosis (N=25)

Diagnosis	No.	Percent
Ischaemic	11	44.0
IIH	2	8.0
Post Viral	2	8.0
Multiple Sclerosis	1	4.0
Metabolic Encephalopathy	1	4.0
Obstructive Hydrocephalus	1	4.0
SOF Syndrome	1	4.0
Subdural Hygroma	1	4.0
Wernicke Encephalopathy	1	4.0
Tolosa Hunt	1	4.0
Birth Asphyxia	1	4.0
Compressive	1	4.0
Covid	1	4.0

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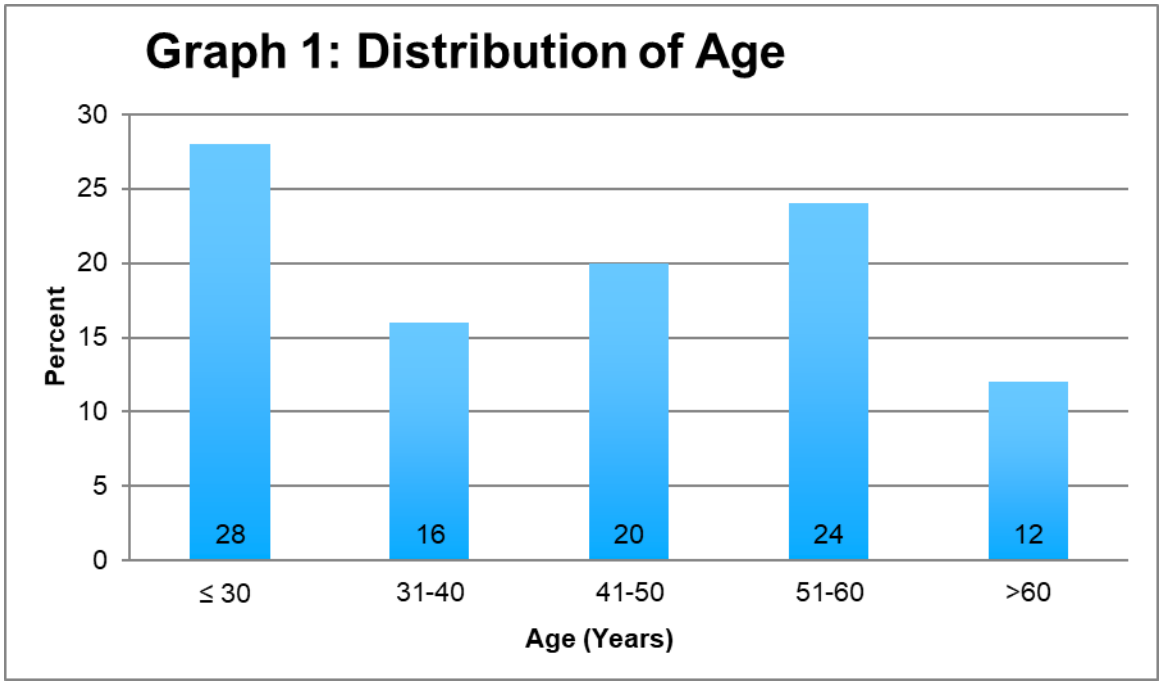

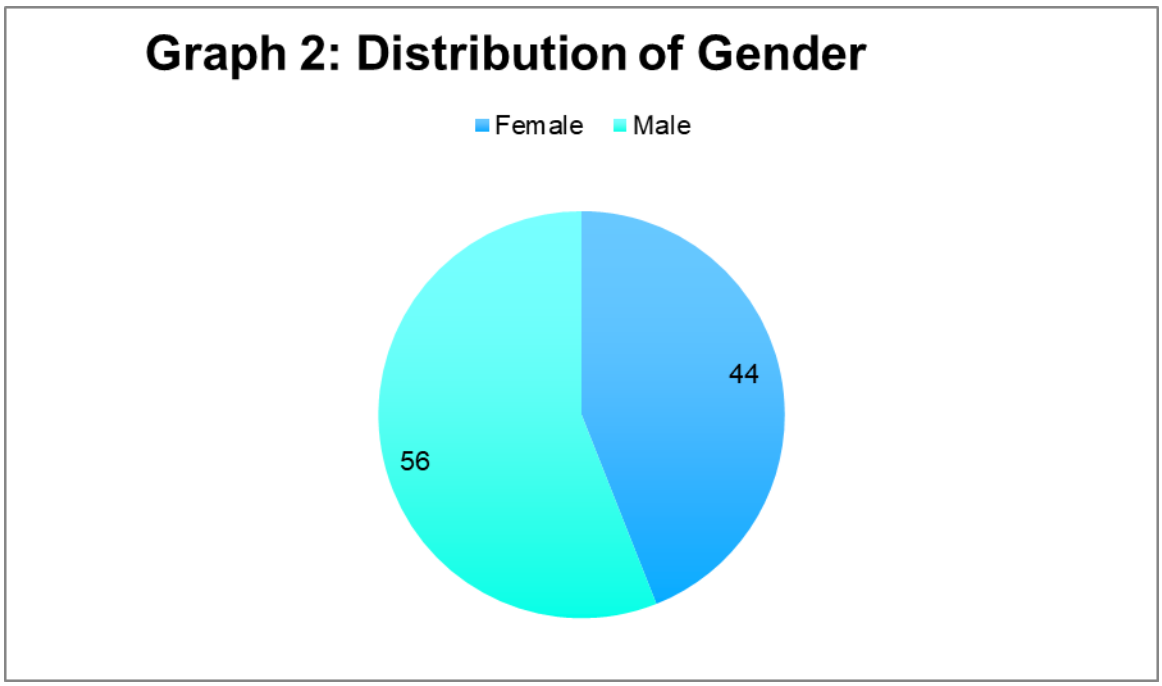

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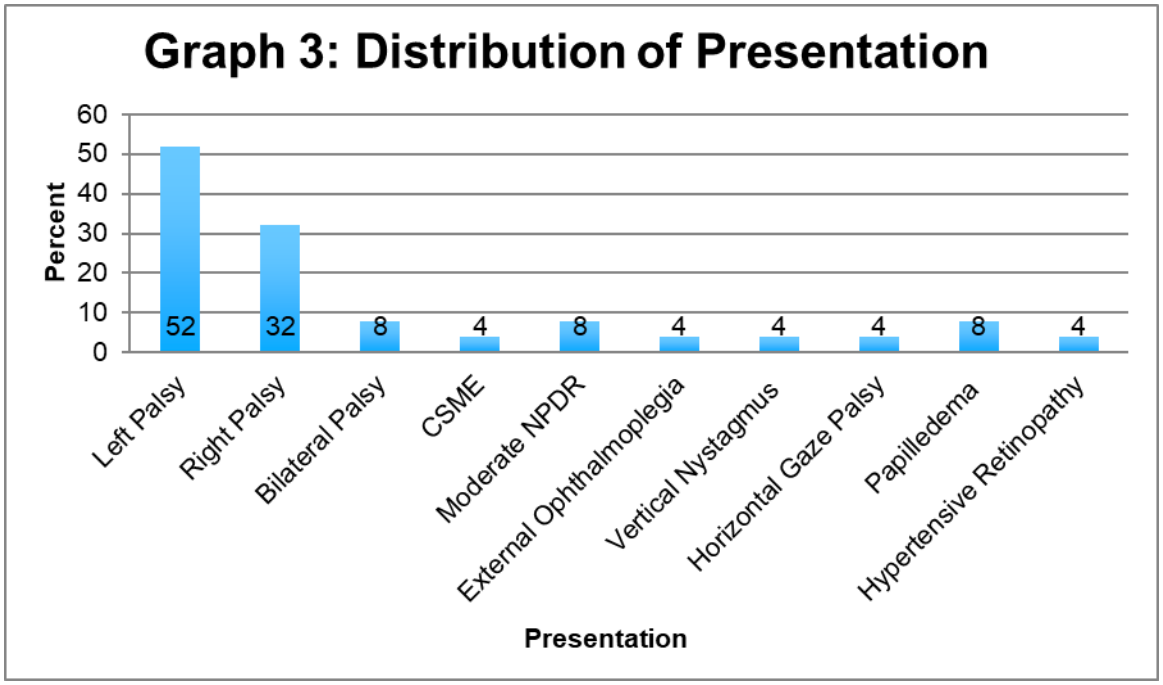

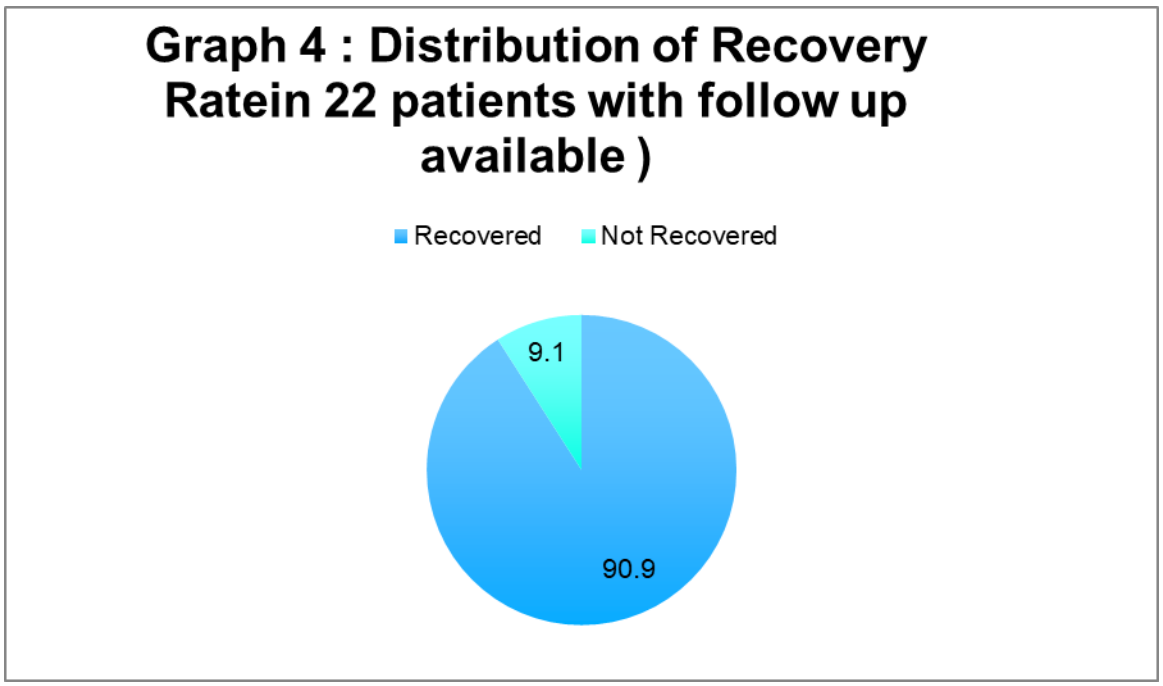

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