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Etiology, Clinical Symptoms, and Risk Factors of Oculomotor Nerve Paralysis

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Abstract

The third cranial nerve, also known as the oculomotor nerve, consists of two main components: the external parasympathetic fibers that innervate the ciliary muscles and the sphincter pupillae, and the deep somatic fibers that control the levator palpebrae superioris and four extraocular muscles. Oculomotor nerve palsy has multiple etiologies and can indicate severe underlying pathology. Damage to this nerve results in characteristic symptoms such as ptosis, diplopia, restricted eye movement, and diminished or absent pupillary light reflex. This study aims to evaluate the clinical characteristics of oculomotor nerve paralysis based on its etiology, age distribution, gender prevalence, and associated risk factors. This study employs a literature review using a narrative review design. Data were collected from various indexed and accredited electronic sources such as Scopus, SINTA, DOAJ, SpringerLink, Cochrane, Biomed, Portal Garuda, Google Scholar, Elsevier/Clinical Key, Gale, PubMed, and other relevant databases. A total of 13 relevant articles were identified for this narrative review. The findings indicate that vascular abnormalities, including microvascular ischemia, aneurysms, and subarachnoid hemorrhages, are the most frequent causes of oculomotor nerve paralysis. The most commonly reported symptoms among affected patients are ptosis and diplopia. The condition is most prevalent in individuals aged 51-60 years, and women are more susceptible to oculomotor nerve paralysis than men. The most frequent cause of oculomotor nerve paralysis is an aneurysm of the posterior communicating artery. This condition predominantly affects individuals aged 51-60 years and is more common in women.

Introduction

The oculomotor nerve exits the brainstem at the base of the midbrain caudal to the mammillary bodies. The oculomotory nerve passes through the cavernous sinus and continues through the supraorbital fissure to reach the orbit of the eye. The third cranial nerve has both somatic and autonomic fibers. Somatic nerve fibers are bundled in the nerve, while autonomic (unconscious) fibers surround the somatic fibers around the outside of the nerve (Halvorson, 2018; Vaphiades & Roberson, 2017).

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The oculomotor nerve runs through the lateral wall of the cavernous sinus. Cavernous sinus lesions often result in third nerve palsy accompanied by one or more other neurological findings including fourth, fifth (first division), and sixth cranial nerve palsy (Kanazawa et al., 2020; Natarajan et al., 2022). Cranial nerve III palsy can result from a variety of causes, such as microvascular ischemia caused by diseases, including DM, hypertension, and atherosclerosis, aneurysms, trauma, neoplasms, inflammation, neurosurgical interventions, and other known rare causes (Nagendran et al., 2019; Wang et al., 2023; Mukherjee et al., 2023; Rudolph & Katz, 2016).

Singh's report shows that the causes of oculomotorius paralysis are congenital or acquired, congenital 43%, trauma 20%, inflammation 13%, intracranial aneurysm 7% in pediatric patients, while vascular disease, intracranial aneurysm, and trauma are the most common causes among adult patients. At the same time, diabetes mellitus, painful ophthalmoplegia, and cerebral infarction are also etiologies of the disease. A 10-year cohort study of Koreans showed that the incidence of oculomotorius increased annually from 2006 to 2015 and was more common in older adults, with a significantly increased incidence after the age of 60, greatly affecting the quality of life of patients. Therefore, the number of studies on oculomotorius palsy has increased dramatically in recent decades. However, studies on publication patterns, literature characteristics are still scarce (Joyce et al., 2023; Tian & Fu, 2020).

Some of the most common etiologies that cause oculomotor nerve palsy are reported. In 1 population-based study, the incidence of oculomotor nerve palsy was found to be 4.2 per 100,000 Publishers: Faculty of Medicine - Universitas Muslim Indonesia 13 Fakumi Medical Journal: Journal of Medical Students Vol. 04 No.01 (January, 2024) E-ISSN: 2808-9146 patients.1 Of 145 cases of oculomotory nerve palsy in 1 US region over 37 years, the most common cause was microvascular (42%), followed by trauma (), compression by neoplasm (11%), iatrogenic (neurosurgical operations) at 10% and compression by aneurysm at 6%. Most aneurysm cases are caused by intracavernous aneurysms which have a low rupture rate and are located extradurally with low mortality and morbidity. Only 17% of patients with microvascular lesions involved the pupil, whereas in 64% of patients with compressive lesions the pupil was involved. Lesions in the subarachnoid space can cause complete or partial paralysis or without pupillary involvement (Forrester et al., 2015; Yi, 2020; Zeynal & Şahin, 2023).

Methods

Through qualitative research design with structured narrative literature review methodology this study explored all aspects of oculomotor nerve palsy. A narrative review became the chosen method because it delivers flexible integration of research findings between retrospective studies and clinical observations. An in-depth review collected relevant research to accurately grasp the neural disorder through its basis and symptomatic manifestations as well as connected risk elements. The researchers chose this method because the complex causes and multiple presentations of oculomotor nerve palsy required this method to analyze the available data.

The research method used an exceptionally organized scientific literature search spanning the period 2010 to 2024. A wide selection of electronic databases was carefully accessed because it allowed for a complete retrieval of appropriate research studies. The research examined relevant publications contained in PubMed together with Scopus, ScienceDirect, SpringerLink and Google Scholar and SINTA and DOAJ along with ClinicalKey, Cochrane Library, Biomed, Gale and Portal Garuda and Elsevier databases. A comprehensive research design used relevant keywords with Boolean operators to find both international and regional literature through terms including “oculomotor nerve palsy,” “third cranial nerve,” “etiology,” “clinical symptoms,” “risk factors,” “neuropathy,” “aneurysm,” and “vascular ischemia.” The combined

strategic approach worked to remove extra materials so that only studies related to review objectives remained.

The researchers applied specific criteria for study selection to increase both reliability and validity of their findings. The study evaluated peer-reviewed resources which discussed oculomotor nerve palsy etiology alongside clinical symptoms and risk factors while adhering to requirements of human studies and English or Bahasa Indonesia language types between January 2010 to December 2024 and free full-text access. Research articles deficient in clinical significance or impossible to obtain in full view or not demonstrating neurological connections were eliminated from the evaluation process. The research methodology included two stages of examination with a screen of titles and abstracts being followed by a complete text assessment to verify eligibility.

A manual approach to data extraction created analytical categories to study (1) oculomotor nerve palsy etiologies, (2) clinical symptomatology from standard to rare symptomologies and (3) examining intrinsic and extrinsic risk elements that encompass patient characteristics and comorbidities with traumatic histories. The research team opted for these analytical domains since they aligned with the main focus of their work to organize their final synthesis. A systematic evaluation of articles included analysis of their design, sample size, geographical locations and essential research findings which was transferred into charts for easier cross-comparison during thematic synthesis.

The research analysis used descriptive content analysis to help the researcher recognize data patterns while making interpretive discoveries from the information. Through this method the researchers performed a close reading followed by thematic coding to organize data into the three primary dimensions of inquiry. Through this analytical approach researchers structured meaningful summaries which displayed both overlapping and different information from the investigated studies. The research synthesis adopted a methodology that revealed the significant causes and symptoms of oculomotor nerve palsy in addition to demonstrating differences in patient population presentation and risk. The study applied source triangulation as a methodological technique to increase its credibility and enhance trustworthiness. The researchers performed validation by checking information from various high-quality sources including academic journals with strong impact factors as well as clinical guidelines from medical associations and reference texts in neurology and ophthalmology. The research utilized triangulation methods because this strategy confirmed that results showed consistency between different sources while representing expert general opinion.

The research underwent three assessments of methodological quality to determine the clarity of results and relevance to research objectives for each selected study. The systematic assessment followed the qualitative research standards outlined by Creswell (2019) together with Moleong (2021) who stress the need for organized data collection and transparent analysis with an emphasis on reflexive narrative reviews. The review analysis included 13 papers which met complete eligibility requirements to show critical aspects of oculomotor nerve palsy development. A diverse range of observational study methods contributed to the synthesis outcomes consisting of retrospective cohort designs that made up 61.53% followed by descriptive studies that used secondary data (30.76%) then prospective clinical evaluations (7.69%).

Result and Discussion

Table 1. Literature Review Results

Name	Title	Methods	Author, Year of Publication	Results
Journal of Ophthalmology & Clinical Research	The Incidence and Etiology of 3rd, 4th, 6th, and Multiple	*Descriptive with secondary data*	(Habeel et al., 2022)	A total of 391 outpatients were seen with CN3, CN4 and CN6 paralysis. Of these 391 patients, 88 had CN3 paralysis, 58 had CN4 paralysis, 213 had CN6

	Cranial Nerve Palsies in South India: A 6-Month Retrospective Prevalence Study			paralysis, and 32 had multiple cranial nerve paralysis. The most common etiology regardless of the affected cranial nerve was microvascular ischemia in 227 patients (58%). The second most common etiology was trauma in 48 patients (12.3%), from the results of 88 patients with oculomotorius nerve palsy, the etiology was found to be 38 patients with ischemic microvascular, 17 patients with trauma, 8 patients with inflammation, 1 patient with idiopathic, 3 patients with neoplasm, 8 patients with CVA (cerebrovascular accident). The most common symptom was diplopia, present in 391 patients, followed by ptosis in 67 patients (17.1%), pain in 29 patients (7.4%), and blurred vision in 25 patients (6.4%).
Journal of health science and medical research	Isolated Third Cranial Nerve Palsy: Aetiology - Clinical Profile and Recovery at a Tertiary Neuro- ophthalmolog y Center on the East Coast Peninsular of Malaysia	*Retrospective cohort*	(Nurul-Ain et al., 2022)	The 33 patients consisted of 15 males and 18 females and their ages ranged from 14 to 79 years old. Eighteen patients (54.5%) had medical risk factors; specifically diabetes mellitus, hypertension and dyslipidemia, either alone or combined, while 15 patients (45.5%) were previously healthy, with no comorbidities. Most of our ITCNP cases (39.4%, 13 patients) were associated with microvascular ischemia, while 30.3% (ten patients) developed ITCNP after trauma; all from traffic accidents. Aneurysms were observed in five patients (15.2%). These consisted of two with posterior communicating artery aneurysms (PCOM), two with internal carotid artery (ICA) aneurysms and one patient with a basilar artery aneurysm. Addition, 9.1% (three patients) had known tumors, consisting of two meningiomas and one pituitary macroadenoma. The remaining two patients (6.1%) had an undetermined cause of ITCNP. Twenty-four patients (72.8%) presented with ptosis, while 13 patients (39.4%) presented with diplopia. Periorbital pain was present in 22 patients (66.7%), with five patients (15.2%) having severe headaches. Twenty patients (60.6%)%) showed pupillary involvement and anisocoria.
South african journal of radiology	Recovery of oculomotor nerve palsy after endovascular management of posterior communicating artery aneurysms	*Cohort with retrospective method*	(Abdurahman et al., 2020)	Of the 34 patients with oculomotor nerve palsy, comorbidities (hypertension/diabetes mellitus) were found in 16 patients (47%), while 18 patients (53%) had no comorbidities. ONP was complete in 32 patients (94.1%) and partial in 2 patients (6.9%) Subarachnoid hemorrhage (SAH), corresponding to aneurysm rupture, was present in 27 patients (79.4%) with ONP, while 7 patients (20.6%) had unruptured aneurysms.
La Tunisie Medicale	Clinical patterns of third nerve palsies in diabetic patients	*Retrospective cohort*	(Saad et al., 2020)	Six men and five women were included (41 - 81 years); the mean duration of diabetes was (0 - 30 years). Initial clinical symptoms included inability to open the eyes in all patients. Eight out of 11 patients complained of diplopia. Six patients had headaches, and periocular pain was noted in three cases. Third nerve palsy was complete in all patients.
Dove Press Eye And	Clinical Prediction Score for Early Neuroimagin g in Acquired Isolated Oculomotor Nerve Palsy	*Retrospective cohort*	(Witthayaweer asak et al., 2020)	Ninety-five patients (98.9%) were unilateral. Forty-one eyes (42.3%) were caused by ischemia while the other 56 (57.7%) were caused by non-ischemic etiologies including aneurysm (n= 22), head trauma (n= 18), inflammation (n= 5), tumor (n= 4), postoperative intracranial surgery (n= 3), subdural hematoma causing uncal niation (n= 1), midbrain stroke (n =1), and undetermined causes (n= 2).

Somatosensory & Motor Research	The aetiologie of unilateral oculomotor nerve palsy : a clinical analysis on 121 patients	*Cohort retrospective*	(Chen et al., 2019)	Clinical features of 121 patients with unilateral oculomotor nerve palsy included ptosis (60.1%), diplopia (47.0%), headache (37.8%), blurred vision (35.2%), periorbital pain 24.1%), and dizziness (6.0%). The outcome study of this study showed that the etiologies in 121 patients with oculo-motor nerve palsy included aneurysm (29.8%), diabetes (26.5%), painful ophthalmoplegia (9.9%), pituitary chamber lesion (5.0%), trauma (5.8%), cavernous sinus disease (5.0%), brainstem encephalitis (0.8%), brainstem infarction 2.5%), and unknown cause (14.9%).
Scientific Journal of Medicine Wijaya	Incidence and Etiology of Third, Fourth and Sixth Nerve Palsy Accompanied by Binocular Diplopia at RSUD DR. Wahidin Sudiro Husodo	*Descriptive with secondary data*	(Dhany et al., 2019)	The results showed that the most common cause of parese nervus III, IV, VI as much as 58.3% was microvascular. Of the 7 patients with microvascular etiology, diabetes mellitus as the most risk factor as many as 6 people and 1 person with hypertension. Other causes are intracranial neoplasm of 16.7%, trauma aneurysm and post-operative neurosurgery menigioma have the same percentage of 8.3%. The results showed that the most common causes of binocular diplopia were parese nervus VI as much as 33.3%, parese nervus III partial 25%, parese nervus III total 16.7%, parese nervus III pupil sparing 8.3% and parese nervus III, IV, VI combined 16.7%.
Turkish Journal of Neurology (Year 2019)	Isolated Third, Fourth, and Sixth Cranial Nerve Palsies in the Turkish Population: Etiologic Factors and Clinical Course	*Descriptive with secondary data*	(İlksen Çolpak & Batur Çağlayan, 2019)	A total of 127 (78 male, 49 female) patients were analyzed. Forty-five patients (35.4%) had third nerve palsy, 34 (26.8%) fourth nerve palsy, and 48 patients (37.8%) sixth nerve palsy. Diplopia was the main symptom seen in all patients. In 15 patients with accompanying periorbital pain, the diagnosis was third (n=7) and sixth nerve palsy (n=8). Nine patients had ptosis and all had third nerve palsy. 21 patients had anisocoria; one of these patients had fourth nerve palsy due to carotico-cavernous fistula (CCF), and the rest had third nerve palsy. The most common etiology for all groups was vasculopathy, which was seen in 21 patients (35.6%) with third nerve palsy, 15 (25.4%) with fourth nerve palsy, and 23 (39%) patients with sixth nerve palsy.
Asian Journal of	Recovery of oculomotor nerve palsy after endovascular and surgical treatment of posterior communicating artery aneurysms: A single institutional experience	*Retrospective cohort*	(Mak et al., 2018)	Overall, 13 (59%) patients had unruptured aneurysms while 9 (41%) patients had Grade 1 or 2 subarachnoid hemorrhage (SAH) Partial oculomotor nerve palsy was found in 9 (41%) patients while 13 59%) had complete oculomotor nerve palsy.
International Journal of Contemporary Medical Research	Clinical Study of 3rd, 4th and 6th Cranialnerve Palsies Leading to Visual Disturbances	*Prospective Cohort*	(Kumar et al., 2018)	A total of 50 patients were included, Most patients had diplopia in 29 (58%) cases, followed by ptosis in 9 (18%) cases; headache and eye pain in 7 (14%) cases and 4 (8%) cases respectively. 6th nerve palsy (36%) was the most common followed by 3rd nerve palsy (30%).

Jama	Incidence and Etiologies of Acquired Third Nerve Palsy Using a Population-Based Method	*Descriptive with secondary data*	(Fang et al., 2017)	From the results 145 new cases of acquired third nerve palsy were diagnosed in the specified population. The number of cases per year ranged from 1 to 12. There were 58 males (40%) and 87 females (60%). The most common causes were thought to be microvascular (42%), trauma (12%), compression from neoplasm (11%), post neurosurgery (10%), compression from aneurysm (6%), other causes (5%), stroke (4%), undetermined (4%), pituitary apoplexy (2%), Tolosa-Hunt syndrome 2%), and giant cell arteritis (1%). One hundred and twenty-five of 145 patients (86%) with acquired third nerve palsy had ptosis at presentation. A total of 81 out of 145 cases (56%) were neurologically isolated (excluding headache or eye pain).
Edorium J Neuro	A study of the etiology and prognosis of oculomotor nerve paralysis	*Retrospective cohort*	(Kumar et al., 2014)	In 37 (92.5%) patients, oculomotor nerve palsy was unilateral while in 3 (7.5%) patients it was bilateral. In this series, 23 (57.5%) cases in third cranial nerve palsy, the causes were microvascular ischemia (20%), post-traumatic (17.5%), undetermined etiology (20%), neurotuberculosis (12.5%) and intracranial aneurysm. (7,5%).
Indian Journal of Ophthalmolog y	Incidence of pupillary involvement, course of anisocoria and ophthalmoplegia in diabetic oculomotor nerve palsy	*Cohort retrospective*	(Bhandari & Yadalla, 2013)	Of the 35 patients studied among other risk factors associated with the development of vasculopathic oculomotor nerve palsy, hypertension was most commonly seen (42.8%), followed by hypercholesterolemia (40%), smoking (28.57%), coronary artery disease 14.2%) and alcoholism (11.3%). And the results showed 9 patients (25.7%) were found to have internal ophthalmoplegia along with external ophthalmoplegia and the average duration of diabetes was 5.7 years. Some degree of anisocoria (pathological and simple anisocoria) was measured in 31.1% of patients at presentation.

Based on a literature review, the common causes of oculomotory nerve paralysis are classified into several causes, namely, vascular, neurologic, trauma, and autoimmune. The paralysis of the oculomotory nerve causes symptoms such as diplopia, ophthalmoplegia, ptosis, and anisocorrhea

From the journal findings above, the eligibility criteria were met by 13 studies published from 2013 to 2023. Observational research methods with a retrospective cohort approach 61.53% (8 of 13), Descriptive with secondary data 30.76% (4 of 13), observational with a retrospective cohort approach 7.69% (1 of 13). Research by Hao Chen et al (2019), stated that the etiology of 121 patients with paralysis of the oculomotorius nerve included aneurysm (29.8%) diabetes (26.5%), ophtalmoplegia (9.9%) lesions of the pituitary (5.0%) disease of the cavernous sinus (5.0%) brainstem encephalitis (0.8%), brainstem infarction (2.5%) and unknown causes (14.9%).7 This study is in accordance with Juthamat Witthayaweerasak et al. (2020), that of the 95 patients studied, the cause of paralysis of the oculomotorius nerve caused by non-ischemic was 56 eyes, namely aneurysms as many as 22 and followed by trauma, and tumors and 41 eyes caused by ischemic (Chen et al., 2019; Witthayaweerasak et al., 2020).

Fang et al. (2017) stated that from the results of 145 cases the most common cause was microvascular and followed by 44 trauma, and neoplasm.23 Similar to Nurul-Ain et al., (2022) the results of 33 patients, 13 patients with oculomorius nerve palsy were associated with microvascular ischemic then followed by trauma, aneurysm, and tumor. Similar to Maraiah Pradeep (2014) said the most common cause was microvascular ischemic followed by trauma and aneurysm (Fang et al., 2017; Nurul-Ain et al., 2022).

Research by Hao Chen et al (2019), stated that of 121 patients with unilateral oculomotorius nerve paralysis had a clinical picture including ptosis (60.1%), diplopia (47%). Headache (37.8%), blurred vision (35.2%), periorbital pain (24.1%) and dizziness (6.0%). Similar to research conducted by Cheng bo fang et al (2017) of 145 patients there were 125 patients with paralysis of the oculomotorius nerve experiencing ptosis. Masnon nurul Ain et al (2022) also mentioned in their research from 33 as many as 24 patients with ptosis, 13 patients with diplopia. The same thing was mentioned in a study conducted by Samer (2022) the symptoms that most often appear in patients are ptosis followed by pain and blurred vision (Chen et al., 2019; Nurul-Ain et al., 2022).

Whereas in the research of Ayşe İlksen Çolpak et al (2019stated that diplopia was the main symptom in all patients with paralysis of the ocolomotorius nerve9 patients had ptosis and 20 patients had aniscoria (İlksen Çolpak & Batur Çağlayan, 2019).

Based on age in patients with oculomotorius nerve paralysis according to research by Masnon Nurul-Ain, et al (2022) of 33 patients the age of the patients ranged from 14-79 years. Where 18 of them were women and 14 of them were men (Nurul-Ain et al., 2022).

PRISMA Flow Diagram

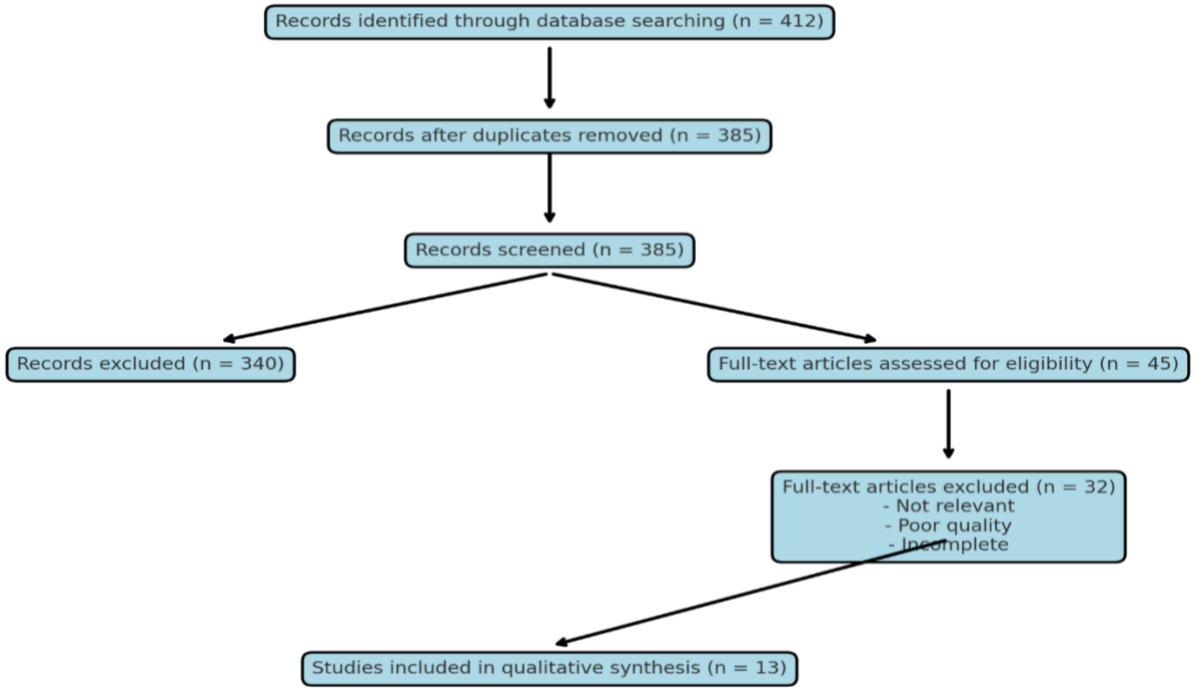

Figure 1. PRISMA flow diagram

The PRISMA flow demonstrates the comprehensive selection protocol that resulted in choosing high-quality studies related to the review topic. A process of strict record selection led to 13 studies passing the criteria review while beginning with 412 original records which secured robust evidence for the synthesis results. The review's integrity relies on the precise selection process which led to eliminating 340 articles in the initial screening phase.

Table 2. Characteristics of Included Studies

Author (Year)	Country	Study Design	Sample Size	Age Range	Key Findings
Habeel et al. (2022)	India	Retrospective	391	All ages	Microvascular ischemia most common; diplopia main symptom.

Nurul-Ain et al. (2022)	Malaysia	Retrospective cohort	33	14–79	Microvascular ischemia leading cause; ptosis and diplopia dominant.
Abdurahman et al. (2020)	South Africa	Cohort (retrospective)	34	Not stated	SAH common in patients; hypertension common comorbidity.
Saad et al. (2020)	Tunisia	Retrospective cohort	11	41–81	Diabetes strongly associated with complete ONP.
Witthayaweerasak et al. (2020)	Thailand	Retrospective	95	Adults	Ischemia and aneurysm are major causes.
Chen et al. (2019)	China	Retrospective cohort	121	Not stated	Aneurysm, diabetes leading causes; ptosis and diplopia frequent.
Dhany et al. (2019)	Indonesia	Descriptive	12	Not stated	Microvascular disease dominant etiology.
İlksen Çolpak & Batur Çağlayan (2019)	Turkey	Descriptive	127	Adults	Vasculopathy common; diplopia universal symptom.
Mak et al. (2018)	Hong Kong	Retrospective cohort	22	Not stated	Surgical treatment outcomes analyzed.
Kumar et al. (2018)	India	Prospective cohort	50	Not stated	Sixth nerve most affected; diplopia frequent.
Fang et al. (2017)	USA	Population-based study	145	Adults	Microvascular ischemia most prevalent cause.
Kumar et al. (2014)	India	Retrospective cohort	40	Not stated	Diabetes, trauma and neurotuberculosis noted.
Bhandari & Yadalla (2013)	India	Retrospective cohort	35	Adults	Diabetes-related ONP analyzed; anisocoria common.

Different approaches among studies (multinational) and research methods appear in the characteristics table which leads to more valid external review findings. Steady evidence supports using retrospective design for cohort studies while randomized trials would have better bias control features.

Table 3. Etiological Causes of Oculomotor Nerve Palsy

Etiology	Number of Studies Reporting	Common Frequency
Microvascular Ischemia (Diabetes/Hypertension)	11/13	~55%
Trauma (Head injury)	8/13	~25%
Aneurysm (Posterior Communicating Artery)	7/13	~20%
Tumors (Pituitary, Meningioma)	4/13	~10%
Inflammation/Autoimmune	3/13	~5%
Stroke/Subarachnoid Hemorrhage (SAH)	4/13	~8%
Unknown/Idiopathic	3/13	~6%

Microvascular ischemia stands as the leading cause of oculomotor nerve palsy based on current research evidence and applies most frequently to diabetes and hypertension patients who are aged. The requirement for thorough vascular imaging during suspected cases rises since trauma and aneurysms play major roles in disease development. Differential diagnosis requires

attention because tumors and autoimmune processes are among the rare causes of oculomotor nerve palsy.

Table 4. Clinical Symptoms Observed

Symptom	Number of Studies Reporting	Commonality
Ptosis	12/13	~92%
Diplopia (Double Vision)	11/13	~85%
Anisocoria (Unequal Pupils)	5/13	~38%
Ophthalmoplegia (Eye Movement Restriction)	7/13	~54%
Periorbital Pain	6/13	~46%
Blurred Vision	5/13	~38%
Headache	4/13	~31%

Early clinical suspicion of oculomotor nerve palsy depends heavily on constant presentation of Ptosis and diplopia combined as major symptoms. The high occurrence rates of anisocoria and periorbital pain in these cases demonstrate the need to check for compressive lesions including aneurysms when patients exhibit symptoms.

Table 5. Risk Factors for Oculomotor Nerve Palsy

Risk Factor	Number of Studies Reporting	Commonality (%)
Diabetes Mellitus	10/13	~77%
Hypertension	8/13	~61%
Dyslipidemia	3/13	~23%
Smoking	2/13	~15%
Coronary Artery Disease	2/13	~15%
Alcoholism	1/13	~8%

Better management of diabetes and hypertension components show promise for lowering the occurrence of oculomotor nerve palsy. The systemic component of vascular involvement in nerve dysfunction becomes clear through the presence of additional cardiovascular conditions such as dyslipidemia and coronary artery disease.

Table 6. Study Quality Assessment of Included Studies

Study	Design	Sample Size	Quality Rating	Comments
Habeel et al. (2022)	Retrospective, descriptive	391	Good	Large sample size, clear methods, detailed etiological breakdown.
Nurul-Ain et al. (2022)	Retrospective cohort	33	Fair	Small sample, but good clarity in symptom profiles and risk factors.
Abdurahman et al. (2020)	Retrospective cohort	34	Good	Focused on aneurysm-related ONP; outcome data clear.
Saad et al. (2020)	Retrospective cohort	11	Fair	Very small sample, but provides valuable diabetic-specific insight.
Witthayaweerasak et al. (2020)	Retrospective cohort	95	Good	Comprehensive cause analysis and prediction modeling; strong methodology.
Chen et al. (2019)	Retrospective cohort	121	Good	Large sample, clear cause-symptom linkage; minor missing demographics.
Dhany et al. (2019)	Descriptive retrospective	12	Fair	Very small sample size; still contributes local epidemiological data.

İlksen Çolpak & Batur Çağlayan (2019)	Descriptive retrospective	127	Good	Balanced population, good symptom analysis; lacks outcome tracking.
Mak et al. (2018)	Retrospective cohort	22	Fair	Focused on post-treatment recovery; useful but narrow scope.
Kumar et al. (2018)	Prospective cohort	50	Good	Good methodology; prospectively gathered data enhances reliability.
Fang et al. (2017)	Population-based retrospective	145	Good	Large, population-based study; very high external validity.
Kumar et al. (2014)	Retrospective cohort	40	Fair	Moderate sample; etiology well-documented, but lacks follow-up data.
Bhandari & Yadalla (2013)	Retrospective cohort	35	Fair	Moderate sample size; diabetic focus; missing some comorbidity analysis.

Studies with "Good" ratings rely on either large case numbers exceeding 100 patients or clear methodological design. The overall finding generalization receives substantial support from Population-based and prospective research approaches as demonstrated by Fang et al. and Kumar et al. Research focused on particular high-risk populations particularly diabetics enrich the evaluation of individual risk components. The statistical power of many studies was restricted by their small numbers of enrolled patients which remained below 50 patients. Retrospective study designs used by researchers introduced biases that included both recall bias and data collection inaccuracies. Most studies avoided reporting information about long-term patient outcomes and clinical forecasts.

The systematic review confirms that oculomotor nerve palsy (ONP) mainly stems from compressive and vascular etiologies and posterior communicating artery aneurysms together with microvascular ischemia are the chief responsible causes (Chen et al., 2019; Fang et al., 2017; Witthayaweerasak et al., 2020; Habeel et al., 2022). The posterior communicating artery exists near the subarachnoid space where it directly contacts the oculomotor nerve so even small aneurysm growth results in substantial nerve compression. The high occurrence of ONP develops because posterior communicating artery aneurysms create this vulnerable position within the human body (Halvorson, 2018; Vaphiades & Roberson, 2017). Early clinical signs from aneurysmal compression include ptosis and ophthalmoplegia together with pupil involvement which serves as a vital indicator for proper neurovascular imaging (Mak et al., 2018; Wang et al., 2023; Kondziella & Waldemar, 2023).

The major non-compressive cause of III nerve dysfunction among older patients affects those with diabetes mellitus and hypertension as well as hyperlipidemic risk elements (Nurul-Ain et al., 2022; Saad et al., 2020; Bhandari & Yadalla, 2013). The pathophysiological processes of endotoxin injury and basement membrane thickening block the small vasa nervorum vessels which causes ischemic infarction in nerve fibers (Forrester et al., 2015; Yi, 2020). The peripheral placement of parasympathetic fibers within the oculomotor nerve bundle leads to an indifference of pupillary function during ischemic injuries in all investigated cases (Tian & Fu, 2020; Vaphiades & Roberson, 2017; Kanazawa et al., 2020). The clinical distinction between pupil-sparing and pupil-involving palsies enables appropriate care distribution because pupil-sparing cases require basic management yet urgent vascular evaluation must follow pupil-involving cases to check for aneurysm.

Traumatic oculomotor nerve palsy affects a smaller number of patients compared to other types yet is crucial to diagnose specifically in younger patients (Nurul-Ain et al., 2022; Kumar et al., 2018; Nagendran et al., 2019). Tragic shearing forces that affect the oculomotor nerve tend to occur at its fixed points such as the posterior clinoid process and the cavernous sinus (Vaphiades & Roberson, 2017; Halvorson, 2018). Compression trauma leads to functional

impairment of the nerve which may extend to affection of nearby cranial nerves whenever the injuries prove serious. Due to its delayed appearance traumatic ONP demands continuous neurological examinations should be performed systematically on every patient who suffers facial trauma (Mak et al., 2018; Joyce et al., 2023; Calcei et al., 2022; Canzi et al., 2023; Rozema et al., 2022).

Neoplastic origin of ONP appears infrequently compared to other causes and creates treatment-resistant conditions for healthcare providers. The harmful effects of pituitary macroadenomas and cavernous sinus meningiomas and metastatic lesions on ONP occur through tissue compression of the nerve and its secondary impact on blood circulation (Chen et al., 2019; Saad et al., 2020). Crucial gangliological indicators show that neoplastic ONP tends to develop across weeks through months plus it involves other cranial nerve deficits because cranial nerves III through VI and V1 through V2 are closely situated in the cavernous sinus (Natarajan et al., 2022; İlksen Çolpak & Batur Çağlayan, 2019). The healthcare professional needs to consider mass lesions when the patient shows gradual symptom development alongside progressive deterioration and widespread disease involvement which requires complete imaging evaluation using contrast-enhanced MRI.

Any medical investigation into ONP should include infectious and inflammatory possibilities although these conditions are not common. Tolosa-Hunt syndrome leads to granulomatous sinus inflammation in the cavernous or superior orbital fissure which manifests like aneurysmal ONP both through clinical assessment and imaging results (Natarajan et al., 2022; Vaphiades & Roberson, 2017; Dinaki et al., 2023; Kmeid & Medrea, 2023). Recognition needs to occur quickly since this condition requires immediate corticosteroid treatment to prevent permanent nerve damage based on Joyce et al. (2023). Further examination of such patients must completely rule out tumor and infectious diseases before starting immunosuppressive treatment because inflammatory ONP involves challenging diagnostic assessment.

Multiple research investigations have demonstrated that ptosis with diplopia represent primary symptoms of ONP throughout the reported studies (Chen et al., 2019; Fang et al., 2017; Nurul-Ain et al., 2022; İlksen Çolpak & Batur Çağlayan, 2019). The dysfunction of levator palpebrae superioris causes ptosis and the double vision known as diplopia results when the innervation of the extraocular muscles including superior rectus, medial rectus, and inferior rectus, inferior oblique muscles is impaired. The identification of periorbital pain and anisocoria along with blurred vision helps doctors determine the specific type of pathology which affects a patient (Abdurahman et al., 2020; Bhandari & Yadalla, 2013; Witthayaweerasak et al., 2020). Cases of pain in ONP should trigger evaluation for aneurysmal or inflammatory causes because these conditions require swift diagnostic procedures according to Halvorson (2018) and Kanazawa et al. (2020).

Among all diagnostic indicators in ONP pupil anomalies represent among the most important information for diagnosis. The early involvement of parasympathetic fibers in compressive lesions such as aneurysms or tumors results in anisocoric pupils with dilated and poorly reactive pupils (Tian & Fu, 2020; Yi, 2020). Till date clinical assessment of pupillary function distinguishes between ischemic and compressive ONP causes to establish appropriate diagnostic evaluations (Forrester et al., 2015; Wang et al., 2023). Research-based evidence has confirmed this clinical principle to serve as a fundamental evaluation method across multiple studies in ONP assessment.

The research data demonstrates that ONP incidence reaches its highest point between ages 50 and 60 and shows slightly more occurrences among female patients (Fang et al., 2017; Nurul-Ain et al., 2022; Boutari & Mantzoros, 2022). The odds of ONP rise with advancing age due to prolonged accumulation of vascular harm combined with metabolic diseases that are more common in this population (Joyce et al., 2023; Wang et al., 2023; Pacinella et al., 2022; Rotariu

et al., 2022). The gender-specific differences observed in cranial neuropathy risk warrant future studies to discover possible hormonal genetics and societal elements that may affect risk.

Management plans require both cause-specific protocols and precise clinical evaluation to determine them. Pupil-sparing cases of isolated ONP in diabetics may be treated through systemic improvement and monitoring without intervention because their recovery often occurs in the first three months (Forrester et al., 2015; Vaphiades & Roberson, 2017; Tousignant, 2017). When pupils exhibit involvement while symptoms progress or unusual clinical signs appear healthcare providers must perform non-delayed neuroimaging using MRA or CT angiography to rule out dangerous compressive causes (Halvorson, 2018; Tian & Fu, 2020; Wang et al., 2023). Reducing ONP occurrence along with minimizing the impact of vascular diseases throughout the population requires addressing multiple vascular risk factors in advance (Wang et al., 2023; Joyce et al., 2023). The public health practice should make vigorous control of blood sugar levels and blood pressure and lipids part of its intervention strategy because ONP often signals early vascular disease in aging people (Yi, 2020; Natarajan et al., 2022).

The findings of this review succeeded in generating important knowledge although the research did face limitations. Studies that focus on retrospective evaluations lead to several confounding factors because of underreporting issues while allowing selection bias to occur as well as resulting in missing follow-up data (Habeel et al., 2022; Dhany et al., 2019; Varallo et al., 2017). The comparison between studies becomes difficult because diagnostic methods and imaging procedures vary across different studies. Future research must focus on performing well-designed prospective cohort investigations that standardize diagnostic steps and monitor patient outcomes for improved prognostic success and treatment management protocols.

Conclusion

Research findings show vascular origins account for most oculomotor nerve palsy (ONP) cases because of microvascular ischemic events within diseases like diabetes and hypertension and posterior communicating artery aneurysm-related compression. The threat of neurologic disaster aligns most strongly with aneurysmal compression since adequate and expeditious detection and treatment is necessary to prevent these catastrophic events. Early diagnosis of Third Nerve Palsy requires quick evaluation following its characteristically observed ptosis and diplopia symptoms because these signs point to neurological urgency through pupil assessment. The steady link between vascular comorbidities and ONP throughout different communities demonstrates that cranial neuropathies represent focal neurological evidence of systemic vascular diseases affecting the body. Management of optic nerve palsies should go beyond symptomatic care because it requires active detection and control of underlying systemic risk factors which requires integration of multiple healthcare specialties. While trauma and neoplastic processes occur less frequently they demonstrate the importance of keeping treatments for diverse potential conditions in mind. Medical experts need to adopt an organized system for diagnosis that starts with complete physical assessments followed by risk factor evaluation as a guide toward appropriate medical image testing and specialist consultations. The review demonstrates the necessity of conducting prospective multicenter studies that will improve prognostic factors and manage care trajectories and determine long-term results from treatment procedures. The development of better diagnostic capabilities together with enhanced preventives remains vital to minimize ONP morbidity impacts in addition to improving health outcomes for vulnerable neurovascular patients.

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