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Risk Factors of Opthalmoplegia in Diabetes Mellitus

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Abstract: The purpose of this research is meaningful, namely to find out what are the risk factors for ophthalmoplegia in diabetes mellitus. Ophthalmoplegia, although rare in DM, is associated with great anxiety for the patient and often appears to be a serious problem from a diagnostic and therapeutic standpoint. This study took the library method in accordance with the objects involved in the research. The results of the study found that there were several risk factors for ophthalmoplegia in patients suffering from Diabetes Miletus. Diabetes is everything related to sugar or glucose, meaning how the body produces or uses insulin effectively to control blood glucose. In this case what is meant by glucose is related to the energy needed and urgent for the body's cells, perhaps the kidneys, heart and blood vessels and small blood vessels in the eyes. Older people are more likely to experience diabetic ophthalmoplegia. Some of the risk factors include micro factors and macroangiopathy factors of chronic diabetes, which include retinopathy, nephropathy, neuropathy and severe vascular disease.

Keywords: Diabetes mellitus; Ophthalmoplegia; Risk factors

Introduction

The International Diabetes Federation states that the global prevalence of diabetes is 425 million cases worldwide in 2017 and it is also predicted that this will continue to increase to 629 million cases in 2045 (Goyal et al., 2020). The IDF divides the whole world into regions Diabetes Map, which is published annually.

Diabetes mellitus (DM) is a clinical syndrome associated with insufficient insulin secretion or action (Balaji et al., 2019). It is considered as one of the greatest emerging health threats of the 21st century. It is estimated that by 2025 there will be 380 million DM sufferers (Talagadadeevi et al., 2023). In addition to the classic complications of this disease, DM has been associated with impaired T-cell response, impaired neutrophil function, and impaired humoral immunity (Ayelign et al., 2019). Consequently, DM increases susceptibility to infections, both most common and almost always only in DM patients (e.g. rhinoceros mucosa).

Diabetics are more susceptible to cataracts. The risk of cataracts increases with increasing duration of diabetes and severity of hyperglycemia. Cataracts occur at an earlier age and are 2-5 times more common in patients with diabetes. The Wisconsin study identified that the ten-year cumulative cataract surgery incidence was 27% in patients with early-onset diabetes and 44% in cases with older-onset disease.

A common disease that affects millions of patients worldwide, one of which is diabetes mellitus (DM) (Deng et al., 2021). DM varies from country to country based on population genetics, exposure to risk factors, and health care for affected patients. These complications include micro and macrovascular events that can significantly impact the affected patient's health and quality of life. Peripheral neuropathy is a common microvascular complication of DM among diabetic patients, with a prevalence of up to 60% and is well studied.

Cranial neuropathy, although other microvascular events, are rare in diabetics and are not well explored (AlZailaie et al., 2023). Despite extensive research on the epidemiology of diabetic neuropathy in general, there is a relative dearth of knowledge regarding the factors that are associated with cranial neuropathy in diabetics. Cranial neuropathy in people with predominant

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diabetes is often seen or appears in older individuals with long duration of diabetes (Bellary et al., 2021).

In diabetes mellitus, it has several risk factors in ophthalmoplegia. The risk factors in it also have some impact on the sufferer. The risk of ophthalmoplegia can be found from a variety of causes. The causes of diabetes mellitus include unbalanced nutrition, unbalanced physical activity, consuming drinks accompanied by artificial sweeteners and unhealthy snacks (Pang et al., 2023). More severe risks can also occur, for example, such as patients who do not maintain their lifestyle.

In the West Pacific is the highest share in the incidence of diabetes. In 2017, there were one hundred and fifty-nine million cases of diabetes in almost all parts of the West Pacific countries. Indonesia is one of the western Pacific countries according to the IDF Diabetes Atlas and is included in the top ten (10th) with the highest diabetes rates in the world, China, India, USA, Brazil, Mexico, Russia, Egypt, Germany and Pakistan (Magliano et al., 2021).

Diabetics have a predisposition to certain acute mononeuropathies, including cranial neuropathies involving the ocular motor nerves (Luna et al., 2021; Yavuz, 2022). Clinical characteristics of diabetes-associated ophthalmoplegia include sudden onset, often short-lived ipsilateral pain, absence of other neurologic findings, and resolution in most cases within months (Choi et al., 2019; Welborn & Benjamin, 2023). Clinicopathological studies have suggested that diabetic ophthalmoplegia results from microvascular infarction of the ocular motor nerve in the subarachnoid or cavernous segment (Chévez-Barrios & Cykowski, 2022).

However, recent reports have also documented similar events resulting from brainstem infarction. Some authors favor the more general term vasculopathy mononeuropathy to describe this condition to emphasize the fact that such ophthalmoplegia may occur in nondiabetics who have open blood vessels or no other known risk factors.

Diabetics tend to experience certain acute mononeuropathies, including cranial neuropathy, which can involve the oculomotor nerve (Billerot et al., 2023). The oculomotor nerve is quite commonly involved in diabetes (Wei et al., 2020). The size and reactivity of the ipsilateral pupil is generally considered a useful guide to help the clinician differentiate oculomotor nerve injury, which is caused by compression of an aneurysm (a dilated and poorly reacting pupil) from an infarcted peripheral nerve in which the pupil is normally spared.

Many patients present with pupillary involvement of the oculomotor nerve associated with diabetic paralysis (H. Chen et al., 2019). Similarly, there are incidents of oculomotor nerve palsy associated with aneurysms but present with pupillarying. As oculomotor nerve palsies caused by a posterior communicating artery aneurysm can lead to devastating outcomes, a dilemma arises in patients with pupils involving oculomotor nerve palsies with diabetes.

Neuro-ophthalmological manifestations are the most common ocular pathology in diabetics after diabetic retinopathy, cataracts and glaucoma (Kowsalya et al., 2022; Rai et al., 2023). The severity of these affections is variable, but they can cause important visual function impairment. Oculomotor nerve palsy (ONP) generates less interest in the literature than diabetic retinopathy which is a public health problem in our country. Early disease can be explained by altered metabolism, inflammation or vascular occlusion resulting in ischemic degeneration of the nerve, infarction or hemorrhage in the nucleus or in the cranial nerve pathways from its emergence to the orbit. Our aim was to study the clinical, epidemiological and evolutionary therapeutic features of ONP in diabetics.

Ophthalmoplegia may be seen in the preclinical phase of diabetes and also up to the first manifestations of the disease (B. S. Chen et al., 2023). The pathogenesis of cranial neuropathies is conventionally postulated as vascular ischemia, and the prognosis is good. Ophthalmoplegia is serious and not a common problem among patients with diabetes mellitus; The oculomotor nerve was most commonly affected in our case report. The fact that the coexistence of diabetic complications and cardiovascular risk factors is slightly higher in patients with VI palsy is compatible with the hypothesis that these ischemic events may be more closely related to diabetes and the metabolic syndrome in their pathogenesis (Rossi et al., 2022).

Sometimes, the first sign of diabetes mellitus is ophthalmoplegia. This disturbance may originate in third, fourth, or sixth cranial nerve palsies, and recent onset diplopia is characteristic. Damage to the oculomotor (third) nerve causes the eye to deviate downward and outward, and palpebral ptosis is also seen. Trochlear nerve palsy (fourth cranial nerve palsy), on the other hand, causes vertical deviation with vertical diplopia, whereas abducens nerve palsy (sixth cranial nerve palsy) causes the affected eye to enter.

The most common causes of acute ophthalmoplegia include diabetic neuropathy, pressure from an aneurysm or other space-occupying lesion, brainstem ischemia or other cerebrovascular problems, nerve trauma, infectious or toxic neuritis, multiple sclerosis, and syphilis. Although diabetes is frequently involved, the differential diagnosis is critical Modern Medicine July 1979 Weakness of accommodation Diplopia cal. For example, pupillary dilatation indicates a structural lesion (usually an aneurysm) compressing the third

nerve; However, if the pupils are not dilated, the cause is more likely to be diabetic neurosis.

Diabetes is thought to produce an ischemic form of optic neuropathy by contributing to small vascular occlusion in the vessels serving the affected nerve. However, cranial nerve palsies are not related to the severity of diabetes or the degree of control, and usually resolve spontaneously within 1 to 3 months. No maintenance required; however, as noted above, it is very important to rule out other potential (and more serious) causes. A full neurological examination is therefore in order.

According to Kautzky-Willer et al. (2016) argues that in this case there is sufficient evidence that the mechanisms underlying the pathogenesis of complications of diabetes include certain epigenetic and genetic changes, including dietary and lifestyle factors that are not in accordance with a healthy lifestyle that should be. Basic risk factors for microvascular complications as well as macro conditions, (Tracey et al., 2015). The Irish Longitudinal Study on Aging (TILDA) identified risk factors for macro and microvascular complications in older or older people with type 2 diabetes: The results identified aging, including male gender, also smoking, and low physical activity and high cholesterol.

If Ophthalmoplegia is a manifestation of a benign, self-limiting diabetic neuropathy is certainly to be expected. Demonstration However, the symptoms can be consistent with those of serious, life-threatening diseases such as intracranial tumors and aneurysms, which can also occur in people with diabetes. Brain or arteriography may be required for complete assessment of a Pneumoencephalogram, one of which indicates an inherent risk. Is diabetic ophthalmoplegia indicated? Care must be taken with this procedure on a case-by-case assessment. Therefore, it is important to identify the characteristics of diabetic ophthalmoplegia.

As an independent predictor of macrovascular complications. Then in terms of hypertension, smoking and diabetes are reliable predictors of microvascular complications for ten years. According to Chilelli et al. (2013) important microvascular complications caused by chronic hyperglycemia through various mechanisms, including: Advanced Glycation End Products (AGEs), the formation of proinflammatory microorganisms and the induction of oxidative stress are part of diabetic nephropathy. As a macrovascular complication, atherosclerosis occurs more frequently in people with diabetes than in people without diabetes.

In people aged 20 to 65 years diabetes mellitus increases the risk of stroke more than five times (Khoury et al., 2013). Acquired diplopia, ophthalmoplegia, and painful ptosis are relatively common manifestations of ocular motor nerve dysfunction in diabetics. When this disease occurs, it triggers worry and anxiety in these patients. Compared with diabetics, the incidence of ophthalmoplegia is 5-10 times higher than non-diabetics and is around 0.97% in diabetics compared to 0.13% in non-diabetics (Watanabe et al., 1990).

Cranial mononeuropathies, especially ophthalmoplegia, are common in people with diabetes. (Fraser et al., 1979). The oculomotor and abducens nerves are more likely to be affected than the trochlear nerve (Rucker, 1958; Walsh & Hoyt, 1969). Since both diabetic ophthalmoplegia and diabetic retinopathy are caused by disturbances in normal microvascular function, it is reasonable to assume that the prevalence of the two diseases is directly proportional. Although the presence and degree of neuropathy and retinopathy usually correspond to the duration and severity of diabetes, ophthalmoplegia may occur in the preclinical stages of diabetes and be the first manifestation of the disease (Zaino et al., 2023).

In most developed countries, data showing diabetic ophthalmoplegia has also never been stated to have been collected in the Makassar area even though there are risk factors for it. Therefore, researchers must know what are the risk factors in diabetics that can cause ophthalmoplegia. Researchers hope that this research can predict several other risk factors in the prevention of diabetic ophthalmoplegia besides a decrease in the blood sugar index.

Method

In this study using literature search research. This study also uses qualitative methods. In library research, it means collecting library information from various library information sources related to research objects, such as research abstracts, indexes, reviews, journals, and reference works (Sugiyono, 2019). In this study, researchers obtained various sources and evidence regarding the factors of diabetic ophthalmoplegia. The research flow is summarized in the form of Figure 1.

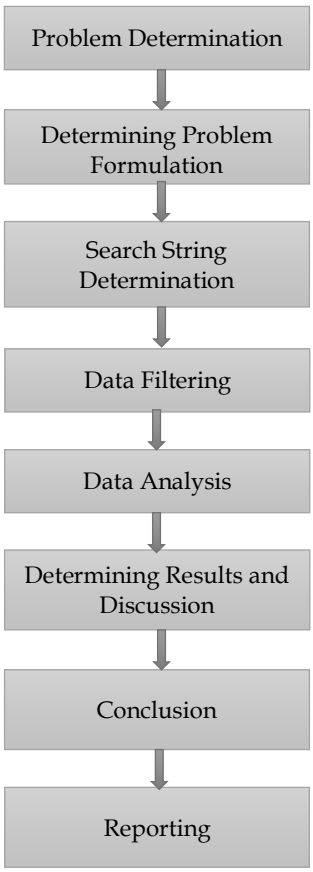

Figure 1. Research Flow

The research begins with determining the problem to be researched (Lai, 2020). After the problem is found, the problem formulation is determined so that the research can be focused. at the stage of determining the search string, the determination of synonyms and other pronouns is carried out so that the accuracy of the data collected can be guaranteed. The data that has been collected is then filtered to facilitate data analysis. The data that has been filtered will be analyzed in accordance with the objectives so that conclusions can be drawn. If the research has been completed, then reporting is carried out which makes a manuscript of the research that has been carried out.

Result and Discussion

Diabetes and Macrovascular and Microvascular Complications

Glucose is a source of power or energy that is important enough for the body's cells. However, an excess of glucose in the blood over a long period of time can damage almost all parts of the body, starting from parts of the body such as the kidneys, heart, blood vessels and small blood vessels in the eyes. Diabetes mellitus or diabetes is a disease that affects the body's ability to use insulin or produce it in an effective way to regulate blood glucose. In this case, it is important to protect the body from something called hyperglycemia; with direct and indirect effects on human blood vessels which are a major cause of morbidity and mortality in type 1 and type 2 diabetes.

In general, the side effects of hyperglycemia can be categorized into macrovascular complications (coronary heart disease, peripheral arterial disease, and stroke) and microvascular complications (such as diabetic nephropathy, neuropathy, and retinopathy). Opinion from Fowler (2008) patients who have diabetes mellitus which is related to microvascular complications are at much higher risk of experiencing accelerated atherosclerosis, which can then eventually become a cause of cerebrovascular events and causes of cardiovascular events and premature death.

The microvascular system is a category of the basic functional units of the cardiovascular system, some of which are arterioles, capillaries, and venules. These things are of course different from macrovascular starting from its architecture to its cellular components. Then in contrast to the macrovascular system where it supplies blood to the organs, the microvascular system plays an important role in maintaining blood pressure and proper nutrition. The microcirculation also has regulatory systems that regulate vascular permeability and myogenic responses that can adjust blood flow to local metabolic needs. Alterations in microvascular function may occur before hyperglycemia and pathologic vascular changes become apparent. Diabetes also causes pathognomonic changes in the microvessels affecting and increasing the thickness of the capillary basement membrane, ranging from arterioles in the glomeruli, retina, and myocardium, to the skin as well as muscle, leading to the development of diabetic microangiopathy.

According to Orasanu & Plutzky (2009) has the opinion that eventually this thickening causes disruption of vascular function and also leaves some clinical constraints such as delayed wound healing, hypertension and tissue hypoxia. Neovascularization due to vasa vasorum can combine microangiopathy and macro, and is able to predict platelet damage and cause atherosclerosis.

Various biochemical pathways are associated with hyperglycemia and microvascular complications. These include polyol accumulation, formation of advanced glycation end products (AGEs), oxidative stress and protein kinase C (PKC) activation. This process is believed to modulate disease processes by influencing cell metabolism and growth factors (Fong et al., 2004).

Polyol accumulation in hyperglycemia is associated with thickening of the basement membrane, loss of pericytes and microaneurysm formation. High

concentrations of glucose increase flux through the polyol pathway due to the activity of the aldose reductase enzyme, resulting in increased intracellular concentrations of sorbitol (Niimi et al., 2021). This increased accumulation of intracellular sorbitol was hypothesized to be the cause of osmotic damage to vascular cells (Cortese et al., 2020). Aldose reductase inhibitors (ARIs) have been studied to prevent retinal and nerve damage in diabetes.

However, several clinical trials of ARI in humans have shown no efficacy in preventing the occurrence or development of retinopathy (Arauz-Pacheco C, 1992). Another well-characterized pathway is damage due to the accumulation of Advanced Glycation End Products (AGEs). High serum glucose levels can lead to non-enzymatic binding of glucose to protein side chains, resulting in the formation of compounds called AGEs (Sadeghi et al., 2023).

Hyperglycemia studies in rats show accumulation of AGEs and loss of pericytes in retinal capillaries. In addition, diabetic rats treated with aminoguanidine (an inhibitor of AGE formation) showed reduced accumulation of AGEs and fewer histological changes, including microaneurysm formation and loss of pericytes (Kang & Yang, 2020). The effects of aminoguanidine in humans are currently being analyzed in ongoing clinical trials. Preliminary results indicate that aminoguanidine reduces the development of retinopathy but is associated with anemia.

Ophthalmoplegia

Weakness (paresis) or paralysis (plegia), also called ophthalmoplegia, refers to one or more of the six muscles responsible for eye movement. According to Vaughan & Hardie (2002) states that diseases that can affect eye movement can be divided into several categories, namely: Injuries or diseases of the cerebral hemispheres, midbrain, pons and cerebellum, eye motor neurons, extraocular muscle disease (EOM), and secondary cortical diseases affect EOMs. Classification can be based on the cause of the ophthalmoplegia or the direction of movement associated with it. There are many causes of ophthalmoplegia related to deficiencies or diseases of any body system.

The central nervous system (CNS), which is responsible for eye movement, can be influenced internally or externally, starting from the medulla, brainstem, cisterns, skull base, sinuses, and ending with the orbits; EOM can be affected primarily or secondarily by pathological processes near the orbit. This neural pathway begins in the supranuclear, internuclear, nuclear and fascicular pathways of the brainstem and then continues into the subarachnoid region, sinuses, superior orbital fissure, and then the orbit. ends at the neuromuscular junction of the extraocular muscles. Usually, lesions involving the cranial nerves or connective tissue cause neurologic deficits other than ophthalmoplegia (Xie et al., 2020).

The ophthalmoplegia is paralysis or weakness of the eye muscles. It can affect one or more of the six muscles that hold the eye in place and control its movement. The prevalence of ophthalmoplegia is estimated at around 0.32%. Among those with ophthalmoplegia, the most common lesion was due to involvement of cranial nerve VI in 53.11% of cases followed by cranial nerve III in 36.36% of cases and 2.8% of cases of paralysis due to cranial nerve IV. Older age over 45 years, prolonged diabetes is an important risk factor for ophthalmoplegia. Other factors such as having retinopathy or those with nephropathy are at increased risk of developing ophthalmoplegia. There is paralysis of not only the extraocular muscles but also intraocular muscle weakness. These muscles are supplied by cranial nerves III, IV and VI.

Ophthalmoplegia can be congenital or acquired. It can be partial or complete. It may be internal or external. In some cases, the students are involved while in some cases the students involved are avoided. Some patients may feel pain and some may not. It may be isolated or in some cases it may be multiple where there is more involvement of the neurological damage.

Diabetic ophthalmoplegia

Ophthalmoplegia due to paralysis of cranial nerves III, IV and VI in diabetics is considered a type of microvascular cranial nerve palsies with atherosclerotic changes in small vessels; However, general recovery within 12 weeks after the onset of symptoms is common.

Ophthalmoplegia diabetes was reported ten times higher in diabetics by 0.97% compared to non-diabetics up to 0.13% (Watanabe et al., 1990). In Saudi diabetics, cranial nerves VI and III are the most commonly affected cranial nerves. Diabetic ophthalmoplegia is more common in elderly people with advanced diabetes. Other risk factors are micro and macroangiopathy of chronic diabetes, namely: Retinopathy, nephropathy, neuropathy and major vascular disease.

Degree of Ocular Motor Dysfunction

Complete third nerve palsy causes outward and downward rotation of the eye with ptosis and mydriasis. Ocular motor dysfunction is often incomplete, with partial or partial paralysis of all motor ocular muscles or complete or total paralysis of the motor ocular muscles. Some have total paralysis while others have partial paralysis. In two published case series: N-III microvascular palsy. IV nerve palsies cause diplopia (disappearance of the vertical oblique muscle from the image) due to superior oblique muscle paralysis. In NVI

palsy, the eyes cannot see outward and are deviated inward, resulting in double vision due to paralysis of the lateral rectus muscle.

Conclusion

The main cause of infectious disease in tuberculosis (TB) is Mycobacterium tuberculosis. Pulmonary tuberculosis is an intractable infection that has a long history in humans and remains a major global public health problem. The microvasculature is a fundamental part of the cardiovascular system and consists of arterioles, capillaries and venules. Unlike the macrovascular system which supplies blood to the organs, the microvascular system plays an important role in maintaining blood pressure and proper nutrition. The microcirculation also has regulatory mechanisms that regulate vascular permeability and myogenic response to meet local metabolic demands. Ophthalmoplegia (OP) is weakness or paralysis of one or more of the six eye muscles that control eye movement. Risk factors include micro- and macroangiopathy in chronic diabetes such as retinopathy, nephropathy, neuropathy and significant vascular disease.

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This article was prepared by four people, namely, N.L, H.S, S.T, and W.W. The writing of this paper was carried out simultaneously at each stage.

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Conflicts of Interest
The authors declare no conflict of interest.

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