

## Significance of Hba1c in Diabetic Ocular Motor Cranial Nerve Palsies

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### Abstract

**Aim of the study:** The aim of this study was to evaluate the cases of Isolated Third, Fourth and Sixth Cranial Nerve (CN) palsies of microvascular etiology in patients with Diabetes mellitus (Type2) and analyse their Glycosylated haemoglobin (HbA1c) levels.

**Materials and Methods:** Retrospective study of patients diagnosed with third, fourth or sixth nerve palsy over three years, 2014- 2017 was done. 61 patients with the nerve palsy of microvascular ischaemic etiology due to diabetes mellitus (Type2) were selected for the study. The latest laboratory investigations that the patient had were recorded. The fasting, post prandial blood sugars and HbA1c levels were analysed. Analysis done using Microsoft excel 2010.

**Results:** The study included 61 patients, of whom 72.13% were males. The age ranged from 40 to 80 years (mean age- 58 years). 30 patients (49.18%) had 6th nerve palsy, 16 (26.22%) had 3rd nerve palsy, while 15 (24.59%) had 4th nerve palsy. The mean HbA1c levels were  $7.8 \pm 1.25$  (range – 4.8 to 11.1). 25% of patients had HbA1c levels in the range of 6 to 7, 27.8% of patients had 7 to 8, and 36% in the range of 8 to 9, and 11.04% above 9.

**Conclusion:** Elevated HbA1c levels are associated with occurrence of diabetic ocular motor nerve palsies, with 6th nerve being the most commonly affected. HbA1c levels in the range of 7 to 9% make them more prone for ocular motor cranial nerve palsies.

**Keywords:** Ocular Motor Nerve Palsy; Diabetes, HbA1c

### Introduction

An isolated ocular motor cranial nerve palsy can be defined as a malfunction of a single ocular motor cranial nerve (Oculomotor, Trochlear or Abducens) without any other neurological signs. In clinical practice, these palsies are most commonly associated with microvascular ischaemic etiology. Diabetes mellitus and Hypertension being important causes of the same. Many studies have been conducted to judge the appropriate line of treatment for these palsies, especially the use of MRI.

The purpose of this study was to evaluate the cases of Isolated Third, Fourth and Sixth Cranial Nerve (CN) palsies of microvascular etiology in patients with Diabetes mellitus (Type 2) and analyse their laboratory investigations, most specifically Glycosylated haemoglobin (HbA1c) levels.

### Materials and Methods

Retrospective study of patients diagnosed with third, fourth or sixth nerve palsy over three years, 2014-2017 was done. There were 181 patients. Of these, 61 patients with the isolated nerve palsy of microvascular ischaemic etiology (due to diabetes, hypertension, hyperlipidemia, etc) were selected for the study.

All these patients had diabetes mellitus (type 2) with or without Hypertension, as diagnosed by an independent physician. The criteria for Diabetic cases were patients who were on oral hypoglycaemic agents or Insulin; while that for Hypertension were those on antihypertensive medication. Any patients who were not known diabetics, but were found to have a random blood sugar greater than or equal to 200mg/dL on presentation were referred to a diabetologist for further evaluation and diagnosis [1].

The latest laboratory investigations that the patient had were recorded. In case of diabetics, the fasting, post prandial blood sugars and HbA1c levels were recorded with the onset of double vision.

Any patients who had multiple cranial nerve palsies and pupil involving third cranial nerve palsies were excluded. This was done to avoid any other intracranial pathology that may lead to these nerve palsies, and these patients underwent MRI scans to confirm the same.

Patients with isolated nerve palsy who had MRI findings that suggested any cause other than a microvascular etiology were also excluded.

Analysis were done using Microsoft excel 2010.

### Results

The study included 61 patients, of whom 72.13% were males. The age ranged from 40 to 80 years (mean age being 58 years). All patients had unilateral nerve palsy, 31(50.82%) being right-sided palsies. 56.14% had coexisting hypertension.

30 patients (49.18%) had 6th nerve palsy, 16 (26.22%) had 3rd nerve palsy, while 15 (24.59%) had 4th nerve palsy (Figure 1).

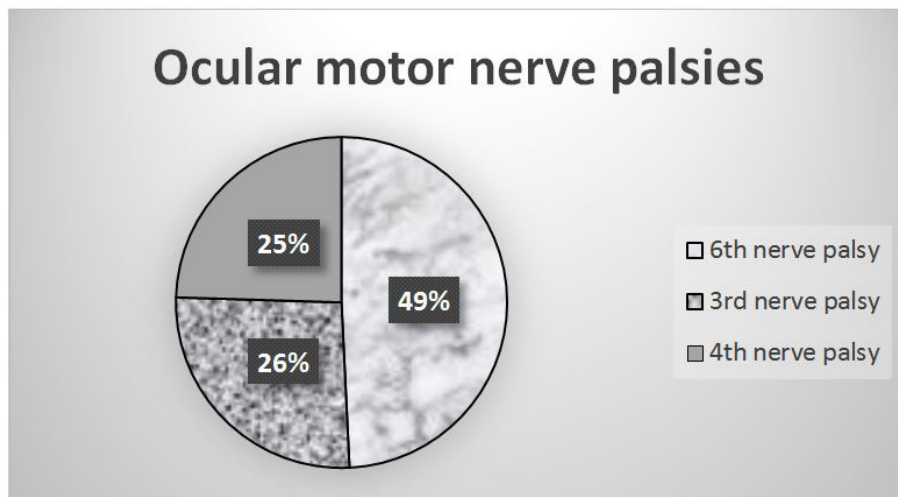


Figure 1: showing the percentage of involvement of sixth, third and fourth cranial nerve palsies

The nerve palsy was graded as partial or complete depending on the extent of limitation of extraocular movements (EOM). 79% had partial, while 21% had complete nerve palsies.

The mean duration of diabetes (Type 2) was  $5.78 \pm 6.19$  years, the minimum duration being diagnosed at presentation and maximum being 30 years. The mean FBS (Fasting Blood Sugar) levels were  $116.61 \text{ mg/dL} \pm 30.17$ . The mean PPBS (Post Prandial Blood Sugar) levels were  $179.62 \text{ mg/dL} \pm 57.08$

The mean HbA1C levels were  $7.8 \pm 1.25$  (range - 4.8 to 11.1). The mean HbA1c level in patients with associated NPDR was  $8.70 \pm 0.8$ , while that in patients without NPDR was  $7.62 \pm 1.27$  ( $p < 0.05$ ). A comparison of HbA1c values between patients with partial and complete nerve palsy showed no significant difference ( $p > 0.05$ ).

25% of patients had HbA1c levels in the range of 6 to 7, 27.8% of patients had 7 to 8, and 36% in the range of 8 to 9, and 11.04% above 9 (Figure 2).

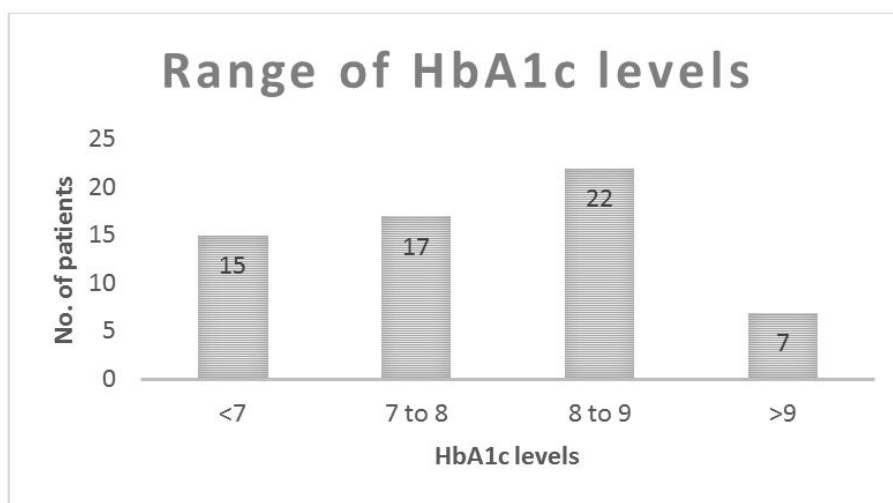


Figure 2: showing the number of patients in different ranges of HbA1c levels

The incidence of diabetic retinopathy (DR) in these cases was 23.22%, ranging from mild to moderate non-proliferative diabetic retinopathy (NPDR). No cases of Proliferative Diabetic retinopathy were seen.

We also observed that prevalence of DR in patients with 6th nerve palsy was 30% and in 3rd nerve palsy was 25%; No patients with diabetic 4th nerve palsy had DR.

## Discussion

Our study was conducted to find the significance of HbA1c levels in diabetic ocular motor nerve palsies, and is the first in this regard, to the best of our knowledge.

There are various causes of Oculomotor, Trochlear and Abducens nerve palsies, and many studies have been performed to analyse the etiology. The causes range from microvascular etiology, space occupying lesions, infections, brainstem infarction, pituitary apoplexy, trauma to demyelinating disorders [2-3].

In our study, the most frequently involved was the 6th cranial nerve (49.2%), followed by 3rd cranial nerve (26.23%) and the least was the fourth cranial nerve (24.5%). These findings were consistent with other studies conducted in this regard [4-6].

Studies suggest that cranial nerve palsies are more common in diabetic patients as compared with non-diabetics, due to atherosclerotic changes in small vessels [7]. The other risk factors for vasculopathic nerve palsies are hypertension, hyperlipidemia, hyper homocysteinuria, smoking and older age.

As a general rule, isolated cranial nerve palsies or ophthalmoplegia, in a known diabetic or hypertensive patient is assumed to be due to microvascular ischaemic changes [8]. These palsies may be associated with pain to begin with, especially in case of third nerve involvement, and resolve spontaneously in about 3 months.<sup>(8,6)</sup> The trend initially was to defer MRI till a specific indications like pupillary involvement, multiple cranial nerve involvement, or any signs suggestive of intracranial space occupying lesions, were found. However, with an increasing number of patients having been diagnosed with some intracranial lesion, like infarction or pituitary apoplexy, there are differing opinions on how an early a MRI is indicated [3]. In the patients showing normal MRI and spontaneous recovery, the cause was assumed to be of microvascular etiology.

Studies conducted to analyse laboratory investigations showed hyperlipidemia in diabetic patients which supports atherosclerotic etiology [9]. Since this is an expected change in such cases, it was not analysed in our study.

The mean FBS and PPBS levels were seen to vary greatly in our patients and were attributed to the fact that most patients were on treatment for a variable time period before presenting with nerve palsy. Only 5 patients (8.19%) were diagnosed with diabetes mellitus, on presentation for nerve palsy.

However, it was seen that the HbA1c levels were elevated, the mean being 7.82%. It is interesting to note that both the lowest and highest values of HbA1c levels were seen in the patients who had duration of diabetes for 5 years and above, showing that glycaemic control need not always correlate with the duration of diabetes.

We also analysed the presence of Diabetic retinopathy, and observed that patients with DR showed significantly higher HbA1c values as compared to those without DR ( $p < 0.05$ ). This indicates that the two complications (DR and cranial nerve palsies) are of similar etiopathogenesis as they correlate with diabetes control.

In our study, DR was seen in 23.22% which is consistent with other studies [5]. Of these, 76.9% had mild NPDR, and the rest had moderate NPDR. No patients had proliferative DR. These findings are consistent with the study by Dhume et al. [10].

The American Diabetes Association (ADA) has designated HbA1C level of  $< 7\%$  as a goal of optimal blood glucose control. The American Association of clinical endocrinologists has further recommended HbA1C levels of  $< 6.5\%$  [11].

64% of patients in our study had HbA1c levels in the range of 7 to 9, suggesting that ocular motor nerve palsies strongly correlate with poor glycemic control.

While it has not always been clear that aggressive glycemic control can reduce the end-organ complications of diabetes, recent evidence indicates that aggressive glycemic control in type 2 diabetes is associated with a 25% lower incidence of microvascular complications [11,12].

There is also evidence to suggest that long-term glycemic variability, which can be predicted by regular monitoring of HbA1c levels, is now emerging to be strongly associated with micro and macrovascular complications, suggesting that this investigation is an important tool in the prediction of outcomes in diabetes related vascular complications [13].

Our study shows that around one third of total nerve palsies are due to microvascular etiology, and there is a significant correlation between the incidence of ocular motor cranial nerves and HbA1c levels in diabetic patients.

The limitations of our study being a small sample size, and that the HbA1c levels at the recovery of the nerve palsy were not studied in our patients, which would have helped us to correlate the influence of glycaemic control on nerve palsy better.

## Conclusion:

Elevated HbA1c levels are associated with occurrence of diabetic ocular motor nerve palsies, with 6th nerve being the most commonly affected. HbA1c levels in the range of 7 to 9% make them more prone for ocular motor cranial nerve palsies.

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