

# Cranial Nerve Lesion in Diabetic Patients

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## ABSTRACT

*The retrospective investigation was done about relationships between diabetes and cranial nerve lesions (CNL) on the sample of hospitalized neurological patients in Clinical Hospital Dubrava (CHD) in 6 yrs. period (2001–2006). The goal was to expand the cognition about CNL as a complication of diabetes, to investigate possibility of better therapy models as well as to investigate the prevention possibilities. The results show that CNL are significantly more present by the diabetic patients vrs. the other hospitalized neurological patients. The main risk factors for CNL development are the duration of diabetes, patient's age and diabetes per se. No significant differences between masculine and feminine patients were registered nor by diabetics neither by other patients. For CNL are also not from significant importance the successfully treatment of diabetes, as well as type of antidiabetic and other medication. This investigation can not confirm the suspicion that some of antidiabetic medicaments are responsible for CNL due to their neurotoxic side effects.*

**Key words:** diabetes, cranial nerve lesions, hypoglycaemics, inzulin, retinopathy, diabetes duration

## Introduction

Diabetes is the most common endocrine disease. Today's lifestyle, associated diseases, as well as longer life expectancy of the population, will surely contribute to increasing prevalence of diabetes, and increased incidence of diabetic complications.

Review of available literature, particularly since 1990 until now, it is evident that a lot of attention was devoted to peripheral polyneuropathy, as one of the complications, but we do not find many papers on the topic of mononeuropathies, and especially among them do not find much about the central mononeuropathy.

Recent research on the topic craniopathy is retrospective, with the aim of getting to know all the risk factors and early detection of lesions. It may be observed that the most affected by the frequency are n. abducens, n. oculomotorius, n. trochlearis, and finally facial nerve. Other brain nerves are rare or sporadically affected<sup>1–3</sup>.

A correlation was seen with age, sex, comorbidity, diabetes control, the method of treatment. It is not found

the correlation between any of these parameters and the incidence of central neuropathy<sup>6,7,12</sup>.

In several studies etiological factor has been sought for the occurrence of craniopathies, and in them was found that over 50% of all patients have neuropathy as a complication of diabetes, also a total of 18 different possible other causes of neuropathy, one of which is the most common chronic inflammatory demyelination. Among the other causes were mentioned aneurysms, tumors, trauma, vascular lesions<sup>1,3–5,8,10,13</sup>.

## Materials and Methods

A retrospective study were performed on a sample of 7229 patients, representing all hospitalized patients at the Department of Neurology, Clinical Hospital Dubrava during the period of six years (2001–2006).

From the sample (7229) we have extracted patients with diabetes besides the neurological symptoms, which were the reason of hospitalization (310).

Also, we are especially singled out from above 7229, all persons who had CNL (70) and divided them into two groups, diabetics (29) and nondiabetics (41).

Observed group was named a group of patients who suffer from diabetes and have CNL (29). We used two control groups, the first group consisted from patients who suffer from diabetes and have CNL (310), a second group consisted from patients who have CNL and no diabetes (41).

A statistical form was created for all patients, which included: full name of patient, medical history identification, gender, year of birth, reason for admission, discharge diagnosis, habits (drinking coffee, alcohol, cigarette smoking), medication, and the essential information about diabetes (family burden of diabetes, duration of diabetes, age when the therapy was introduced, treatment of diabetes on admission, diabetes treatment at discharge, blood glucose levels on admission, specific complications of diabetes), lesion of cranial nerves, the outcome of therapy of craniopathies during hospitalization.

If the treatment of diabetes differed at discharge compared to treatment on admission, it was considered as treatment failures.

Habit of enjoying coffee, alcohol and cigarettes were processed qualitatively. The persons who have practiced stated every day for more than three years, were rated positively.

### Statistics

Study was made with descriptive statistics.

All qualitative data are presented in tables in the absolute number and percentage. Differences of quantitative variables between two groups were tested with a nonparametric test for independent samples (Mann-Whitney U-test). Quantitative data are presented in median and corresponding range. The differences of qualitative variables between two groups were tested by  $\chi^2$ -square test with Yates correction. Effect of some parameters on the occurrence of cranial nerve lesions was tested by logistic regression.

Results were considered statistically significant if  $p < 0.05$ .

Data analysis was done on the PC statistical program Statistica 6.0.

### Results

Total patients with CNL was 70. *N. facialis* was affected in 31 patients (44.3%), *n. abducens* in 27 (38.6%), *n. oculomotorius* in 17 (24.3%), *N. glossopharyngeus* in 3 patients (4.3%) (Table 1).

In patients with diabetes *n. facialis* was affected in 14 (48.3%), *n. oculomotorius* them 10 (34.5%), and *n. abducens* them in 8 (27.6%) (Table 2).

**TABLE 1**  
DISTRIBUTION OF LESIONS IN HOSPITALIZED NEUROLOGICAL PATIENTS WHO ARE SUFFERING AND NOT SUFFERING FROM DIABETES, ACCORDING TO A PARTICULAR CRANIAL NERVE INVOLVEMENT

Affected nerve	N	%
<i>N. facialis</i>	31	44.3
<i>N. abducens</i>	27	38.6
<i>N. oculomotorius</i>	17	24.3
<i>N. glossopharyngeus</i>	3	4.3
<i>N. trigeminus</i>	1	1.4

**TABLE 2**  
DISTRIBUTION OF THE INVOLVEMENT OF SOME CRANIAL NERVES IN PATIENTS WITH DIABETES

Affected nerve	N	%
<i>N. facialis</i>	14	48.3
<i>N. oculomotorius</i>	10	34.5
<i>N. abducens</i>	8	27.6

**TABLE 3**  
DISTRIBUTION CNL IN PATIENTS WITH RETINOPATHY

Affected nerve	N
<i>N. abducens</i>	3
<i>N. oculomotorius</i>	2
<i>N. facialis</i>	1
Total Nr. of patients	6

In this group we didn't have patients with lesions of *n. glossopharyngeus* and *n. trigeminus*. We are particularly singled out patients with retinopathy and patients with diabetes. In patients who have retinopathy *n. abducens* was affected in 3 patients, *n. oculomotorius* in 2, and *n. facialis* in 1 patient (Table 3).

In the group of patients with CNL suffering and not suffering from diabetes, we found a statistically significant difference in age. Patients suffering from diabetes and have CNL on average are older than patients without diabetes and have CNL ( $p=0.0038$ ) (Table 4).

We did not find statistically significant differences by gender ( $p=0.5449$ ), the therapeutic outcome of craniopathy ( $p=0.6558$ ), the drugs that patients were taking beside the antidiabetics ( $p=0.0563$ ). In the group of patients with diabetes with and without CNL we found a statistically significant difference in duration of diabetes. In patients suffering from diabetes and have CNL on averageduration of diabetes lasted longer ( $p=0.0001$ ) (Table 5).

In the same group of patients we found a statistically significant difference according to the specific complications of diabetes. In patients who have CNL statistically significantly higher is prevalence of retinopathy ( $p=0.0078$ ) (Table 6).

**TABLE 4**  
DISTRIBUTION OF PATIENTS WITH CNL, PATIENTS WITH AND WITHOUT DIABETES BY AGE

	Diabetic patients with CNL N=29	Non-diabetic patients with CNL N=41	Statistically significance of difference
AGE			
Median (span)	66.0 (32–86)	50.0 (16–79)	p=0.0038

**TABLE 5**  
THE DISTRIBUTION OF DIABETIC PATIENTS WITH AND WITHOUT CNL THE DURATION OF DIABETES

	With CNL N=29	Without CNL N=310	Statistically significance of difference
Hystory of DM (yrs)	12.0 (8–25)	10.0 (0–35)	p=0.0001

**TABLE 6**  
THE DISTRIBUTION OF DIABETIC PATIENTS WITH AND WITHOUT CNL USUALLY ACCOMPANIED BY COMPLICATIONS OF DIABETES

complications OF DM	With CNL N=29	Without CNL N=310	Statistically significance of difference
Retinopathy	6 (20.7%)	21 (6.8%)	p=0.0078
Polyneuropathy	6 (20.7%)	39 (12.6%)	p=0.2637
Nephropathy	2 (6.9%)	20 (6.5%)	p=0.7633

We did not find statistically significant differences by gender ( $p=0.9155$ ), by age ( $p=0.3787$ ), according to diabetes treatment ( $p=0.7771$ ), according to the outcome of treatment of diabetes ( $p=0.8630$ ), the medication patients were taking beside antidiabetic ( $p=0.2312$ ). The influence of certain parameters on the occurrence of cranial nerve lesions was tested by logistic regression. It was found that the risk factors for the occurrence of CNL are diabetes ( $OR=1.812$ ,  $p=0.0001$ ), duration of diabetes ( $OR=1.125$ ,  $p=0.0001$ ), retinopathy ( $OR=3.590$ ,  $p=0.0129$ ) (Table 7).

## Discussion

Patients who are involved in the research groups were selected among the 7229 patients who were hospitalized during six years in the Department of Neurology Hospital Dubrava in Zagreb within the period 2001 to 2006. Without exception, all documents are reviewed for all patients who were hospitalized during this period. The study was retrograde. The main reason for hospitalization of patients on admission was neurological problems. Frequently, patients were admitted in hospital as emergencies, which means that they developed acute neurological problems. If it is a fact that one patient was admitted several times, and entered in the studied group, they take into account the data of his last stay in the ward. The most common reason for admission to the Neurology Department was a stroke.

By the patients who have had CNL, the lesion was usually the only reason for admission to a neurological hospital, in 95% of cases in patients who had as well as

those who didn't have diabetes, and among them there was no statistically significant differences.

Among 7229 medical histories of hospitalized patients, 380 patients were allocated and divided into three groups. The first consisted of all patients who had at least one lesion of cranial nerve (70), a second group gathered all patients who had diabetes (310). These two groups were called control. The third, study group, comprised patients who suffered from both diabetes and CNL (29). Mutual comparisons were performed with each of the observed control group for better understanding the relationships between diabetes and CNL.

It was found that CNL is significantly present more frequently in people with diabetes than other neurological population that does not suffer from diabetes, making clear that diabetes is a significant risk factor for appearing of CNL. In fact in more than 95% of cases this was the only neurological outburst in hospitalized patients and the only neurological complications in patients with diabetes and other population without diabetes, considering that the frequency of occurrence CNL by groups and size of groups of diabetics and nondiabetics clearly indicates that the CNL is significantly more frequent by diabetic patients vs. the nondiabetic patients. In the earlier published studies we found similar result<sup>2,6,17</sup>.

In our study we didn't find significant differences between the two groups by gender. So there is no statistically significant differences in gender representation among diabetic and nondiabetic patients with CNL, as well as by the diabetic patients regardless whether or not they have CNL.

**TABLE 7**  
RISK FACTORS FOR THE OCCURRENCE OF CRANIAL NERVE LESIONS

	OR	95 % Confidence limits		p
		Lower	Upper	
Diabetes	1.812	11.10	29.59	0.0001
Gender	1.035	0.48	2.22	0.9297
Age	0.966	0.93	1.00	0.0818
Antihypertensives	0.520	0.21	1.28	0.1552
Anticoagulants	0.827	0.23	2.92	0.7674
Psychotropic medications	0.420	0.05	3.25	0.4049
Other medications	0.582	0.17	2.04	0.3973
Irregular medication	4.606	0.87	24.32	0.0718
Duration of diabetes	1.125	1.06	1.19	0.0001
Diet	1.091	0.24	4.95	0.9099
Oral hypoglycemics	0.478	0,27	1.07	0.0734
Insulin	0.773	0.28	2.13	0.6176
Diabetic Retinopathy	3.590	1.31	9.81	0.0129
Polyneuropathy	1.813	0.69	4.75	0.2250
Nephropathy	1.074	0.24	4.86	0.9259
Successful therapy of DM	1.154	0.54	2.49	0.7142

Similar results were found in other studies of correlation between CNL and diabetes<sup>6</sup>.

If we compare each group with CNL depending on whether or not they have diabetes, then it is evident that examinees with diabetes and CNL were significantly older than those without diabetes complicated with CNL. Simultaneously among diabetic patients with and without CNL, there is no significant differences by age. The result is a little bit surprising. We expected that this complication, CNL, like most other health complications occurs much earlier in people who suffer from diabetes than other neurological patients, and they would consequently be a younger population. However, the results are interpreted in other etiological factors that cause CNL by the nondiabetic population, which occur in the population of middle and younger age<sup>1,10</sup>.

There was a question in the survey outcome of CNL therapy in diabetic and nondiabetic individuals. It was believed that treatment of CNL in diabetic patients must be much more obstinate than in nondiabetics. However, the results showed no statistically significant difference whether CNL occurred among the other risk factors or diabetes. During hospitalisation there wasn't no one single case with deterioration of the disease, and the extent of improvement vrs. no change situation has no statistically significant differences. Such a result is not found in previous works which deal with this issue.

If one looks at the people who suffer from diabetes, with and without CNL it is evident that there is a statistically significant difference regard to duration of diabetes. Specifically, those diabetes patients who were hospitalized because of the acute CNL, had significantly

longer average of diabetic medical history than those with diabetes who were hospitalized due to other neurological reasons, and no CNL.

A similar result is found by other researchers, although they have based their papers on different, in our opinion incomplete groups of patients with CNL, partly unclear and inconsistently selected, which is not the case in our study<sup>14</sup>. Specifically, among them were observed only those patients who had the disorder eye movements. Because they belonged to »hormonal population« they were not compared with CNL among patients with no diabetes, as we have done since our respondents were »a neurological hospital population«.

There was a question whether the treatment of diabetes has an impact on the CNL occurrence, due to suspicion that the neurologic complications can be prevented by the early introduction of insulin therapy in combination with or without oral antidiabetics. There is also dissenting opinion that some antidiabetics are neurotoxic, increasing the risk of occurrence of neurological complications in diabetes. This primarily refers to insulin.

We note here that this was a major stimulus for our research: to investigate whether insulin in addition to his »irreplaceability« in the treatment of diabetes is also neurotoxic with specific effects on cranial nerves, and then beyond. However, research has clearly shown that CNL, as well as neurological complications in diabetes, is not dependent on the method of treatment of diabetes. No statistically significant differences between treatments for diabetes in diabetic patients with and without CNL<sup>6</sup>.

Also, in this study we could not confirm the hypothesis that there is any difference among patients with diabetes with and without CNL depending on the success of glycemia control and treating diabetes<sup>3,6,7,12</sup>.

According to the above, we can not claim that a major risk factor for CNL is exclusively poor control of diabetes, although we can not exclude its importance because it violates the very nature of diabetes and previous theses. Specifically, poor regulation sometimes and often is almost equally represented on average in all of our patients with diabetes, so its not noticed a significant influence on neurological complications.

By poor regulation of glycaemia, in fact diabetes, it would be interesting considering the CNL to see which type of acute complications is more risky, whether hypoglycaemic, hyperglycaemic or combined crisis. In our study we have had the intention to explore the area, but the data we found in the medical histories didn't enable this. Research of this type would lead to interesting results, and probably should be prospective.

The result of poor control of diabetes were always hyperglycemia, and in no any case hypoglycemia.

If we compare the other most common complications that occur in diabetes such as retinopathy, nephropathy and polyneuropathy, it is clear that CNL is associated with retinopathy. The retinopathy are significantly more likely occurs in diabetics with CNL than in those without CNL<sup>15,16,18</sup>.

The obtained result is ascribed to the fact that the retina of the peripheral nervous system, but functionally and anatomically very close to the central nervous system that belongs to the cranial nerve, n. opticus. As such, the retina is also susceptible to damage in people with diabetes.

Also, in people with diabetes is the question of whether certain chronic therapy poses a particular risk factor for the occurrence of CNL. That is, whether some of the chronic drug therapy is »especially neurotoxic« in diabetes if it is not among individuals without diabetes.

Our results could not confirm this assumption, namely there was no statistically significant differences between individuals with diabetes with and without CNL

depending on the drugs that are taken as a chronic therapy.

It is interesting to note that among CNL the most common affected is n. facialis, and at least n. trigeminus. Among the others the most common are oculomotoric nerves. This result is consistent with results of other researches<sup>1–3</sup>.

## Conclusion

The results show that diabetes is a significant risk factor for the occurrence of cranial nerve lesions. The probability of a patient who suffers from diabetes to get CNL is 18 times higher than if he does not suffer from diabetes.

The statistically significant difference was found among diabetic patients with and without CNL due to the duration of diabetes. Logistic regression was found that with each year of diabetes duration increases the probability of CNL occurrence by 12.5%.

Among the patients who are suffering and not suffering from diabetes and have CNL there was a statistically significant difference in age. Diabetic patients that suffer also from CNL are on average older than nondiabetic patients with CNL.

There was a statistically significant correlation between CNL and retinopathy. Diabetic patients with retinopathy have a 3 and a half times more probability to get CNL than patients with diabetes and no retinopathy.

Gender is not a risk factor for CNL appearance for diabetic as well as nondiabetic patients.

There was no statistically significant differences in the occurrence CNL among patients in the way of treatment of diabetes, which waste the hypothesis that the antidiabetics are neurotoxic.

It was not found that the success of treatment is a significant factor in the emerging CNL, even though we booked it because our approach to the concept of successful treatment of diabetes was limited and framed by a possibilities of a retrospective study.

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## **LEZIJE KRANIJALNIH ŽIVACA U OSOBA OBOLJELIH OD DIJABETESA**

### **S A Ž E T A K**

Rađeno je retrospektivno istraživanje povezanosti dijabetesa i LKŽ (lezije kranijalnih živaca) na uzorku hospitaliziranih neuroloških pacijenata u KB Dubrava tijekom 6 godina (2001–2006. god.). Cilj istraživanja je bio da se proširi spoznaja o LKŽ kao komplikacije dijabetesa, istraži mogućnost uspješnijeg liječenja, te istražiti mogućnost prevencije iste. Rezultati ukazuju da se LKŽ značajno češće događa kod osoba koje boluju od dijabetesa nego kod ostalih neuroloških bolesnika koji su zahtjevali hospitalizaciju. Glavni rizični čimbenik za nastanak LKŽ je dužina trajanja dijabetesa, dob bolesnika s dijabetesom, te sam dijabetes. Spol nije rizični čimbenik za nastanak LKŽ, kako kod bolesnika s dijabetesom tako niti kod bolesnika bez dijabetesa. Značajnim se, po nastanak LKŽ, nije pokazala niti uspješnost liječenja dijabetesa, vrsta antidijabetika, kao niti vrsta druge kronične terapije koju su bolesnici uzimali pored antidijabetika. Ovo istraživanje ne potvrđuje sumnju da su neki antidijabetici neurotoksični u smislu LKŽ.