VISUAL EVOKED POTENTIALS IN DIABETIC PATIENTS AND THEIR RELATIONSHIP WITH PERIPHERAL NEUROPATHY – A CASE CONTROL STUDY

Dissertation submitted in partial fulfillment of the requirements for the degree of

D.M. (NEUROLOGY)

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CERTIFICATE

This is to certify that the dissertation entitled "**VISUAL EVOKED POTENTIALS IN DIABETIC PATIENTS AND THEIR RELATIONSHIP WITH PERIPHERAL NEUROPATHY – A CASE CONTROL STUDY**" was done under our supervision and is the bonafide work of **Dr.B.BINDU**. It is submitted in partial fulfillment of the requirement for the D.M. (Neurology) examination.

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CONTENTS

INTRODUCTION

Diabetes mellitus is a systemic disorder characterized by chronic hyperglycaemia and derangements in the metabolism of carbohydrates, lipids and amino acids secondary to absolute or relative deficiency of normal insulin and or insulin resistance and relative or absolute excess of glucagon.

Having been recorded as early as 1500 BC in the Abers Papyrus of Egypt, diabetes mellitus is one of the oldest diseases affecting mankind. It is now a widely prevalent global health problem. The global prevalence of diabetes in adult is around 4% **(Park K, 2000)**. The prevalence is especially high in India, which by 2025 AD, will become the country harbouring the largest number of diabetics (King H et al 1998).

Every cell in our body rely on the metabolism of carbohydrates, aminoacids and lipids for the integrity of its structure and function. The substrates for the intracellular metabolism are taken up from the interstitial fluid and plasma. The concentration of these substrates in these fluids depends to a great extend on the metabolism by insulin sensitive tissues such as hepatocytes, adipocytes, myocytes etc. Thus

the insufficiency of insulin action in diabetes mellitus indirectly affects every cell in the body besides directly affecting the metabolism of insulin dependent cells.

Diabetes mellitus is a syndrome which has metabolic and vascular components. The metabolic component consists of derangement in the metabolism of carbohydrates, lipids and aminoacids. (Ronald Kahn C, Gordon C Weir, 1996). The vascular component consists of accelerated atherosclerosis, capillary basement membrane thickening, hyperplasia of endothelial cells, occlusion of capillaries, hyperfiltration, microaneurysm formation and neovascularisation.

Diabetes mellitus, being a chronic disease, causes a variety of complications, which account for the great morbidity and mortality due to this disease. The complications of diabetes mellitus include diabetic ketoacidosis, nonketotic hyperosmolar coma, neuropathy, retinopathy, nephropathy, atherosclerosis, hypertension, ischaemic heart disease, peripheral vascular disease, stroke, decrease in immunity, increased susceptibility to infections, teratogenicity and intrapartum complications. With the better understanding and better

methods of management, the lifespan of diabetic patients have been lengthened to a great extent and so the incidence of long term microvascular and macrovascular complications have also increased.

Neuropathy is the commonest diabetes–specific complication. Neuropathy is known to occur even with a short duration of diabetes mellitus. Many of these patients lack symptoms and signs of neuropathy i.e., subclinical diabetic neuropathy is common **(Akbar DH et al, 2000)**.[1] It is often undiagnosed for a long period until the patient develops clinical features suggestive of sensory, motor, or autonomic dysfunction. Electrophysiological investigations such as nerve conduction studies are sensitive in detecting the presence of asymptomatic neuropathy

Diabetic neuropathy primarily affects the peripheral nervous system, including the cranial nerves **(Aminoff, 1989)**[(2)]. Though it is often peripheral neuropathy that we diagnose in the diabetics (Daniel Tarsy) the involvement of the central nervous system has also been well-documented **(Das T, 2001[3]; Eaton SE[4])**. Only few studies have so far been conducted regarding prevalence of central nerve conduction abnormalities.

Evoked potentials is a convenient and non invasive tool for evaluation of central nervous system Visual evoked potentials (VEP) could be used to evaluate disturbances in the central visual pathway [5,6,7] Fullfield VP is excusitively sensitive to lesion of optic nerve and anterior chiasma.

Evoked potentials are also helpful in determining subclinical lesions in the optic nerve, spinal cord & brain stem. Therefore it is a convenient tool in the diagnosis and follow up for neurological disorders[8,9,10].

In diabetes mellitus, Visual deficits appears to result from both Vascular disease and metabolic abnormalities, which can affect retina, optic nerve and Visual pathway. There are conflicting results regarding optic neuropathy in diabetic patients. Tests for optic neuropathy have been performed in children and adult on a comparatively small scale[5]. Therefore the aim of present study was to evaluate, Visual evoked potentials in diabetic patients and if altered its relationship with peripheral neuropathy.

VEP is primarily a reflection of activity originating in the central 3 to 6° of Visual field which is relayed to surface of occipital

cortex. All portions of PVEP are probably of cortical origin and are classified as middle latency evoked potential. However the exact source of different PVEP components are unresolved. The earliest definable wave P50 begins within 50 ms. N 75 may represent the initial excitation associated with the arrival of Visual Signal at layer of IV of the calcarine cortex. Kraui et al proposed that P 100 arises from a secondary wave of inhibition of pyramidal cells mediated by GABA. Experiment with magnetic interference over the occipital cortex indicate that the interval from 80 to 100 ms after a retinal stimulation is critical for Visual perception. This time frame correlates well to P 100 and suggests that later, does in some way reflect active processing of Visual information.

TRANSIENT VEP & STEADY STATE VEP

When the interval between Visual stimuli is greater than the duration of the VEP & responses are averaged immediately the result is called transient VEP. This is the type generally used in clinical situation.

At stimulus faster than 4 / sec, sequential VEP run together and form train of rhythmic activity called steady state VEP. Used to measure visual acuity objectively.

VEP STIMULUS

1) **Pattern reversal** – the most commonly used stimuli for VEP recording is a pattern of light and dark check, bar or strips that is repeatedly reversed. Most clinical lab use black and white checker board pattern. Evoked potential guideline of ACNS

(American Clinical Neuro physiology society) recommend a check size in the range of 24 – 32 minutes of arc. At this size effects of Visual blurring reduced and foveal sensitivity remains high.

2) **Flash evoked potential**. Cortical response to flash stimuli is much more wide spread complex and variable than that resulting from pattern shift. The great variability of FVEP limit their utility. FVEP can be recorded through closed eye and through all but the most dense ocular opacities. It is unaffected by refractory errors, so useful in assay of function of optic nerve and central visual pathway in patients with ocular scarring and hemorrhage.

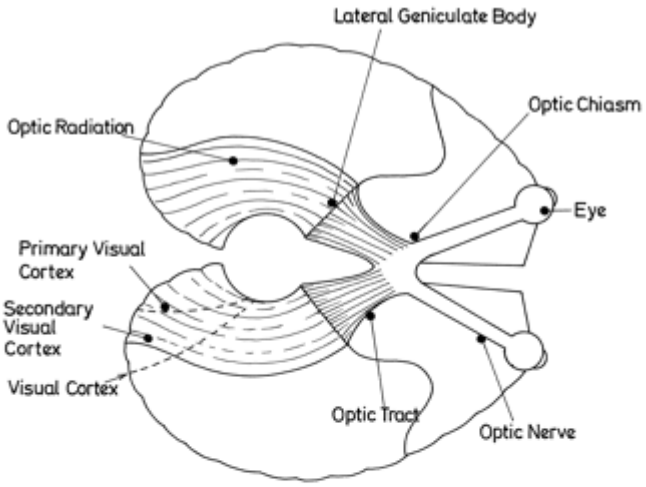
Retrochiasmatic lesions are not often detected by fullfield VEP. Hemifield techniques increase the sensitivity of VEP to retrochiasmal lesions.

P 100 LATENCY

P 100 response as part of VEP wave from, is an average, event related brain electrical potential. It derives its name from the fact that it occurs 100 ms after the stimuli onset. The choice is not attributable to any special physiologic significance of P 100. It is simply one that is highly consistent and reproducible wave form [11, 12,13] which is generated in the striate and parastriate visual cortex in response to a visual stimuli.

Current methods of clinical assessment using this wave form require the subject to look at a checker board which is a more sensitive than flash method. The position of its maximal amplitude is variable occuring, at the ionion in some individuals and corresponding to electrode position of Oz in the standard 10-20 electrode placement system. In other subjects amplitude is greatest in the midline parietal region (Pz). Therefore in standard clinical measurement waveforms are recorded both at Oz and Pz. The majority

of the P 100 waveform is generated by the lower half of the visual field and a number of variables will influence the resultant waveform, such as visual angle subtended by the stimulus and the size of check on the checkerboard, Luminance and ambient room illumination. The P 100 is greatest in children during the first decate of life declining thereafter to remain at a lower level that is stable throughout adult life. P latency increases in people over 60 years of age. The P 100 latency has better correlation with head circumference than with gender and no significant correlation of P100 with head length.



Visual Tracts & Cortex
: VEP (P100)

TECHNICAL RECOMMENDATIONS FOR VEP STUDY

Channel 1 0Z – FPZ

Channel 2 0Z – A1A2

Ground CZ

Recording condition

Band pass 1 – 300 Hz

Analysis time 250 ms

No.of epochs – atleast 100

STIMULATION

Black & White checker board or vertical grating.

Contrast 50 – 80%

Full field size > 8°

Size of pattern 14 X 16 min

Rate of stimuli 1 Hz (transient)

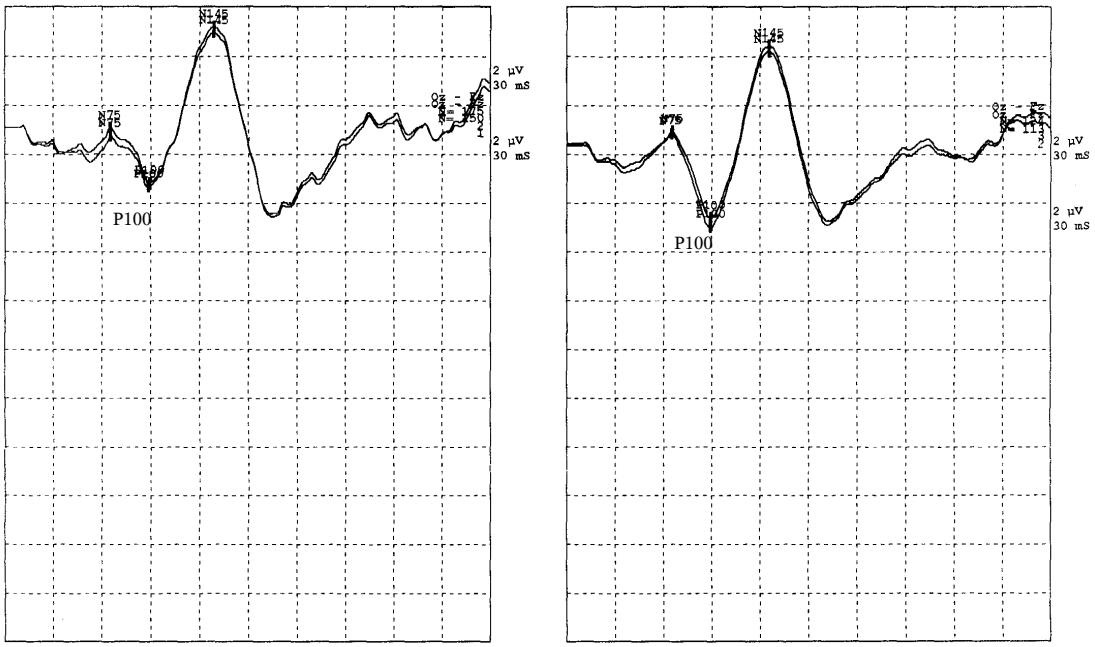
4 – 8 (steady state)

Mean luminance of central field 50cd / m2

Background luminance 20 – 40 cd /m2.

NORMAL VEP

Left **Right**



DIABETES MELLITUS AND ITS COMPLICATIONS

Diabetes mellitus, being a systemic endocrine disorder; is a disease involving all organ systems of the body. It is a disorder of energy metabolism with a significant deleterious impact on the nervous system. With the increase in the prevalence of diabetes and the increase in the lifespan of diabetics, the long term degenerative complications of diabetes are increasingly becoming a global public health problem.

The complications of diabetes, as classified by Jean D. Wilson et al in 1998 are:

I. Acute metabolic complications

1. Diabetic Ketoacidosis

2. Nonketotic hyperosmolar coma

II. Degenerative complications

3. Microvascular complications (microangiopathy and its sequelae)

a. Neuropathy

b. Retinopathy

c. Nephropathy

2. Macrovascular complications:-

(1) Hypertension

(2) Ischaemic heart disease

1 (3) Cerebrovascular accidents

(4) Peripheral vascular disease

III. Miscellaneous complications such as

Impairment of immunity

Foetal macrosomia, lung immaturity

Intrapartum and postpartum complications

Diabetes is a common cause of disability and death through its complications Data from Chennai show that the prevalence of complications of type 2 diabetes mellitus are high (Ramachandran A et al, 1999) as follows:

Hypertension	38.2%
Peripheral neuropathy	25.5%
Retinopathy	23.7%
Coronary heart disease	11.4%
Nephropathy	5.5%
Peripheral vascular disease	4%
Cerebrovascular accidents	0.9%

In general, the complications and their pathogenesis seem to be similar in type 1 diabetes mellitus and type 2 diabetes mellitus.

Diabetic Neuropathy

Diabetic Neuropathy is defined as the presence of symptoms and or signs or other objective evidence of peripheral nerve dysfunction in diabetics after exclusion of other causes **(Boulton AJM et al, 1982).**[12] Most authors use the term diabetic neuropathy as a synonym for diabetic peripheral neuropathy because most of the neurologic complications of diabetes mellitus involve the peripheral nervous system including the cranial nerves.

The estimated prevalence of diabetic neuropathy varies with the sensitivity of the diagnostic methods and the type of patients studied. Pirart J reported a prevalence of 7.5% at the time of diagnosis of diabetes mellitus. The prevalence increases with the duration and severity of hyperglycaemia to affect 60-75% of the diabetics during the course of diabetes. Neurophysiological techniques have revealed a higher incidence of 70-90% (Gallai V et al, 1988). Thus, neuropathy is the commonest microvascular complication of diabetes.

Classification of Diabetic Peripheral Neuropathies

The complexity of clinical presentation as well as the imprecise information on the pathophysiology make the classification of diabetic neuropathies difficult and imperfect. Considering the topographic distribution, the mode of onset and progression, the type of nerve fibres affected, and the nature of dysfunction, diabetic peripheral neuropathies may be arbitrarily classified into

I. Acute symmetrical polyneuropathies

1. Acute painful neuropathy

2. Rapidly reversible neuropathies.

(i) Hyperglycaemia induced/ hyperglycaemic neuropathy

(ii) Treatment induced neuropathy

II. Chronic symmetrical polyneuropathies

1. Distal sensory ± autonomic polyneuropathy

2. Distal sensori -motor polyneuropathy

3. Large fibre neuropathy

4. Small fibre neuropathy

5. Autonomic neuropathy

6. Symmetric proximal lower 1imb motor neuropathy

7. Chronic Inflammatory Demyelinating Polyneuropathy

III. Asymmetrical focal or multifocal neuropathies

1. Diabetic amyotrophy (Asymmetric proximal lower limb motor neuropathy)

2. Mononeuropathies

(1). Cranial neuropathy (single or multiple)

(2). Truncal neuropathy (Thoracoabdominal radiculopathy/ plexopathy)

(3). Lumbosacral radiculoplexopathy

(4). Focal limb neuropathies (limb mononeuropathy- single or multiple)

(i) Mononeuritis multiplex

(ii) Entrapment neuropathies

IV. Combinations

1. Polyradiculoneuropathy

2. Diabetic neuropathic cachexia

Diabetic cranial nerve palsies

Vascular infarct with resulting ischaemia is considered to be the cause of diabetes-related cranial nerve palsies. The third cranial nerve is the most commonly affected. The sixth, fourth, seventh cranial and optic nerve may also be affected. Diabetes induced third, fourth and sixth nerve palsies are self-limited. The complete recovery from oculomotor palsy within three months indicates that focal demyelination without axonal destruction is the responsible lesion.

Aetiopathogenesis of Diabetic Neuropathy

The aetiological role of diabetes mellitus in neuropathy has been proved beyond doubt. Most of the neurologic complications of diabetes involve the peripheral nervous system. Diabetes is known to cause central nervous system dysfunction also.

The pathogenesis of diabetic neuropathy *is* not precisely known despite recent advances. So several hypotheses have been put forward. These hypothesis can be broadly classified into:-

1. Ischaemic /hypoxic hypothesis
    a. Haemodynamic hypothesis
    b. Microvascular hypothesis

c. Prostaglandin hypothesis

d. Hypercoagulability hypothesis

2. Metabolic hypotheses

a. Axonal hypothesis

b. Schwann cell hypothesis

c. Osmotic hypothesis

d. Myoinositol depletion hypothesis

e. Overglycation hypothesis

f. Oxidative stress hypothesis

g. Deranged lipid metabolism hypothesis

h. Taurine depletion hypothesis

i. Magnesium deficiency hypothesis

j. Carnitine deficiency hypothesis

3. Impaired neurotrophism hypothesis

Neurotrophin deficiency hypothesis

4. Autoimmune hypothesis

The present day diabetologists and neurologists favour the microvascular hypothesis (Singh & Gupta, 2002). But the general consensus is that diabetic neuropathy is a disease of multifactorial aetiology, the various pathogenic factors acting synergistically (Feldman EL et al, 1997).

REVIEW OF LITERAUTRE

The significance and prevalence of diabetic neuropathy has increased in recent years because of the increase in the prevalence of diabetes mellitus. The increase in life span of diabetics and the availability of more sensitive methods of detection of neuropathy.

According to WHO, 19% of world diabetic population is in India. Present diabetic population of 35 million projected to go up by 80 million by 2030.

Boulton AJM et al (1982)[12] defined diabetic neuropathy as the presence of symptoms and or signs or other objective evidence of peripheral nerve dysfunction in diabetes after the exclusion of other causes for the peripheral neuropathy. The presence of certain diabetic complaining of sensory symptoms even when physical and electrophysiological examination reveal to neurological abnormality, made it necessary to redefine the term. So in the San Antonio conference of Diabetic Neuropathy, The American Diabetic Association and the American Academy of Neurology came to a consensus that diabetic neuropathy is a descriptive term meaning

demonstrable disorder, either clinically evident or subclinical, that occurs in the setting of diabetis mellitus without other causes for peripheral neuropathy.

More recently, electrophysiological investigation have demonstrated the presence of chronic diabetic neuropathy affecting the central nervous system. Hence it is advisable to use the term diabetic neuropathy in a broader prespective to designate all chronic neurologic manifestation (central as well as peripheral) of diabetes.

History of Neurodiabetology

In 1975, when ***Rou J***[13] become the first person to document symptoms of peripheral neuropathy in diabetic patients. The next 100 years saw many relevant works on neurodiabetology which contained valuable descriptions relating to symptomolocolgy of nervous system damage in diabetes.

In ***1893***[14] ***Pyre TD*** observed that the neurological disturbances in diabetic patients were associated with pathological changes of peripheral nerve at autopsy.

In 1950 a great number of works were published, in which correlation of nervous system was studied by electrophysiological, histochemical, electron microscope biochemical and other methods. This enabled the development of a detailed clinicophysiological picture of various types of diabetic neuropathy, and also revealed certain mechanisms responsible for central and peripheral neuropathy.

Recently electrophysiologcal screening of central and peripheral nervous system involvement and many interventional studies using essential fatty acids, antioxidants, neurotrophins, genetherapy and various other drugs are being conducted in different part of world.

Prevalence of diabetic peripheral neuropathy

The neuropathy that we often diagnose in the diabetes is peripheral neuropathy (***Daniel Tarssy and Roy Freeman 1996***).

The most comprehensive study of the incidence and prevalence of neuropathy in a diabetic population was the prospective study on 4400 diabetics during 1947 to 1973 conducted by ***Piart J***. The prevalence of neuropathy was 7.5% at the time of diagnosis which

increased more or less linearly at the rate of about 1.7% / year to 20 – 30% after 10 – 15 years and to 50% after 25 years.

Pyrce PJ et al **(1993)** have reported that neurological complications occur equally in Type I and Type II diabetes and additional in various forms of acquired diabetes mellitus. But United Kingdom multicentric study (Yound NJ et al) showed the peripheral neuropathy was more common in Type II.

Cabezas Cerrato J (1998)[15] carried out a multiregional cross sectional study of clinical diabetic poly neuropathy among 2644 Spanish diabetic patients. Using a standard system for scoring symptom and signs of polyneuropathy the prevalence of diabetic neuropathy was found to be 22.7% in the whole sample, 12.9% in Type I diabetes and 24.4% in Type II diabetes. The prevalence was 14.2% among diabetes < 5 years.

Nihalani KD et al[16] ***(1999)*** reported an overall prevalence of peripheral neuropathy of 55.6% among non geriatric Indian diabetics. A Chennai based study by ***Ramachnadran A. et al (1999)*** revealed that the prevalence of peripheral neuropathy in type II diabetes was

25.5% and that the neuropathy was the commonest microvascular complication.

In the study by ***De Wyh Ch*** and Colleagues ***(1999***) on Australian outpatients attending a diabetic clinic, polyneuropathy defined as Lower Limb Sensory and motor nerve conduction velocity on latency outside ± 25D of most measured in age matched control, was present in 40% of patients.

Vinik A(1999)[17] **et al** has reported that among the patients attending a diabetic clinic 25% had symptoms of neuropathy 50% had signs of neuropathy revealed by simple clinical host such as ankle jerk or vibrator preparation test and almost 90% tested positive to sophisticated tests of antonomic function or peripheral sensation.

Ashok S et al (2001)[18] determined the prevalence of peripheral neuropathy using biothesiomtry in a large group of South Indian type 2 diabetes in Chennai 19.1% of patients had evidence of peripheral neuropathy. The prevalence of neuropathy increased with increase in the age and duration of diabetes.

Barbosa et al (2001)[19] studied 93 type 2 diabetes in Portugal 72 (80%) patients had symptoms of polyneuropathy but clinical signs of distal symmetric polyneropathy was present only in 29 (32.2%) significant positive association with age, duration, feet skin changes and myocardial resistance.

Central neuropathy in diabetes mellitus

Though neurons do not require insulin for glucose uptake. Insulin acts on nervous system. Insuline receptors are widely distributed in the brain. They are also present in the peripheral nervous system.

A number of autopsy studies have documented spinal cord lesions in diabetics (***De Jorg RN 1976***). Autopsy studies conducted by ***Ohnishi A et al (1983)***[22] revealed degeneration of posterior column, which probably was secondary to disease of dorsal root ganglia or the peripheral nerves. ***Eaton*** and ***Colleagues (2001)***[23] using MRI found that diabetics having distal symmetrical polyneuropathy had significant smaller cord area at C4/5 and T3/4 when compared to healthy controls. This indicates distal symmetric polyneuropathy is

not simply a disease of the peripheral nerve, but there is substantial involvement of the spinal involvement of the spinal cord. ***Olssen et al (1968)*** have correlated the corticospinal tract degeneration 10 diabetics to lesion higher in the nervous system.

An Indian study by ***Das et al (2001)*** has revealed that subclinical dysfunction of central nervous system is common in diabetes, particularly in NIDDM and this can reliably detected by measuring sensory evoked potential. 57 IDDM and NIDDM patients and 25 controls who were found to be absolutely normal by clinical examination of CNS and computerized tomogram of brain were selected for the study. Reduced VEP was found in 16.7% of NIDDM and 11% of IDDM.

Mariani E. etal (1990)[22] found prolongation of P100 latency significantly longer in diabetics with polyneuropathy than those in without, particularly after binocular stimulation. He had studied VEP in 35 patients without retinopathy (4 IDDM + 31 NIDDM). Positive correlation was found between latencies of VEP and HbAI and duration of diabetes.

ALgan et al (1989)[5] evaluated 50 IDDM and 19 NIDDM and reported p100 latency above normal n 28% of them. P100 latency was significantly larger in patients with diabetes. There was no correlation between P100 latency and type, duration of diabetes, quality of metabolic control or presence of degenerative complication.

Puvanendran K et al (1983)[6] reported abnormal PVEP in 10 of diabetic patients and suggested this could be a confusing factor in the diagnosis of multiple sclerosis.

Ponte F et al (1986)[23] studied VEP in 62 IDDM without retinopathy and attempted to correlate the duration of diabetes, insulin requirements, blood glucose and glycosylated Hb with VEPs. He found prolongation of P100 latencies in diabetes and VEP detected by small check was more involved. Positive correlation was found between VEP and duration of diabetes.

D criillo et al (1984)[24] reported significant VEP abnormalities in 30% of subjects he studied. He studied VEP in 30 IDDM children and adolescent. No correlation was found between VEP and age, duration of diabetes and metabolic control and retinopathy.

Maritinelli et al (1991)[25] using electrophysiological tests (ERG, VEP, Oscillatory potential) studied function of visual system in IDDM. He studied 10 IDDM & 10 control subjects before and after photostress and suggested by the presence of impaired basal VEP an early involvement of nervous condurtance in optic nerve.However preserved flash ERG and normal recovery time after photostress, indicated a short disease duration does not induce physiopathological changes in the outer retinal layers or in the macular function.

Yalt Kayak et al (1988)[26] looked into whether there is a peripheral and central involvement of nervous system. He studied 30 normal subjects and 25 diabetics in whom apart from VEP, Sural nerve conduction velocity was also determined. He found prolongation in P100 and N140 components. The N90 – 140 inter peak Latency was also prolonged. Pathologic changes in VEP did not show any correlation with sural nerve conduction abnormalities.

O Ziegler et al (1994)[27] found short term blood glucose normalization improved P100 latency in uncomplicated diabetic patients and suggested abnormal VEP are partially reversible and include functional disturbance related to glucose metabolism. He

studied 12 poorly controlled. Diabetic patients before and after 3 days of near normoglycemia obtained by continuous insulin infusion. The p100 latencies were longer in diabetics. After 3 days of blood glucose control the mean P100 latencies were significantly shorter.

G.Pozzesseere et al (1988)[28] reported that neurophysiological abnormalities are present at different levels in IDDM and NIDDM patients only a few years after clinical diagosis and before the appearance of overt complications and these abnormalities seem to be correlated with metabolic control status. He recorded VEP, BAER and SEP in 4 groups, group1 – 11 IDDM, group 2 – 14 NIDDM, group 3 and 4 control group. In group 1 and 2 significant abrnormalities were found in the latency values of VEP.

G Pozzcssere et al (1991)[29] found evidence that higher cognitive function may be affected in diabetes as documented by P300 analysis and short term memory test. Electrophysiological analysis highlights neuropsychological changes not detectable by psychometric tests. Alteration of evoked potential was present in half of IDDM subjects studied. VEP, BAER, SEP was carried in 16 IDDM patients. Abnormal VEP was recorded in 1/16.

G.Tamburrano et al (1988)[30] demonstrated that earliest hypoglycemia induced EEG alterations occur in the frontal regions and VEP is less effective. He studied the effects of hypoglycemia per se on EEg and VEP in 8 normal young patients.

KJ Hardy et al (1995)[31] suggested that short term changes in blood glucose are not the mechanism for visual pathway dysfunction in aretinopathic IDDM patients as hypothesized by many. Colour discrimination was measured in 10 uncomplicated aretinopathic IDDM patients during hyperglycemic, euglycemic and hypoglycemic state and there was no difference.

Uberall MA (1996)[32] assessed 29 adolescents with IDDM and 29 controls steadily increasing latency delay for VEP (N80, P100, N150, P200) and ERP components in IDDM group was found. A pathological VEP/ERP latency delay of more than 3SD above the reference value range was observed in 21 IDDM patients (72.4%).

Alessandrini M et al [33] evaluated whether correlation existed between saccadic eye movements and visual pathways function in diabetic patient. Saccadic or fast eyemovement (EMS) and VEP were

assessed in 20 IDDM. VEP showed a significant delay in N75, P100, N145, latencies and significant reduction of N75 100 and P100 N145 amplitudes. No relationship was found between saccadic eyemovement and VEP abnormalities.

Parsi et al (1994)[34] studied VEP after photostress in IDDM patients with or without retinopathy. VEP recorded under basal conditions showed a P100 latency significantly higher in IDDP and IDDP WR than in control eyes and in IDDPWR than in IDDP eyes. N75 – P100 amplitude was significantly lower in diabetic compared to control. In all eyes VEP after photostress showed an increase in latency and decrease in amplitude.

Dolu H (2003)[35] evaluated central neuropathy in type II diabetes mellitus by multimodal evoked potential and concluded that central and peripheral neuropathies in DM are related to the duration of the disease and not to degree of hyperglycemia and metabolic control.

Lip Yang Y[36] explained the alteration of PVEP in 30 NIDDM patients and compared with 30 cases of healthy subjects. The

abnormality of PVEP is related to blood sugar in empty stomach course of NIDDM, peripheral nerve lesions and diabetic neuropathy.

U CCicoli L et al (1995)[36] assessed visual function in newely diagnosed IDDM patients electrophysiologically. In 10 IDDM patients and 10 controls he studied ERG, oscillatory potential & VEP in basal condition and after photostress. The VEP under basal condition showed that P100 latency was significantly increased in diabetic patients compared to control. The impaired basal VEP suggests an early involvement of nervous conduction in optic nerve.

Martinelli V (1992)[38] evaluated effects of hyperglycemia on VEP in 10 IDDM patients in 10 patients and suggested that. neurophysiologic abnormalities detected in IDDM patients are due to structural involvement of central nervous pathways and not due to functional damage induced by acute short term hyperglycemia.

Pan CH et al (1992)[39] conducted PSVEP study on 46 cases of NIDDM and 13 cases of IDDM. The peak latency, IPL and evoked amplitude of P100 were analysed. Motor and sensory nerve conduction velocities of the median nerve, blood sugar, HbA1c and

duration of DM were measured simultaneously. Prolongation of all peak latency and IPL and decreased amplitude of P100 were found.

Fierro B et al (1996)[40] evaluated central nervous system involvement in diabetes, IDDM > 10 years duration using SEP and VEP. Both parameters were abnormal in 10(28%) patients. VEP and SEP components were not generally significantly associated with the indices of peripheral function.

Khardori R et al (1986)[41] measured VEP and BAER in 34 type I diabetic patients. 15% had abnormal VEP. These abnormalities was not related to duration of diabetes, diabetic control or individual diabetic complications.

Comi G et al (1981)[42] investigated for central neuropathy in 71 IDDM type I diabetic children & 33 controls. The P100 latencies of P100 were significantly lengthened in 17 patients (27%) but no correlation was found between VEP and age, duration, insulin requirements and HbA1 level. Negative correlation was found between VEP and peripheral nervous conduction velocity.

Moreo G et al (1995)[43] performed longitudinal study in 18 NIDDM patients and 35 control. At first recording the peak P100 latency were significantly delayed in diabetic and peripheral neuropathy was detected in 5. The second recording no significant alteration in P100 but peripheral neuropathy increased to 7. He concluded VEP abnormalities remain stable and peripheral neuropathy progressed.

Verrotti A et al (2000)[44] suggested that glycemic control reverse VEP abnormalities. VEP was recorded before and after photostress. HbA1c was 9.4% P100 latency was significantly prolonged and test repeated 6 months later with good glycemic control HbA1 7.2%. At second recording a complete normalization of parameters was observed.

Collier A et al (1988)[45] using SEP and VEP looked for evidence for central neuropathy in IDDM with mild peripheral neuropathy. The VEP showed a small but significant delay.

Aguggia et al[46] looked into correlation of VEP polyneuropathy in diabetic patients without retinopathy. Among 35 patients (4 IDDM

and 31 NIDDM) VEP was studied and four peripheral nerve conduction velocity (sensory and motor conduction of median nerve, peroneal nerve and sural NCV). Delay in cerebral evoked potential was mostly attributable to the peripheral neuropathicv change and no firm evidence was in favour of central diabetic neuropathy.

Parisi et al (1998)[47] assessed whether VEP abnormalities are due to impaired function of retinal layers and or delayed. Conduction in post retinal visual pathway. Simultaneous recordings of VEP and PERG were performed at 2 intervals, at entry and 3 months later in 14 newly diagnosed IDDM patients. In comparison to controls VEP P100 latencies, significantly delayed, impairment of all PERG parameters and retinocortical time and latency window. No correlations were found between the paratmeters. The two sources, one retinal (impaired PERG) and one post retinal may independently contribute to the abnormal VEP.

Akinci et al (1994)[48] studied BAER, VER and NCV in 18 IDDM patients. VER latencies were prolonged. There was a positive correlation between NCVs of n.peroneal and median (motor and sensory) and VER latencies.

Millingen (1987)[49] ***KS et al*** performed PVER in 60 diabetic inpatients. Only one patient had unequally prolonged VER and 2 others it was prolonged unequally in association with proliferative retinopathy. The study does not strongly support the concept of optic neuropathy.

Anastasi M et al (1985)[50] studied VER in 50 diabetics IDDM. The latency was prolonged in relation to duration of the disease. The VEP alteration probably indicate alteration of membrane imbalance or demyclinisation.

Pozzessere G (1989)[51] performed a longitudinal study in 9 IDDM and 12 NIDDM. At first recording abnormalities present in both type I and II. In follow study the number of patients with pathological values remained unmodified, a tendency to progression, namely the number nervous level with electrophysiological abnormalities was observed.

Thomas SV et al (1993)[52] evaluated P100 latency in 20 patients with Tropical pancreatic diabetes and 20controls. No statistically significant difference in P100 latency between the two groups. There

was no correlation between P100 latency and duration and severity of diabetis, retinopathy.

Comi G et al 1986, [53] performed VEP in 85 type I IDDM and investigated all of them for peripheral neuropathy. The P100, IPL latency were prolonged and P100 amplitude decreased. Platency increased with duration of diabetes. A negative correlation was found with NCV. He concluded the above results could be due to desynchronisation of the impulses travelling along the optic pathway.

Pierzchala et al, (2002)[54], assessed conduction in central afferent tracts and the velocity of blood flow in pre and intracerebral arteries in 63 diabetic patients. VEP, BAER and SEP were studied. The latencies of assessed potential was significantly longer.

Fierro et al,1999[55] carried a neurophysiological (SEP, VEP) followup study in 30 diabetic patients ,type I IDDM, to investigate the effect of improved glucoregulation. Patients showed a decrement of HbA1c and VEP abnormalties improved. The results suggest VEP abnormalities are reversible in diabetic patients with improved glycemic control.

Celiker R et al, (1996)[56] investigated in the absence of neuropathic symptoms. 49% had peripheral NCV slowing, 40.6% F wave abnormality and 33.7% carpel tunnel syndrome.

Schneck et al, (1997)[57] studied whether specific chromatic pathway are selectively affected by short term variation in blood glucose level and found it to be affected.

Yin SY et al, ***(1991)***[58] found P100 latency to be particularly prolonged for blue color and positive correlation with blood sugar and duration of diabetes.

Lovasik JV et al (1988)[59] examined the neural function of retina and macular cortical pathway by VEP in 30 IDDM. Results showed small but measurable difference in amplitude and timing characteristics of retinal and cortical potentials for the test and control group.

Suzuki C et al, (2000)[60] investigated peripheral and central somotosensory conduction in patients with diabetes and found both to be affected.

Omer Azal, (1996),[61] studied VEP in 45 diabeteic patients and P lantency prolonged in diabetics significantly.

MAS Abdel Megeed et al in 2002[64] evaluated ERG, and PVEP in 29 children with IDDM and found P100 to be significantly delayed in eyes of diabetic patients even in those with IDDM < 5 years.

Kate dra et al,[65] studied VEP in 40 diabetic patients and found abnormality in 35% and coexisted with worst metabolic control, longer duration &older patients.

Geert Jan Biessels et al (1999)[66] compared the course of development of neurophysiological changes in the central and peripheral nervous system in streptozotocin diabetic rats. The study demonstrated the peripheral impairments develop within weeks after diabetic induction, where as central impairments take months to develop. Insulin can reverse both central and peripheral aterations.

PG Ramon et al[67] recorded VEP in 25 diabetic patient and 15 control. P100 latency were significantly prolonged and P100 amplitude decreased in diabetics.

AIM OF THE STUDY

To evaluate visual evoked potential abnormalities in diabetic patients and its relationship to peripheral neuropathy.

MATERIALS AND METHODS

The aim of the present study was to determine the Visual evoked potential abnormalities in diabetics and check their relationship with peripheral neuropathy.

The present study was a case control study including a study group consisting of 34 diabetes (19 female and 15 males) mean age (46.8 ± 12.54) and a control group consisting of 20 healthy subjects (11 females and 9 males) mean age (41.25 ± 9.39).

A total of 34 patients were chosen according to inclusion and exclusion criteria from among the diabetic patients attending the diabetology out patient clinic of Govt. Hospital, Madras Medical College during the period from Jan – 2005 to Aug 2005.

INCLUSION CRITERIA

1) Patients who were diagnosed to have diabetes mellitus according to revised criteria for diagnosing diabetes issued by the consensus panel of experts from the National Diabetic data group and world health organisation (American Diabetes Association 2000) i.e. fasting plasma glucose more than 126

mg / dl or 2 hr post prandial plasma group more than 200mg / dl.

2) Patients on regular treatment.

3) Age 18 to 60 years

EXCLUSION CRITERIA

1) Patients with diabetic retinopathy and maculopathy

2) Long standing hypertension

3) Consuming alcohol > 100ml / day

4) Those with peripheral nervous system disease unrelated to diabetes mellitus.

5) Cataract, glaucoma, Vitreous opacities, or any evidence of optic neuropathy.

6) Past history of Cerebrovascular accident.

All patients were either NIDDM (31) or IDDM (3) proved by blood glucose studies. The duration of diabetes ranged from 3-20 years. Fasting blood glucose level was estimated prior to recording VEP. Detailed opthalmological check up of all patients was done

which included, visual acuity, recording of ocular tension and fundus examination under full mydriasis. Only those patients with normal visual acuity at base line were included in the study. Clinical evidence of peripheral neuropathy was sought for by means of pinprick testing, cottons touch and vibration testing with 128 tuning fork. Motor power and reflexes were studied for evidence of motor neuropathy.

Visual evoked potentials were recorded with RMS equipment, both eyes were stimulated separately by checkerboard pattern size 8 x 8 reversal at 1.7/sec. The screen was placed at the 1 meter from the nasion. The response was recorded by surface electrode that were placed at the occipital region, the active one week being placed Oz and reference at Fz. Patients were advised to come without applying oil to scalp and to shampoo the hair and dry. Preparations of skin was done by abrading and degreasing. The aim was to achieve maximal stimulation of the foveal and parafoveal fibres at 75% contrast and reversal rate of 1.2Hx. Uniform illumination was maintained in the laboratory and electrode impedance was kept less than 5 ohms. An average of 200 sweeps was given to each eye. This was repeated twice and the averages of were superimposed to

demonstrate reproducibility. Any difference of more than 3 ms in the latencies between trials were not included. The peak P 100 latency and amplitude were studied.

The Right median and common peroneal nerve motor and sensory conduction were studied recording the distal latency, CMAP and Nerve conduction velocity.

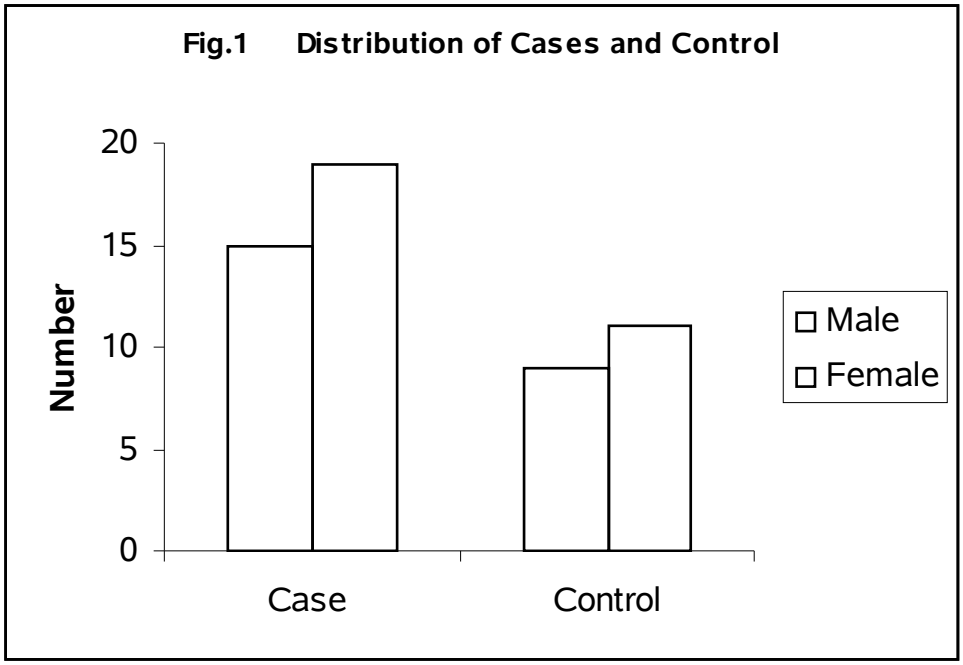
RESULTS

Students t – test was used to statistically analyze for significance in difference in VEP in diabetics and controls

1) **Distribution of cases and control**

Sex	Cases	Control
Male	15	9
Female	19	11
Total	34	20

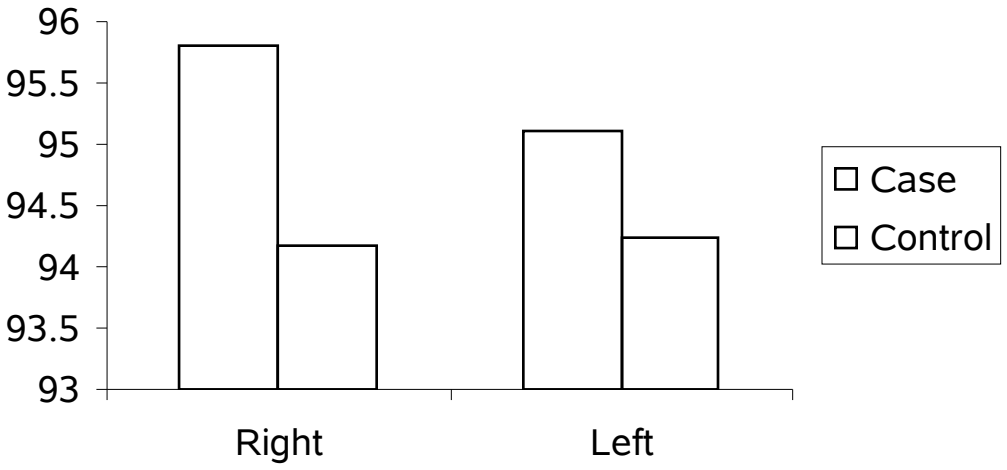
Fig.1 Distribution of Cases and Control



2) P 100 LATENCY

P 100 Latency	Cases		Control		P Value
	Mean	SD	Mean	SD	
Right	95.81	7.34	94.17	4.55	0.356
Left	95.10	5.30	94.25	3.41	0.522
Mean	95.48	5.65	94.21	3.61	0.370

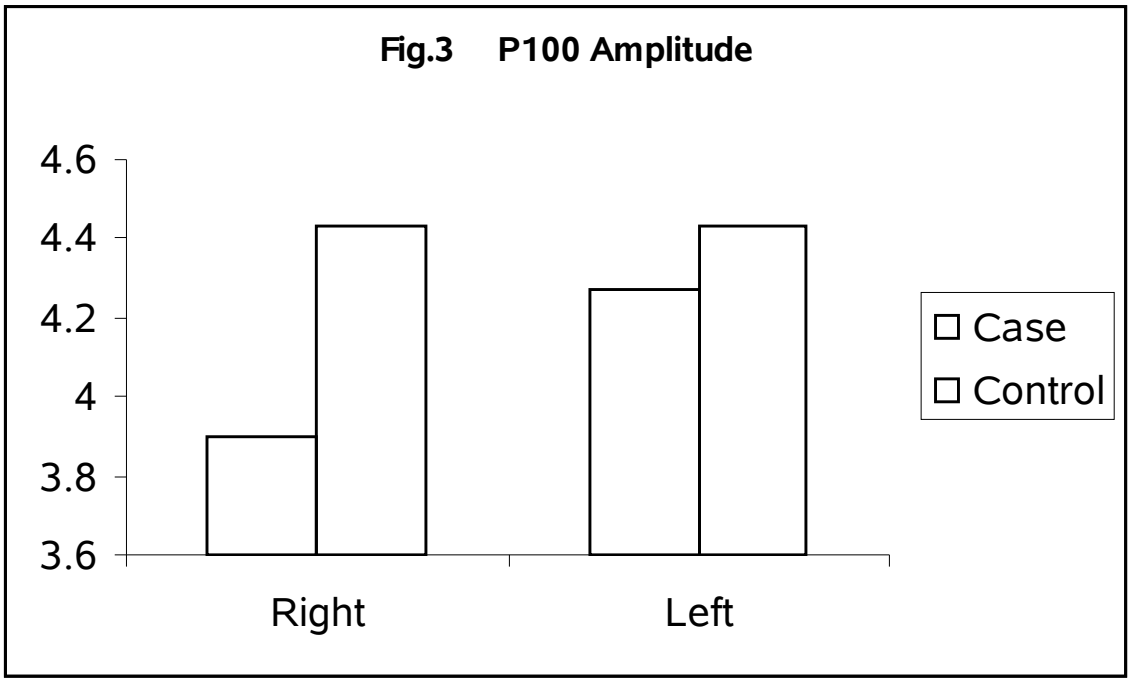
Fig.2 P100 Latency



No statistically significant difference in P 100 Latencies of cases and control.

3) P 100 AMPLITUDE

P 100 Amplitude	Cases		Control		P Value
	Mean	SD	Mean	SD	
Right	3.90	2.17	4.43	2.16	0.384
Left	4.27	2.43	4.43	2.33	0.813
Mean	4.09	2.25	4.43	2.19	0.582



No statistically significant difference in P 100 Amplitude of cases and control.

4) DIFFERENCE IN P 100 LATENCY IN MALES / FEMALES

Mean P 100 Latency					
Sex	Cases		Control		P Value
	Mean	SD	Mean	SD	
Male	96.94	5.16	94.29	3.52	0.185
Female	94.33	5.89	94.14	3.85	0.925

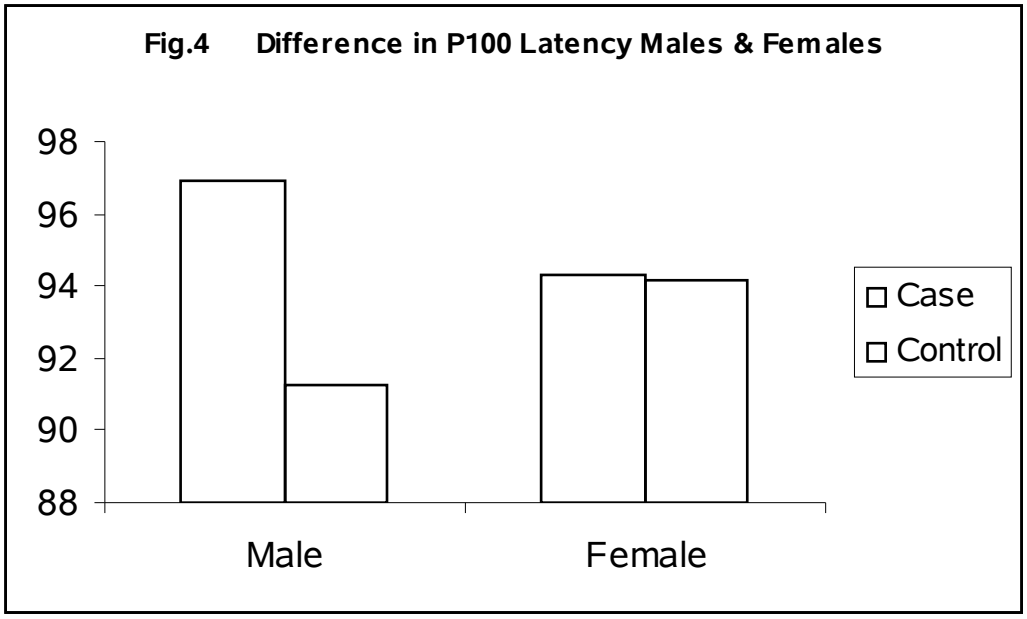
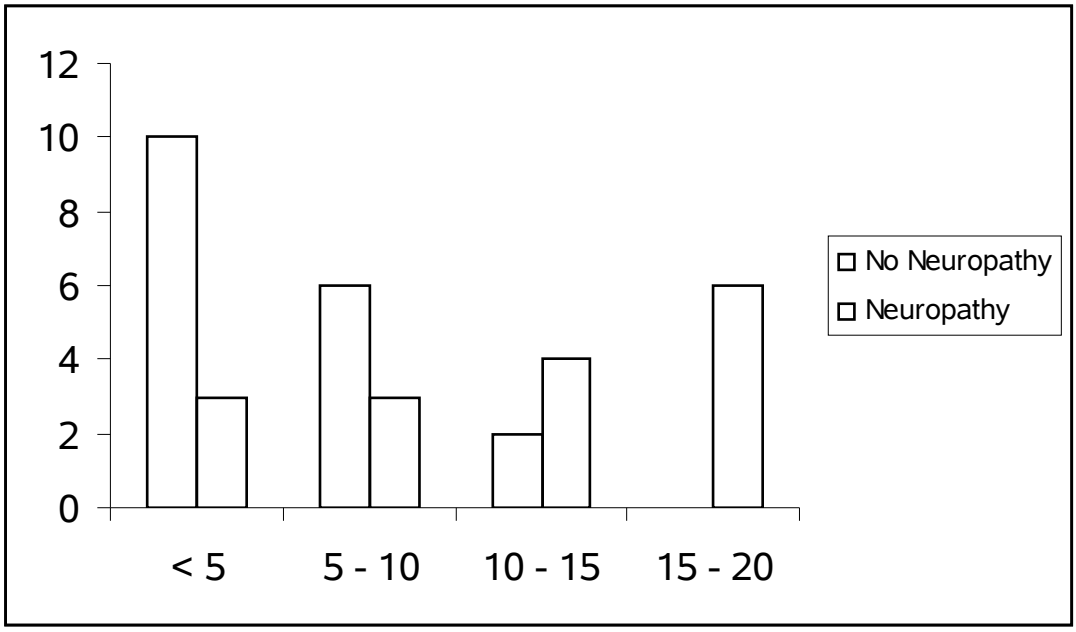


Fig.4 Difference in P100 Latency Males & Females

5) **PERIPHERAL NEUROPATHY WITH RELATION TO DURATION OF DIABETES**

Years of Diabetes	Number of Cases		
	No -Neuropathy	Neuropathy	Total
0-5	10	3	13
5-10	6	3	9
10-15	2	4	6
15-20	-	6	6

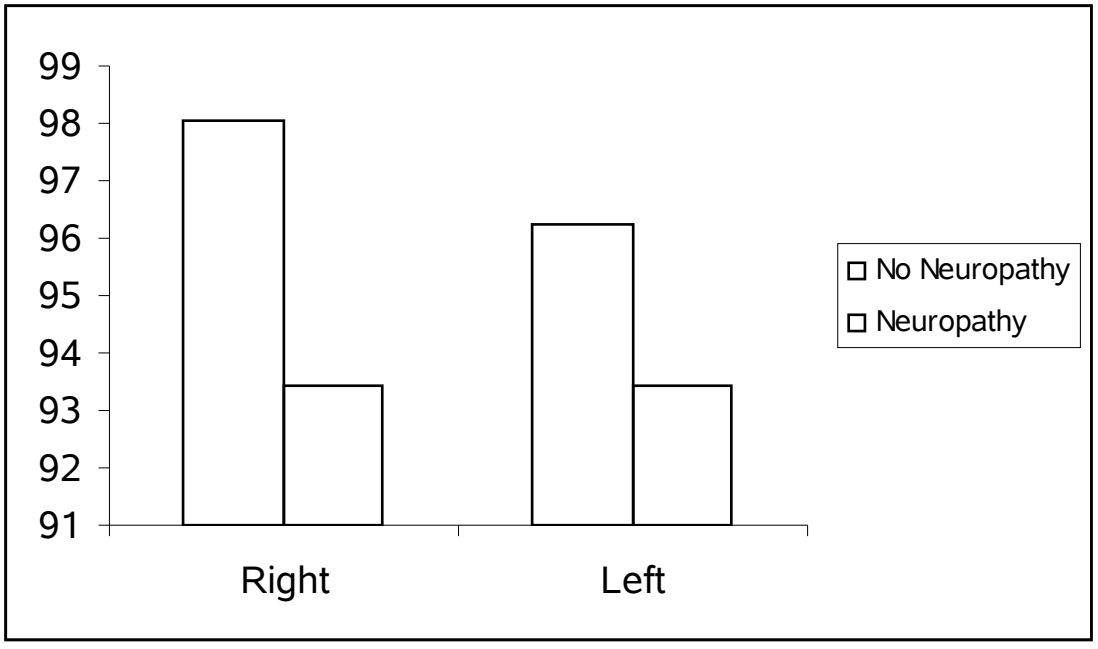
Fig.5.Peripheral Neuropathy With Relation To Duration Of Diabetes



6) P 100 LATENCY IN CASES WITH NEUROPATHY & NO NEUROPATHY

P 100 Latency	No Neuropathy		Neuropathy		P Value
	Mean	SD	Mean	SD	
Right	98.05	5.88	93.41	8.18	0.064
Left	96.25	5.25	93.44	5.01	0.086
Mean	97.31	4.96	93.43	5.82	0.046*

Fig.6. P 100 Latency in Cases with Neuropathy & No Neuropathy

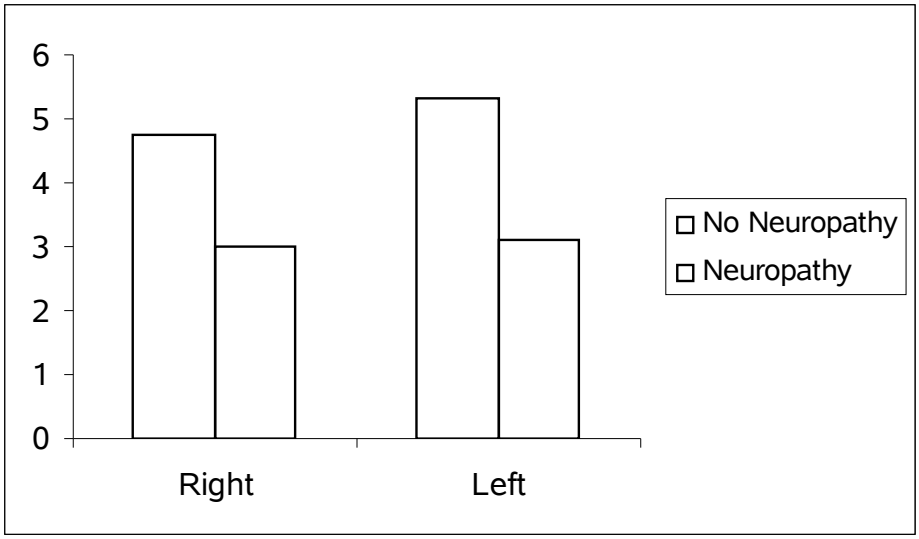


P 100 Latency was smaller in patients with peripheral Neuropathy ($P < 0.05$).

7) **P AMPLITUDE IN CASE WITH NEUROPATHY AND NO NEUROPATHY**

P 100 Amplitude	No Neuropathy		Neuropathy		P Value
	Mean	SD	Mean	SD	
Right	4.74	2.49	2.99	1.22	0.013
Left	5.31	2.65	3.11	1.51	0.006
Mean	5.03	2.54	3.05	3.61	0.008

Fig.7. P Amplitude in Case with Neuropathy and No Neuropathy

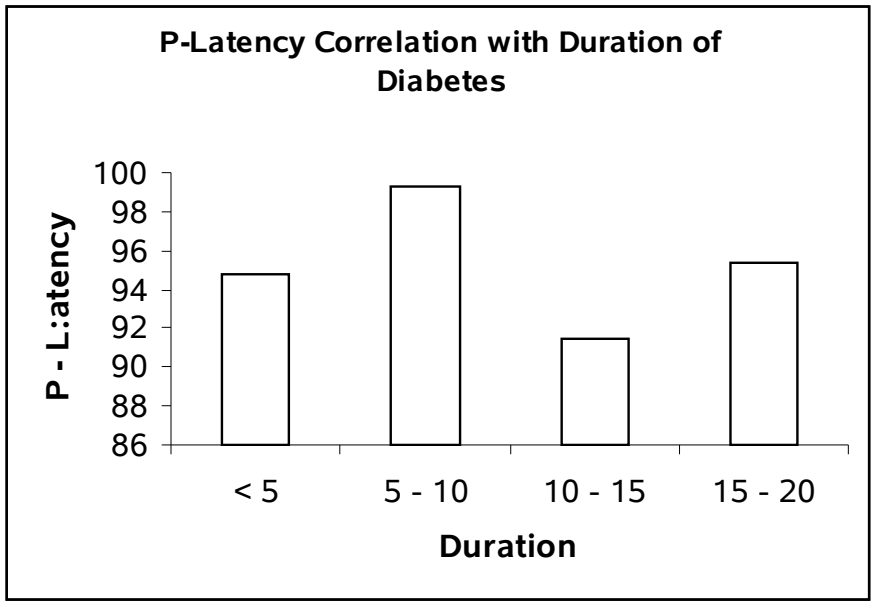


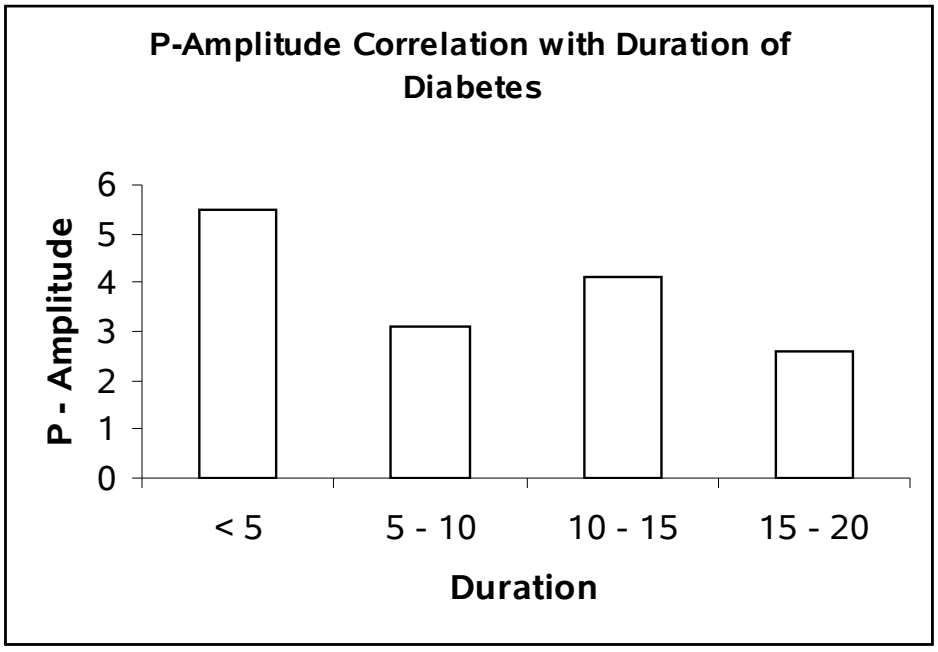
Significant (P <.01) reduction in P amplitude of patients with Neuropathy compared to without Neuropathy.

8) **P 100 LATENCY AND AMPLITUDE CORRELATION WITH DURATION OF DIABETES**

Diabetes in Years	P –Latency		P –Amplitude	
	Mean	SD	Mean	SD
< 5	94.82	4.74	5.47	2.62
5-10	99.26	5.05	3.09	1.71
10-15	91.41	5.67	4.10	1.10
15-20	95.33	6.09	2.58	1.26

Fig. 8 P 100 Latency and Amplitude Correlation with Duration Of Diabetes

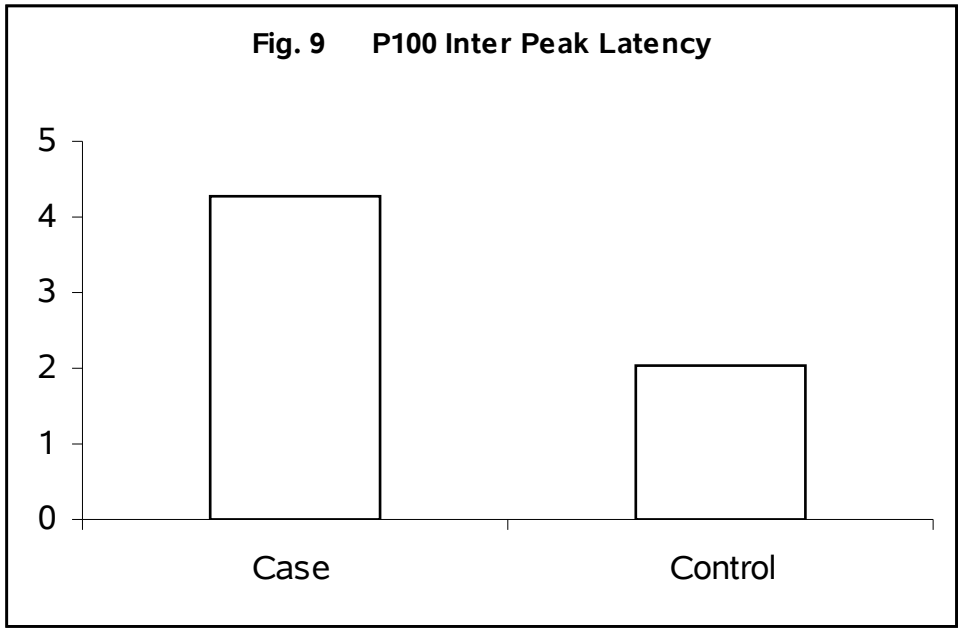




By Annova (Multiple range tests: student newman kauls test) no correlation P100Latency/Amplitude with duration of diabetes .

9) **P 100 INTER PEAK LATENCY**

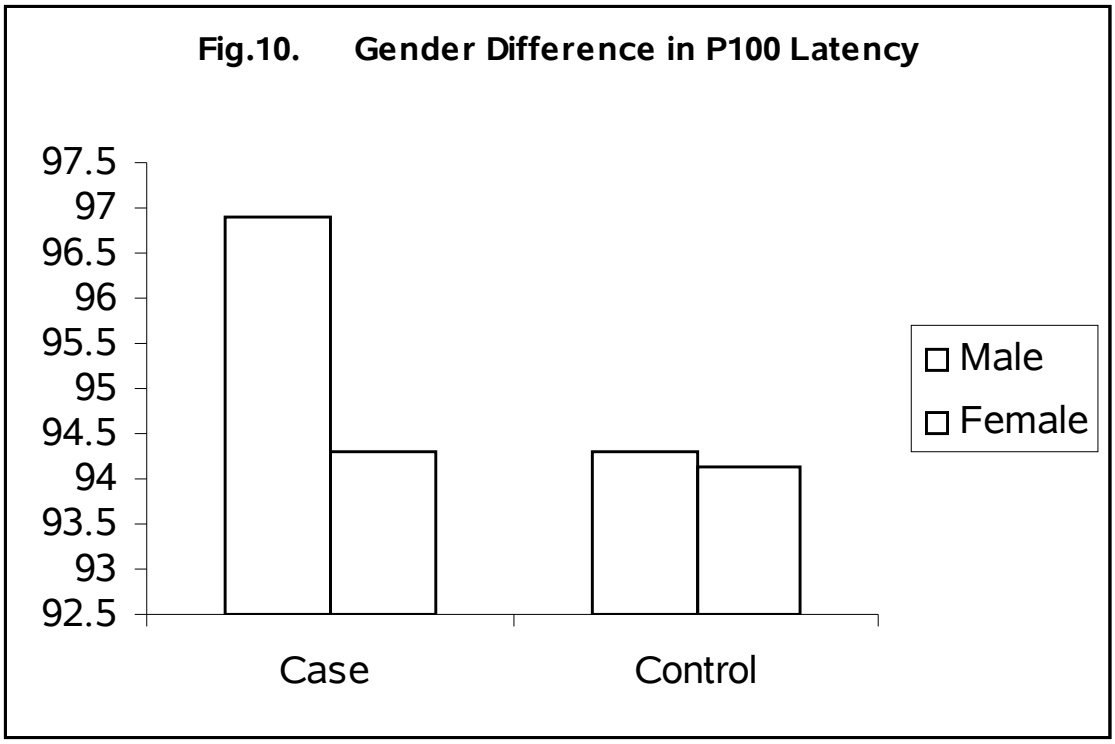
INTER PEAK LATENCY			
	Mean	**SD**	**P –Value**
Cases	4.29	4.22	0.041
Control	2.05	2.87	



Inter Peak Latency shows significant difference ($P < 0.05$) between cases and control

10) **GENDER DIFFERENCE IN P100 LATENCY.**

Sex	Diabetes		Control		P value
	Mean	SD	Mean	SD	
Male	96.9	5.16	94.20	3.52	0.165
Female	94.3	5.89	94.14	3.85	0.92



DISCUSSION

Evoked potentials are simple, sensitive and objective technique for evaluating impulse conduction along the central nervous system pathway.

P 100 Latency:

Evoked potential abnormalities have been described in Diabetes Mellitus but the proportion of patients with increased latencies of visual P-100 is variable ranging, 9% to 77% [5,6,11,51] .Such high variability could be explained by several factors, such as criteria of ascertainment inclusions or diagnosis, the presence of retinopathy or peripheral neuropathy and the difference in stimulus recording conditions.

In our study the mean P 100 Latency of cases was (95.48 + 5.65) greater than the control (94.21 +3.61) but the difference was not statistically significant. Similar was the observation of Thomas SV et al[52], Oziegler[27], Milligen et al[49]. Only 11.8% of the cases 4/84 had P 100 Latency prolongation in the abnormal range i.e. more than 2.5SD above the mean P100 control (94.21 + 9.02 = 103.23).

However most of the studies have demonstrated significant increment in P100 Latency in the diabetic compared with non diabetic controls. Algan et al[4] found prolongation of P-100 Latency in 50 diabetic patients of which 6 of them had diabetic retinopathy. Mariani et al[22] found prolongation of P 100 in 35 diabetic patients but they did not have retinopathy. Ponte F et al[23] reported prolongation of VEP latency in 50 asymptomatic IDDM without retinopathy. Puvanendrian K et al[6], Cirillo D et al[24] & Anastasi M et al[50] also reported VEP abnormalities in diabetic patients. Although collier et al found VEP abnormalities in diabetic patients with retinopathy they did not find any abnormality in other patients without retinopathy. Yaltkaya et al[26] found prolongation of N 140 latency and N 70, N140 inter peak latencies as well as P 100 latencies and they explained it with existence of retrochiasmal involvement. Bortek L et al[70] found 77% VEP abnormalities and did not find any correlation with retinopathy. Sima et al have recently shown that diabetic BB rat develop a central sensory neuropathy in which there are prolonged latencies of VEP related to axonopathy of optic nerve fibers.

P 100 AMPLITUDE:

In our study P 100 amplitude mean in diabetic (4.09 + 2.25) was lower than the control (4.43 + 2.19) but the difference was not statistically significant. Significant low mean P amplitude has been observed by Lip P Yang Y et al[36]. & Panch et al[39].

P 100 AMPLITUDE and LATENCY in relationship to Peripheral Neuropathy.

In our study 47% of patients (16/34) had peripheral neuropathy based on the presence of median or peroneal nerve motor or sensory. Velocity or latency below the lower limit of normal. There was no correlation between prolongation of P 100 latency and presence of peripheral neuropathy. The mean P 100 in patients with peripheral neuropathy was smaller (93.43 ± 5.82) than in patients without evidence of neuropathy (97.31 ± 4.96) Comi G et al had observed a negative correlation at 30' check size between P 100 latency and motor sensory nerve conduction velocity in all examined nerves. Khardori et al studied 34 IDDM patients and did not find any relationship with VEP abnormalities and presence of peripheral neuropathy. Yaltkaya et al[26] also reported no correlation in P100

latency in 25 diabetics he studied with sural nerve conduction abnormalities. The same was also stated by Algan M et al[4], Uberrall MA et al[32], Pozzessere et al[29] identified significant abnormalities both in peripheral and central nerve conduction in IDDM and NIDDM subjects, but no correlation between these phenomena were performed. In contrast to the above studies other authors Puvanendran et al, Mariani E et al[22]. LiP yangy[36] and Akinci et al[48] have found positive correlation between abnormalities in peripheral nerve conduction and changes in P 100 Latency.

In our study mean P 100 amplitude was significantly ($P < 0.01$) reduced in those with peripheral neuropathy (3.03 ± 1.26) than those without (5.03 ± 2.54) this has not been observed in other studies.

DURATION OF DIABETES

Our study did not show any linear correlation between P 100 latency and amplitude and duration of diabetes. (Table –8) .Of the 10 studies that have examined this association significant positive correlation with duration of diabetes was described only in 3 reports. Prolonged P 100 latency have been found within 4 years of diagnosis in patients with IDDM and NIDDM and in different study within 6

years of onset of IDDM. Alteration of P 100 latencies have been demonstrated within a few weeks of diagnosis of IDDM.

Over all the evidence for an association between duration of diabetes and VEP abnormalities is limited in keeping with the presence of P 100 abnormalities in people with recently diagnosed diabetes. Few have reported no correlation with duration of diabetes as was our observation, Algan et al[4], G. Pozzessere et al[29], Uberall[32], Khardori et al[41], Collier et al[45].

TYPE OF DIABETES

In our study IDDM patients constituted only 9% (3/34) of the study group and rest where NIDDM. Among the 3 IDDM one had prolonged P 100 latency (33%). Among the 31 NIDDM 3 had prolonged latency (9.7%). Being a small study group it is difficult to give correct interpretation for this finding. More et al reported that 39% of their NIDDM group had P 100 Latencies more than 2 SD greater than non diabetic control. Pozzessere et al[28] found P 100 Latency changed in a similar proportion of each group. (21 % of NIDDM & 18% of IDDM). Algan et al[4] also found no significant

difference between subjects with IDDM and NIDDN, demonstrating increased latency in approximately 28% of each group.

GLYCEMIC CONTROL

In our study long term glycemic control by glycosylated hemoglobin was not estimated. In some study evoke potential have been correlated with hyperglycemia and in others, the evidence for an association with glycemic control in less compelling than for duration of diabetes with only one of the ten studies demonstrating, Marian et al, significant correlation. Ziegler et al[27] had VEP measurements in poorly controlled diabetics before and after three days of insulin to achieve normoglycemia and demonstrated significant shortening in P 100 latency although these still remained significantly prolonged in comparison with non diabetic value. In view of the rapid improvement author proposed that the changes in P 100 latency resulted from metabolic effects rather than structural changes as suggested by many others.

AGE OF PATIENTS

Our study was confined to patients more than 18 years. But there are several studies that have assessed VEP P 100 in children and adolescence with IDDM, the majority of whom had no overt retinopathic changes. Two studies reported prolonged latency 30% and 27% both in Pre and post pubertal diabetic children which are comparable in magnitude to the results observed in adult with IDDM. However in a different study, Lovasit et al[59] observed no changes in P 100 latency in a chort of young patients with IDDM. In our study P 100 latency increased with age but correlation was better in controls (34%) compared to cases.

INTER PEAK LATENCY

The P 100 inter ocular latency difference was more in diabetic compared to control and was statistically significant (table-9). Pan CH et al[39] had analysed this and did not find statistically significant different between IDDM and age matched control group.

SEX OF PATIENT

In our study P latency was longer in adult male compared to female in both diabetic and control (table –10) but statistically no significant difference. The same was observed in normal adult by Guthkel CH et al[64].

SUMMARY

1) No significant prolongation of P 100 latency in diabetic patients compared to control. 11.8% of cases (4/34) had P 100 latency prolongation > 2.5SD (94.21 + 9.02) above the mean of control. (1 SD = 3.61)

2) P 100 Latency did not show any correlation with the presence of peripheral neuropathy.

3) P 100 amplitude was significantly decreased in those with peripheral neuropathy compared to those without neuropathy.

4) There was no correlation with duration diabetes.

5) Inter Peak Latency difference was more in diabetics compared to controls and was statistically significant.

CONCLUSION

VEP abnormalities are present in diabetic patients in the form of prolongation of P100 latency and decreased P100 amplitude but are not statistically significant.

P 100 amplitude is decreased in patients with peripheral neuropathy.

S.No	Name	Age	Sex	Case/ Control	Duration of Diabetes	Neuropathy	P LAT R	P LAT L	MEAN PLAT	P AMP R	P AMP L	MEAN P AMP	IPL
1	Veshalakshi	63	F	1	1	1	101.30	91.30	96.30	3.64	4.12	3.88	10.00
2	Sudha	37	F	1	1	1	99.40	99.40	99.40	6.39	6.74	6.57	0.00
3	Sundari	25	F	1	1	1	91.30	96.30	93.80	4.22	4.66	4.44	5.00
4	Senthamari	52	M	1	1	1	90.60	90.60	90.60	8.69	9.98	9.34	0.00
5	Karthikeyan	22	M	1	1	1	102.50	107.50	105.00	3.20	3.40	3.30	5.00
6	Lalitha	40	F	1	1	1	92.50	91.90	92.20	6.89	7.39	7.14	0.60
7	Muthu Lakshmi	42	F	1	1	1	103.80	90.40	97.10	3.62	3.19	3.41	13.40
8	Kandan	50	M	1	1	1	98.80	99.40	99.10	3.80	4.10	3.95	0.60
9	Kali Muthu	55	M	1	1	1	90.63	93.75	92.19	9.12	9.40	9.26	3.12
10	Devaki	29	F	1	1	1	90.60	93.80	92.20	9.10	10.60	9.85	3.20
11	Vasanth	23	M	1	2	1	95.60	95.00	95.30	3.19	6.04	4.62	0.60
12	Rajendran	47	M	1	2	1	105.00	98.10	101.55	1.00	2.10	1.55	6.90
13	Jayachandran	60	M	1	2	1	101.90	101.30	101.60	1.60	2.46	2.03	0.60
14	Pachiamma	50	F	1	2	1	110.00	106.90	108.45	1.75	2.10	1.93	3.10
15	Indirani	45	F	1	2	1	96.90	90.00	93.45	6.13	6.56	6.35	6.90
16	Naseema	25	F	1	2	1	98.80	99.40	99.10	3.80	4.16	3.98	0.60
17	Adhi Lakhsmi	45	F	1	3	1	91.90	94.40	93.15	5.10	3.75	4.43	2.50
18	Naga Booshan	50	M	1	3	1	103.40	98.80	101.10	4.16	4.80	4.48	4.60
19	Gopala Krishnan	60	M	1	1	2	86.30	95.00	90.65	3.98	4.26	4.12	8.70
20	Gandhimathi	39	F	1	1	2	86.30	88.10	87.20	2.92	3.21	3.07	1.80
21	Manjula	42	F	1	1	2	103.80	90.00	96.90	3.60	1.92	2.76	13.80
22	Saraswathi	58	F	1	2	2	90.60	96.90	93.75	1.06	1.47	1.27	6.30
23	Govindhan	60	M	1	2	2	108.80	98.80	103.80	2.20	2.16	2.18	10.00
24	Prabhu	52	M	1	2	2	101.30	91.30	96.30	3.64	4.12	3.88	10.00
25	Sundara Moorthy	53	M	1	3	2	92.50	93.10	92.80	2.58	3.89	3.24	0.60
26	Saraswathi	58	F	1	3	2	84.40	85.60	85.00	5.08	6.81	5.95	1.20
27	Rani	53	F	1	3	2	88.10	88.10	88.10	3.40	2.40	2.90	0.00
28	Nagapooja	59	F	1	3	2	88.10	88.50	88.30	3.40	3.80	3.60	0.40
29	Renganayagi	60	F	1	4	2	105.00	103.80	104.40	4.80	3.80	4.30	1.20
30	Selvarajan	52	M	1	4	2	85.00	97.50	81.25	1.00	1.40	1.20	12.00
31	Israel	59	M	1	4	2	88.80	95.10	91.95	1.44	3.85	2.65	6.30
32	Ramachandran	60	M	1	4	2	103.10	98.80	100.95	1.95	1.38	1.67	4.30
33	Jagadeeswari	60	F	1	4	2	88.00	89.50	88.75	2.40	1.21	1.81	1.50
34	Anjali	50	F	1	4	2	94.40	95.00	94.70	3.60	4.10	3.85	0.60
35	Anaki	45	F	2	0	1	89.40	88.80	89.10	3.81	2.24	3.30	0.60
36	Meenakshi	50	F	2	0	1	82.50	94.40	88.45	2.57	2.29	2.43	11.90

37	Poongodi	45	F	2	0	1	96.90	97.50	97.20	8.49	7.39	7.94	0.60
38	Chitra	45	F	2	0	1	96.90	97.50	97.20	8.41	7.39	7.90	0.60
39	Malli	40	F	2	0	1	100.00	99.40	99.70	4.14	3.07	3.60	0.60
40	Chinnian	42	M	2	0	1	93.80	96.30	95.05	1.38	1.47	1.42	2.50
41	Lakshmanan	36	M	2	0	1	94.40	91.30	92.85	1.91	1.87	1.89	3.10
42	Gopalan	58	M	2	0	1	95.60	95.60	95.60	7.05	6.24	6.65	0.00
43	Amkiah	44	M	2	0	1	99.40	99.40	99.40	3.02	2.65	2.84	0.00
44	Vijaya	30	F	2	0	1	91.90	92.50	92.20	5.85	6.91	6.38	0.60
45	Maruthiayi	55	F	2	0	1	89.40	91.90	90.65	2.97	2.50	2.74	2.50
46	Kannamal	47	F	2	0	1	99.40	94.40	96.90	4.95	7.03	5.98	5.00
47	Rajendran	39	M	2	0	1	100.00	100.00	100.00	5.27	5.83	5.55	0.00
48	Priya	30	F	2	0	1	91.30	91.90	91.60	3.54	3.13	3.34	0.60
49	Raman	30	M	2	0	1	90.60	89.40	90.00	6.38	6.40	6.39	1.20
50	Ramadoss	36	M	2	0	1	94.40	90.60	92.50	4.80	5.00	4.90	3.80
51	Mohan	25	M	2	0	1	91.30	91.30	91.30	1.91	1.87	1.85	0.00
52	Ramesh	50	M	2	0	1	91.90	92.00	91.95	5.85	6.91	6.38	0.10
53	Gheetha	50	F	2	0	1	94.40	96.30	95.35	1.38	1.47	1.42	1.90
54	Valliammal	58	F	2	0	1	99.90	94.40	97.15	4.95	7.03	5.99	5.50

Case → 1, Control → 2.
Duration of Diabetes
0 → No diabetes, < 5 → 1, 5 – 10 → 2, 10 – 15 → 3, 15 – 20 → 4
No Neuropathy (NN) → 1
Neuropathy Present (PN) → 2
P LAT R → P 100 LATENCY RIGHT
P LAT L → P 100 LATENCY LEFT
P AMP L → P 100 AMPLITUDE LEFT
P AMP R → P 100 AMPLITUTDE RIGHT
IPL → INTER PEAK P100 LATENCY

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