

Title

Clinical and Neurophysiological characteristics of a Chronic Sensory Polyneuropathy Associated to Helicobacter Pylori Seropositivity.

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Running title

Polyneuropathy and Helicobacter pylori

Abstract.

BACKGROUND. Interest in Helicobacter pylori (Hp) pathology in organs unrelated to the gastrointestinal system motivated investigating its role in Peripheral Nerve Disease (PND). We wondered if data like gender, race, age, plus Vertigo and New Daily Persistent Headaches (NDPH), could validate etiological association between Hp and Neuropathy (exhibiting paresthesia, decreased reflexes, glove/stocking levels, and abnormal Neuroconduction).

MATERIAL & METHODS. Between 2003 and 2007, from over 1300 new patients, Polyneuropathy was diagnosed in 229. Main sample of 69 cases, with elevated Hp antibody titre (+HpAT) had their clinical and Neurophysiological data compared to remaining 160 PND cases with metabolic, vitamin, idiopathic, immune, and toxic aetiology, without +HpAT (control sample).

RESULTS. In the main sample there were 50(72%) women, 19(28%) men. Forty-nine (71%) were Caucasian, 20(29%) were Hispanic or Black. Age mean 55 yr, duration 15 months; 24(35%) had vertigo, 22(32%) had NDPH and 30(43%) Mononeuropathy. Main sample Neuroconduction showed preponderant sensory abnormalities suggesting myelin damage. In the control sample there were 78(49%) women, 82(51%) men; 82(51%) were Caucasian, 78(49%) Hispanic or Black. Age mean 48 yr, 14 month duration, 31(19%) had Vertigo, 19(11%) NDPH and 45(28%) Mononeuropathy. Their nerve conduction had fewer sensory abnormalities. Other significant differences between samples were determined for gender, race, vertigo, NDPH, Mononeuropathy, none for age or duration.

CONCLUSION. Despite inconsistent reports in the literature of (+HpAT) in healthy subjects, we have characterized Hp with its CagA and VacA cytotoxins, to be associated to a chronic sensory Polyneuropathy. This has an unusual predominance in women and Caucasians, coinciding with vertigo, NDPH, or Mononeuropathy.

Key words. Caucasian women, Vertigo, Headaches, Mononeuropathy.

Abstracto.

FONDO. El interés por las patologías del Helicobacter Pylori (Hp) no relacionadas con el sistema gastrointestinal, nos motivó a investigar su papel en las Enfermedades del Sistema Nervioso Periférico (ESNP). Nos preguntábamos si factores tales como el género, la edad, la raza, o la aparición de Vértigos y Cefaleas Nuevas Diarias Persistentes (CNDP) pudiesen validar la asociación etiológica entre el Hp y una neuropatía con su consabida clínica de parestesias, reflejos disminuidos, niveles de guantes/medias y neuroconduccion anormal.

MATERIAL Y METODOS. Entre el 2003 y comienzo del 2007, de entre 1300 pacientes nuevos, se diagnosticó Polineuropatia en 229. La muestra principal de 69, que tenían seropositividad o títulos elevados de anticuerpos para el Hp (+HpAT), se comparó con una muestra control de los restantes 160 casos con polineuropatias metabólicas, avitaminosiscas, inmunes, toxicas o idiopáticas, pero con seronegatividad al Hp.

RESULTADOS. La muestra principal consistió en 50(72%) mujeres y 19(28%) varones, siendo 49(71%) caucásicos y 20(29%) mixtos o negros. Edad mediana de 55 años; 15 meses de duración. Tenían vértigos 24(35%), CNDP 22(32), y mononeuropatia 30(43%). También se encontró una neuroconduccion anormal preponderantemente sensorial, sugerente de daño mielínico. En la muestra control habían 78(49%) mujeres y 82(51%) hombres, siendo 82(51%) caucásicos y 78(49%) mixtos o negros; edad mediana de 48 años, duración de 14 meses. De los controles 31(19%) tuvieron vértigos, 19(11%) CNDP y mononeuropatia 45(28%). La neuroconduccion sensorial resultó menos afectada. Las diferencias fueron significativas para el género, raza, vértigos, CNDP y mononeuropatia pero no para la edad o la duración.

CONCLUSIÓN. A pesar de la inconsistencia de reportes en la literatura de la seropositividad del Hp en sujetos sanos, le hemos caracterizado, junto con sus citotoxinas CagA y VacA, como asociado a una Polineuropatia Crónica Sensorial. Esta tiene inusual predominancia en mujeres y en la raza caucásica, coincidiendo tal vez con vértigos, CNDP, o mononeuropatia.

Palabras clave. Mujeres caucásicas, vértigo, cefaleas, mononeuropatia

Introduction.

There has been an increase of interest in Helicobacter pylori's (Hp) pathology in organs unrelated to the gastrointestinal system such as endothelial or vasculitic disorders in the Henoch Schonlein Purpura (1) and Behcet's disease (2,3). In Peripheral Nervous System, there is a report of Lewis Autoimmune mechanisms in B12 deficiency (4), in Cerebrospinal fluid of the Miller-Fischer syndrome (5), and of Acute Inflammatory Demyelinating Polyradiculopathy (AIDP), or Acute Motor Axonal Neuropathy (AMAN) forms of the Guillain- Barré Syndrome (GBS) (6, 7).

We joined the expansion of Hp etiological trends by reporting in 1998 Hp, to be another of extra cranial infections triggering cases of New Daily Persistent Headaches (8, 9) and besides, one of us (CJSW) had described a case of Acute Disseminated Encephalomyelitis, with Hp diagnosed by gastric biopsy, which responded rapidly to antibiotic and steroid therapy (10). We have also studied and treated successfully 9 unreported cases of Benign Paroxysmal Vertigo related to Hp (Personal Communication).

Furthermore, before 2003, we had observed that (+HpAT), was found sometimes as the sole laboratory sign, or etiological agent, in many of our Polyneuropathy cases. Since then, HpAT was added to our research battery of metabolic, vitamin, immune, toxic, endocrine, and infectious tests. Thus a clinical and neurophysiological prospective project was started with all cases of peripheral nerve involvement coinciding with +HpAT.

The original 28 cases of such relationship were presented at Sydney's 2005 WCN as a poster, and published as an abstract in the Journal of the Neurological Sciences (11).

By the end of 2006, we had extended our series to 69 cases which comprise this paper's main study sample. We have taken advantage of the 160 other Polyneuropathy cases with different aetiologies, and obviously negative Hp antibody titre, in order to compare epidemiological characteristics like gender, race, age, and other symptomatic and semiological patterns to be able to validate our theory.

Material and Method.

During the 2003- 2007 period, authors examined over 1300 new neurological patients at the Universidad Central del Este's Medical Centre and at the Rehabilitation Centre of Santo Domingo. The latter is a semi-private organization, partially government-patronized, giving

physical therapy, diagnostic (EEG, EMG, Laboratory) and other health services to the lower or middle classes. The Universidad Central del Este's Medical Centre is a teaching hospital, adjacent to our private consulting rooms, giving admission and diagnostic services (Neuroimaging, Cardiac Catheterism, etc) to insured, and possibly higher classed patients. On their first consultation, 229 patients had a tentative diagnosis of Polyneuropathy, based on neurological symptoms like paresthesia, weakness or lack of balance, and confirmed by distal limb sensory losses and diminished O.T. reflexes.

Patient's gender, age and race had been recorded with their physical and gastric complaints and duration, plus "soft" symptoms like vertigo or headaches. We noted in their clinical examination: pupillary reaction, osteo-tendinous (OT) and pyramidal reflexes, limb sensory levels to pain, temperature and vibration, Romberg/Barany signs, and the presence of Mononeuritis. Every patient had routine laboratory tests like Glicemia, TSH, FTA-ABS, HTLV -I/II, HIV, IgE, IgA, IgG, IgM, Vitamin B12, Folic Acid, Uric Acid, FRA, PCR, and ESR. Budget and epidemiological reasons justified testing serum Hp IgG antibodies rather than breath Urease, or direct gastric biopsy staining. Well known clinical laboratories such as "Referencia", "Amadita", and the Rehabilitation Centre's own, provided the following 3 corresponding methods. VIDAS H. pylori IgG, a qualitative automatized enzyme linked fluorescent assay ELFA, and Wampole Laboratories qualitative immunoabsorbent assay ELISA, both with positive Optic Density readings above 0.9. Lambda's Hp rapid chromatographic membrane test reads white as negative, positive when turning Burgundy colour. In the Dominican Republic CagA or VacA direct determinations are unavailable.

From those 229 Cases, 69 patients showed a positive or elevated Hp antibody titre (+HpAT) and were included in the "main sample". After informed consent this entire sample was subjected to a Nerve Conduction (NC) study which aimed at examining at least four nerves. In the right lower limb Common Peroneal and Sural for pure motor and sensory determinations. In the right upper limb Median and Ulnar nerves for both. DeLisa's current guidelines were used for Compound Motor Action Potential (CMAP) distal onset, sensory peak latencies (SPL), as well as motor velocity in Common Peroneal nerve (12). For Sural nerve amplitude we followed Prof. Kimura's guideline (13). Most NC studies were performed with a Cadwell-Sierra II at our laboratory, a few with the Rehabilitation Centre's Oxford-Medelec. All patients in the main sample underwent treatment with

Amoxicillin, Zythromycin or Claritromycin, plus Rabeprazole (Pariet) as PPI.

Methylcobalamin (Methycobal) was indicated for low Vit B-12 levels; oral Prednisone for increased IgE (14).

The remaining 160 Polyneuropathies, whose Hp titre was below 0.75 or 0.9 units, and with dissimilar aetiology (**Table 1**), were utilized as a “control sample” in order to compare epidemiological data like, gender, age, race and complaint duration. We also compared presence of vertigo, headaches or Mononeuritic signs, on account of having previously noticed their unusual clinical prevalence in cases of Polyneuritis with +HpAT.

Well over half of the “control” sample completed a neurophysiological study similar to the main group. Matching these two groups of uneven proportions, may require caution but could be clarified by comparing present results, with our reported experience in the nerve conduction of another sensory Polyneuropathy of immune origin (15).

Miss Julia Hasbun, calculated significance of differences in our original poster, by applying Yates corrected chi square (χ^2), and Odds Ratio (OR) for confidence limits. We are also delighted with the help from CENISMI director, Dr. E. Perez-Then, in our research presentation

Results.

In the Hp positive” main sample”, average age in years was 55.97 with SD of 16.85; symptom duration was 15 months: 19(27.6%) were male, versus 50(72.4%) female. Forty-nine (71%) patients were Caucasian, 20(29%) were not (15 Hispanic, 5 Black). Thirty seven patients belonged to the upper class, 26 to the middle, and 6 to the lower class (27 professionals, 17 workers, 3 students, 22 housewives). Mean antibody titre was 2.22, ranging from 1.3 to 7.5 units (0.75 to 0.9 is considered the normal value). Fifteen had history of Gastric Ulcer, one of Hepatitis. Their clinical neurological symptoms were distributed as follows: 30 had paresthesia, 18 unsteadiness, and 13 limb weakness. There were 24(34.7%) patients with vertigo, and 22(31.9%) with New Daily Persistent Headaches.

As for clinical signs; 16 had Myosis, 1 Midriasis. Fifty-one had diminished reflexes (10 were normal, only 8 brisk). All 69 cases had glove and stocking sensory losses for pain and temperature; ten had vibratory loss. Thirty patients exhibited Mononeuritis (43.4%); mainly

Meralgia Paresthetica. On Romberg or Barany testing, 23 gave a positive sign. Laboratory studies revealed 16 Gammopathies (14 IgE, 1 IgM, and 1 IgA), and 10 had low Vit B12 levels.

Neurophysiological NC testing was meaningful in all +HpAT cases; at least 1 nerve was affected in each patient. The following are the findings from the 389 nerves examined.

From the 197 Peroneal, Median and Ulnar motor nerves, 85(43.1%) had abnormal distal motor latencies (or delays) to CMAP onset or abnormal velocity. For Common Peroneal average of all distal latencies was 4.24 ms, with 10 abnormal delays, plus 3 absent responses; there were 44 abnormal conduction velocities averaging 45.89 mts/s. (9 cases had simultaneous prolonged delay and abnormal CV). Median Motor Nerve conduction had 27 abnormal delays to CMAP onset, with an average of 4.04 ms and no absent response. Ulnar Motor Nerve delays averaged of 3.01 ms to CMAP onset, 9 of them abnormal, with one absent response.

In contrast, out of 192 sensory nerves examined (Sural, Median and Ulnar), 140(73 %) showed absent, or prolonged sensory peak latencies (SPL). In Sural Nerve, sensory delays averaged 4.63 ms, but 36 were abnormal and 10 had absent responses. In Median Nerve sensory studies, peak delays averaged 3.99 ms; while 48 were abnormal, only 2 had absent responses. Ulnar Sensory Nerve peak delays showed an average of 3.94 ms, with 38 of them abnormal, and 6 absent responses.

Amplitudes were diminished in 29 Common Peroneal nerves, in 53 Median motor and 41 Ulnar motor studies. These amplitudes were equally diminished in 41 Sural, 7 Median, and 19 Ulnar nerves. Motor-Sensory abnormality ratio was 85/197 to 140/192. Guidelines, plus affected individual nerves are shown in **Table 2**.

In the limited 160 case “control” sample, 82(51%) were male, 78(49%) female, with an average age in yeas of 48.45, with SD of 18.82, and a duration of 14.4 months. Eighty two (51%) were Caucasian, 78(49%) were not (51 were Hispanic, and 26 Black). Seventy seven patients belonged to the upper class, 54 to the middle, and 29 to the lower class (76 professionals, 29 workers, 25 students, 30 housewives). Out of the 160 case sample, only 31 (19.4%) had vertigo, 19(11.9%) had New Daily Persistent Headaches and 45(28.12%) Mononeuritis,

The following are the Neurophysiological findings from 405 nerves examined in the “control” group. From 203 Peroneal, Median and Ulnar motor nerves, 96(47%) had abnormal distal motor latencies to CMAP onset, or slow velocity. Common Peroneal nerve average of distal latencies was 4.92 ms, with 8 abnormal delays, 6 absent responses; plus 39 abnormal conduction velocities averaging 46.43 m/s (4 cases had simultaneous prolonged delays and abnormal CV). Median Motor Nerve conduction showed 36 abnormal delays to CMAP onset, with an average of 4.63 ms, and no absent response. Ulnar Motor Nerve had average delays of 3.17 ms to CMAP onset, 11 of them abnormal, with no absent response. Out of 202 sensory nerves examined (Sural, Median and Ulnar), 119(58.91%) showed absent or prolonged sensory peak latencies (SPL). In Sural Nerve, sensory delays averaged 5.65 ms, 37 were abnormal and 9 had absent responses. In Median Nerve sensory studies peak delays averaged 4.22 ms, while 51 were abnormal, with no absent responses. Ulnar Sensory nerve peak delays showed an average of 3.62 ms, with 22 of them abnormal, and no absent response. Amplitude was diminished in 39 C. Peroneal, 66 Median and 61 Ulnar motor nerves; as well as in 32 Sural, 15 Median and 25 Ulnar sensory nerves. Axonal pathology seemed to be catching up to myelin damage in this control group. Statistical analysis detected highly significant differences of *p*, and *OR*, between the two groups for gender, race, vertigo, NDPH, and Mononeuritis. In nerve conduction there is a significant sensory nerve involvement in the “main” sample, with no difference for motor nerve conduction between both groups. Although those with +HpAT are apparently older than the control sample (55 vs. 48 years), such a disparity is not significant; neither is duration of symptoms (**Table 3**).

Conclusion

Results for the main sample suggest that Helicobacter Pylori infection could in fact be associated to a Chronic Polyneuropathy. This clinical entity would be characterized by an unusual preference for women, occurring late in life, most likely in Caucasians, with mild clinical symptoms such as paresthesia, unsteadiness, rather than weakness; accompanied by other non PND, but disturbing symptoms like vertigo and NDPH. Neurological examination would reveal glove/stocking sensory losses, diminished reflexes, plus the presence of Mononeuropathy. Neuroconduction tests could confirm diagnosis and suggest

myelin damage by showing abnormal sensory to peak or motor to CMAP onset delays, as well as abnormal NC in Common Peroneal nerve.

Discussion

We could be proposing a faulty hypothesis regarding Hp aetiology for neuropathy, if Hp antibody increase of in the “main” sample would simply represent a proportion usually present in the healthy population. We hope to reject this objection if epidemiological data, showing significant differences between “main” and “control” samples, were accepted.

A) Gender. Our study reveals that Polyneuropathy associated to Hp shows an unusual tendency to occur in women, perhaps late in life, whereas in the literature the majority of papers seem to point a predominance of Hp infection in the male. This concept is sustained by Sipponen and Correa who reported in Finland a delayed increase of gastric Cancer and Hp in females, reversing the “usual male predominance of earlier stages of life” (16). As this reversal occurs after 60, increase in women may be possibly related to a decline in oestrogen metabolism.

B) Race. We feel that the main opposition to our theory comes from gastro-enterology (GE) specialists who believe that a large proportion of Dominicans should have abnormal Hp antibody levels. This is based on local GE hospital sampling (17), and from extrapolating world literature. References range from prevalence in 16.5% of young Japanese volunteers (18), to 43% in Irish blood donors (19), attaining 82% in Tunisia (20).

If we reviewed the literature looking for Hp Genotypes in geographic locations, we may begin to understand racial predominance. Saribasak and colleagues (21) analyze the genomic structure of strains circulating among different geographic locations. In Turkey, their predominant strains are *cagA* type 2a, *vacA* s1a/m1a or *vacA* m2a, associated to a low incidence of gastric cancer but not to Peptic Ulcer Disease (PUD). In contrast, strains *vacA* s1c, m1c, *cagA* type 2a, *cagA* type 1a, *vacA* s1c/m1b and m2b genotypes predominate in East and South Asia, where Gastric cancer is so frequent. We could only speculate that Caucasians with PND from our main sample, together with our low incidence of gastric cancer, could have similar strains to those reported in Turkey. Although the Dominican Helicobacter Society is aware that direct gastric determination of Hp VacA/CagA in DR is not presently available, it is planning for an advanced laboratory. Having promised us access to their studies, we hope to find our national characteristic CagA type.

Race has been rarely documented directly in Hp infection, except for the comparison of poor versus excessive metabolism (efficacy) of PPI and genetic Polymorphism of CYP2C19 in the oriental races. Proinflammatory Cytokines (IL 1b) and TNF, responding to Hp infection, show a variation in eradication rates of Hp to triple therapy (22). Could it be that enzyme CYP2C19, related to excessive or poor metabolism of PPI, varies in different Ethnic groups (23)? A report by Kidd and others points to some defective or null alleles of CYP2C19, only present in African Americans and not in Caucasians (24). Could this enzyme function be inversely related to damage in peripheral nerve?

C) Neurophysiology. Evidence of damage to peripheral nerve appears emphasized for sensory nerves with increases in the average of SPL, and a decrease in the NCV of Common Peroneal, suggesting myelin damage. This is similar to results we reported in Polyneuritis associated to E Gammopathy (14, 15), where Sural SPL occurred at 4.5 ms, Median at 3.9 ms and Ulnar also at 3.9 ms. A mirror image of our present +HpAT cases. Neuropathology. Helicobacter P is responsible in the Gastrointestinal system for Gastric Ulcer, mucosal atrophy & cancer risk (25) by producing vacA, which together with other Cytokines like IL12, IL10, plus cytotoxin, and provided gastric pH is <5, induce vacuolation of epithelial mucosal cells and inhibits its re-epithelialization. In the presence of its protein s1-m1, vacA allows vacuolation of He-La and Vero cells, plus penetration of cytotoxin to the hydrophobic core of lipid bilayer, forming pores or new membrane channels (26).

Are there other mechanisms provoking systemic or individual damage to peripheral nerve?

1) Hp produces an Angiogenic agent, preventable by Proton Pump Inhibition (PPI) (27), which may be responsible, for the development of Gastric Carcinoma, as well as arterial stiffness in the Japanese younger male population (28). Such Angiogenic agent together with heat shock proteins (29), Gastrin and cyclooxygenase (30), may provoke damaging vascular effects affecting small myelinated and unmyelinated fibres, as expected in our cases.

2) Autoantibody induction against Lewis blood antigens by vacA, evokes increases in anion permeability and depolarization in cell plasma membrane; its 58 kDa fragment inducing K efflux from Liposomes. In the Miller-Fischer cases, vacA added to cells, binds to lipid rafts and involves ion channels in the Node of Ranvier (5). This Lewis antigen autoimmune

mechanism is inferred in a Vit B12 deficient case with Giardia in gastric flora (4) and +HpAT: perhaps one rare common feature of molecular mimicry between Campylobacter Jejuni (Cj) and Hp.

3) Hp vaccine research may be important, by revealing that recombinant rUreA and rUreB induced IL2, plus IL10 secretion from monocyte derived dendritic cells, pulse allogenic CD56 (+) NK cells by TNF alpha/IFN gamma secretion (31). Are oxidative stress, nNOS in Endotoxemia (32), and Hp induced CD4+CD* and T cell migration (33), also responsible for PND?

4) Experiments in recent years have found Hp to produce ICAM-1, sICAM 1, and VICAM (34), even NF-Kappa-B I. These, in turn, provoke systemic inflammation and endothelial dysfunction in gastric ulcer patients, in asymptomatic HP "carriers", and even in healthy male subjects (35, 36). In fact, in Gastro-intestinal affected children there is a reduction of sVCAM-1 after antibiotic Hp eradication; a report that may justify our preventive antibiotic treatment protocol.

5) Clinical and pathological difference between Hp Polyneuropathy and Cj Guillain Barré Syndrome is clear, because Hp causes a chronic demyelinating neuropathy, while Cj is responsible for acute, predominantly axonal, syndromes. Nevertheless, we expect future research will explain PND by exposure to Hp vacA and cagA, as comprehensively and successfully, as GBS resulting from the following protein and carbohydrate mimicry mechanisms in Cj infection (37). First, that Cj triggers Ganglioside induction of anti-Ganglioside antibodies recognizing Ranvier Node epitopes (38). Second, that Cj gene cstII shows polymorphism with antibody reactivities against GM1 GD1a evoking weakness, while GQ1b induces ataxia or ophthalmoplegia (39). Third, that Cj Lipooligosacharides produce anti-GM1 IgG antibodies with flaccid paralysis in rabbits, akin to AMAN in the human (40).

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Table No 1

Table 1							
Aetiologies		n			n	Total	
<u>Metabolic</u>	Diabetes Mellitus	25	Hypothyroid	7	Hyperparathyroid	1	33
<u>Vit deficit</u>	B 12	23	Folic Acid	2	Ferropenic	1	26
<u>Infectious</u>	Syphilis	12	Streptococcal	5	HTLV I - II	4	21
<u>Hereditary</u>	Cha Marie Tooth	14	Roussy Levi	2	Others	5	21
<u>Toxic</u>	Statin, Alcohol	3	Carbamazepin ACD	3	Ciguatera	3	9
<u>Immune Demyel</u>	Gammopathy	13	Post Guillain Barré	3	C. I. D. P.	22	38
						Case Total	160
Abbreviations: ACD anticonvulsant							
CIDP= Chronic Inflammatory Demyelinating Polyneuropathy							
Others=Asthma, Prolactinaemia, Polycystic, L Barré, Hypophysial							

Table No 2

Table 2															
Nerve conduction				Normal				+HpAT				-HpAT			
Nerve	Latency	Distance	Amp	Nerves	Ab D/V	NR	▼am	Nerves	Ab D/V	NR	▼am				
Common Peroneal	5.3 ms	8 cm Ankle	2.5mV	69	10	3	29	67	8	6	39				
Common Peroneal	NCV 49 m/s	Knee Ankle			†44			67	†39						
Median Motor	4 ms	8 cms	5mV	64	27	0	53	69	36	0	66				
Ulnar Motor	3.7 ms	8 cm	3mV	64	9	1	41	67	11	0	61				
total No of nerves				197	*- 9			203	*-4						
Abnormal nerves					85				96						
Percentage					43.14%				47.29%						
Sural	3.75 ms	14 cms	20µV	62	36	10	41	66	37	9	32				
Median Sensory	3.4 ms	14 cm	10µV	64	48	2	7	69	51	0	15				
Ulnar Sensory	3.45 ms	14 cm	15µV	66	38	6	19	67	22	0	25				
total No of nerves				192				202							
Abnormal nerves					140				119						
Percentage					72.91%				58.91%						

Note: example † In Common Peroneal add NR + AbD/V + slow NC = †

* 9, * 4, for subtracting simultaneous delay to CMAP+ diminished NC in C Peroneal from †

Ab D/V is equal to abnormal Delay or Conduction Velocity

NR equals to no response to nerve stimuli ▼am is equal to diminished amplitude

Table No 3

Table 3									
Statistical Significance									
<u>Clinical Features</u>	Main		Control		RR	IC	95-1	P=	Sig
	n	%	n	%					
Caucasian Ethnic	49	78	82	51	1.83	1.17	2.87	0.008	s
Gender (Female Sex)	50	73	78	49	2.08	1.31	3.29	0.001	s
Vertigo	24	34.3	31	19.03	1.69	1.14	2.50.	0.001	s
Headaches	22	31.9	19	11.8	2.15	1.47	3.13	0.0005	s
Mononeuritis	30	43.4	45	28.1	1.58	1.07	2.33	0.034	s
<u>Neuroconduction Features</u>									
Sensory Nerves (S)	192		202						
Abnormal sensory nerves	140	72.91%	119	47%	1.4	1.1	1.79	0.004	s
Motor Nerves (M)	197		203						
Abnormal motor nerves	85	43.14%	96	58%	0.92	0.75	1.12	0.46	ns
Note: p <0.05 is significant, p>0/05 is not significant									