The Prevalence of Dysautonomia in Chronic Inflammatory Demyelinating Polyradiculoneuropathy

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ABSTRACT :

BACKGROUND:

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), an immune-mediated disorder of peripheral nerves and nerve roots. Dysautonomiais has not been studied deeply and many question not answered.

OBJECTIVE:

To estimate the prevalence of dysautonomia in chronic inflammatory demyelinating polyradiculoneuropathy in a group of Iraqi patients .

METHODS:

A cross sectional study of 23 patients fulfilled the diagnostic criteria for definite chronic inflammatory demyelinating polyradiculoneuropathy underwent autonomic function in cross sectional study which has been done in Al-Imamain Al-Kadhmiyain Medical City from December 2008 to November 2010 to detect any abnormalities in sympathetic and parasympathetic autonomic nervous systems tests.

RESULT:

This study includes 23 patients diagnosed with CIDP, 12 patients (52%) were male and 11 patients (48%) were females. Twenty patients had autonomic dysfunction, either clinical or subclinical or both.Eighteen of 20 patients (90%) had abnormal autonomic function tests, 16 of 20 patients (80%) symptomatic, and 14 of 20 Patients (70%) symptomatic with abnormal autonomic function tests. Abnormal autonomic function tests were found in 18 of 23 patients with CIDP (78%). In 8 patients (44%), abnormal results were limited to parasympathetic function test. Five patients (28%) abnormal results were limited to sympathetic function test. Five patients (28%) exhibited dysfunction in both systems.

CONCLUSION:

The findings in this study suggest high frequency of clinical and subclinical dysautonomia and parasympathetic system more likely affected than the sympathetic nervous system in patients with chronic inflammatory demyelinating polyradiculoneuropathy.

KEY WORDS: CIDP**,** dysautonomia

INRODUCTION:

Autonomic function can be impaired in many disorders in which sympathetic, parasympathetic, and enteric arms of the autonomic nervous system are affected. Signs and symptoms of autonomic involvement are related to impairment of cardiovascular, gastrointestinal, urogenital, thermoregulatory, sudomotor, and pupillomotor autonomic functions [(1)] .

Chronic inflammatory demyelinating polyradiculoneuropathy (CIDP), an immune-mediated disorder of peripheral nerves and nerve roots, has a variable clinical presentation and, because of several clinical and laboratory similarities with Guillain–Barre´ syndrome (GBS), has been considered a chronic form of GBS.[(2)]

Prevalence estimates vary at 1.2–7/100,000 population but unlike GBS there are no known predisposing factor.[(3)]

Large-diameter axons are considered to be the major immunological target in CIDP. However, small-diameter sensory fibers may be affected as well.[(4)] Axonal degeneration occurs, to varying degrees in lesions that are attributed primarily to demyelination.[(5)] Motor neuron loss and chromatolysis of neurons in the intermediolateral cell columns have also been reported in CIDP, probably as a result of “bystander” inflammation or axonal degeneration associated with CIDP. [(6,7)] But

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in general_Involvement of somatic nerve fibers in CIDP has been characterized as affecting large myelinated fibers more than small myelinated and unmyelinated fibers. [8]

Dysautonomiais was consider as rare in CIDP patients[9,10] and has not been studied deeply and many question not answered, although there have been isolated reports of minor autonomic abnormalities in CIDP[11,12,13,14,15,16].

The old concept of Disorders of autonomic function are most likely present when small myelinated and unmyelinated nerve fibers are affected or when demyelination with conduction block affects the vagus nerve and the preganglionic sympathetic efferent fibers loss. [17] but later severe dysautonomia with abnormalities in all autonomic function tests (AFTs) has been reported in a chronic axonal subtype of CIDP.[18]

THE AIM OF THE STUDY :

Estimate the prevalence of dysautonomia and the types and the relation to age, gender, course and clinical manifestations in chronic inflammatory demyelinating polyradiculoneuropathy in a group of Iraqi patients

PATIENTS AND METHODS:

This sectional study was designed to evaluate autonomic nervous system in CIDP patients. This study was conducted at Al-Imamain Al-Kadhmiyain Medical City from December 2008 to November 2010. It involved 23 consecutive patients (12 men, 11 women) patients with idiopathic CIDP were studied. Their age ranged from 21 to 64 years and the duration of the disease ranged from 6 months to 4 years. 15 patients had a relapsing– remitting course, whereas 8 followed a progressive course. Patients with relapsing–remitting disease were studied during relapse. They all fulfilled the diagnostic criteria for definite CIDP(19)

Any patient with arrhythmia, ischemic or other heart disease, chronic obstructive airway disease, diabetes Mellitus, amyloidosis, porphyria, Hypothyroidism, alcoholism, or central nervous system disease had been excluded. The patients had not been on immunosuppressive treatment.

Five AFTs were used: for the parasympathetic system, the R–R interval variations to deep breathing (IE Difference) and the response of heart rate to standing (30/15 Ratio) and the Valsalva maneuver (Valsalva-Ratio); for the sympathetic system, blood pressure responses to passive postural change (postural drop-PD test) and sustained handgrip (2) and the results of the AFTs were correlated with various clinical parameters of the disease.

The collected data was organized, tabulated, and statistically analyzed using Statistical Package for Social Sciences (SPSS) version 20. Values were expressed as mean ± SD. The Chi-square test to test the significant association .Significance levels were set at P values < 0.05 in all cases.

RESULTS:

This study includes 23 patients diagnosed with CIDP, 12 patients (52%) were male and 11 patients (48%) were females. The mean age group was 42 ± 21. Twenty patients had autonomic dysfunction, either clinical (symptoms related to autonomic nervous system) or subclinical (abnormal AFTs) or both.

Eighteen of 20 patients (90%) had abnormal AFTs, 16 of 20 patients (80%) had abnormal symptoms, and 14 of 20 Patients (70%) had abnormality of both. In 8 patients (44%), abnormal results were limited to parasympathetic function test. Five patients (28%) abnormal results were limited to sympathetic function test. Five patients (28%) exhibited dysfunction in both systems Figure 2.

Of the patients with dysfunction of parasympathetic test, 69% had abnormality limited to response of HR to standing (HR 30/15), 15% of them limited to Valsalva test, 16% to both. None of the patients exhibit abnormal R–R Interval Variation during Deep Breathing test.

Of the patients with dysfunction of the sympathetic test 90% had abnormal postural drop (PD) test and 10% limited to Handgrip test.

In comparing the results of AFTs in each age, this study show statistically insignificance between AFTs and each age group (p value =0.843 table 1). The p values were for: (HR 30/15) =0.735, For Valasalva test = 0.23, for PD = 0.26 and for Handgrip = 0.92.

In comparing the results of AFTs in gender, we found no significant difference (p value =0.692 table 2)

Sixteen of 23(69.5%) of the patients had clinical symptoms were distributed as the following: erectile dysfunction (8), postural dizziness (11), xerostomia (4) , and disturbance in micturition (6). There was no association between AFTs and clinical symptoms (p value =0.104 table 3), and there is no significant association between AFTs and clinical course (p value =0.782 table 4).

Beside high percentage of HR 30/15 to parasympathetic test also there is a significant association with AFTs (p value = 0.016 table

6).There is no significant association between postural drop and AFTs (p value = 0.065).
No significant difference between clinical symptoms and each age group of patients (p value = o.148). There is no significant association between clinical symptoms and clinical course of patients (p value = 0.679). There is no significant association between clinical symptoms and gender of patients (p value = 0.752).

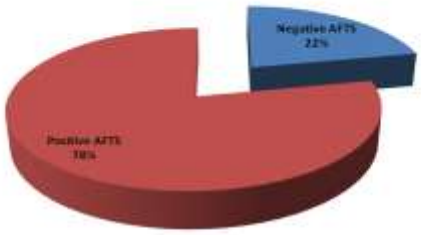

Fig.1
Total Autonomic Function Tests

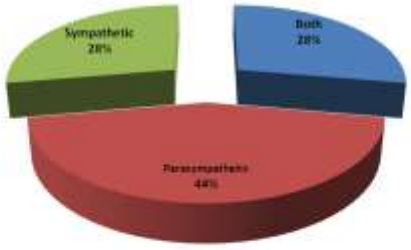

Fig.2
Positive Autonomic Function Tests

Table 1:AFTS and AGE GROUP.

	AGE GROUP					TOTAL
	20-29	30-39	40-49	50-59	60 and more	
AFTs NEG.		1	1	3		5
POST.	2	3	4	6	3	18
Total	2	4	5	9	3	23

P value 0.843

Table 2:AFTS and Gender.

	GENDER		Total
	M	F	
AFTs Neg.	3	2	5
Post.	9	9	18
Total	12	11	23

P value 0.692

Table 3:AFTS and Clinical Symptoms related to autonomic nervous system.

Total	AFTS		Total
	Pos.	Neg.	
Clinical no symptoms	4	3	7
Yes	14	2	16
Total	18	5	23

P value 0.104

Table 4:AFTS and Clinical Course.

	AFTS		Total
	Pos.	Neg.	
Clinical progressive Course	6	2	8.
Relapsing- remitting	12	3	15
Total	18	5	23

P value 0.782

DISCUSSION:

Twenty of 23 patients had autonomic dysfunction, either clinical or subclinical or both. 90% had abnormal AFTs, 80% had abnormal symptoms, and 70% had abnormality of both. In 44%, abnormal results were limited to parasympathetic function test. In 28% abnormal results were limited to sympathetic function test and 28% exhibited dysfunction in both systems.

The patient considers dysautonomia if only one test abnormal and even asymptomatic and abnormality limited to either sympathetic or parasympathetic.

Large series on CIDP report infrequent and mild autonomic complaints. [21] However, severe dysautonomia has been described in anecdotal reports. [22–25] Using quantatitive tests of autonomic function, we found that 78% had autonomic involvement. This is comparable with stamboulis et al. study. (2) Among 18 of our patients with abnormal AFTs, 15 had clinical symptoms indicative of autonomic involvement. Hospitalized patients the assessment was done during the relapse. Studies on dysautonomia in CIDP report variable prevalence of autonomic deficits (21% to 76%) [2,6,16,20] and The low prevelance in other studies may be due to Different inclusion criteria, Different tests, Consider dysautonomia if both para and sympathetic involved, Consider dysautonomia if all tests impaired, The sensitivity of new criteria for diagnosis and Skin test may be less sensitive and need severe and different fibers this may lead probably due to the difference of autonomic tests with low sensitivity, reproducibility, or unknown confounding variables. In previous studies, symptoms of dysautonomiain CIDP patients were considered relatively rare [24].

The prevalence of dysautonomia in CIDP increase since early seventies may be due to increase in the sensitivity of the test used and May be the Involvement of autonomic fibers has not been well characterized and the criteria of diagnosis.

The parasympathetic systems are more likely affected than sympathetic systems which is involved in CIDP as demonstrated by the higher number of patients with abnormalities on testing. Patients with a demyelinating neuropathy such as CIDP are expected to have more prominent vagal dysfunction than sympathetic failure, because the sympathetic nerves, with the exception of the short preganglionic segment, are unmyelinated.[26] Similar findings have been reported in previous studies in CIDP patients'[27].

The 30/15 ratio was most often abnormal, followed by the Valsalva ratio.

An abnormal 30/15 ratio in CIDP patients has also been found relatively more frequently by others.[11,16] which may be more sensitive than other test.

The IE difference test was normal in all our patients. Such intertest differences are not easy to explain because all three tests assess the integrity of parasympathetic cholinergic (cardiovagal) function and are considered equally sensitive, with little to differentiate between them. The physiological substrate of the 30/15 and Valsalva ratios also

involves sympathetic and central mechanisms in contrast to the IE difference, which is considered a test of purely cardiovagal function, [28,29] It is possible, therefore, that predominant involvement of the sympathetic fibers in CIDP patients caused the observed intertest differences. In accord with this hypothesis, the most commonly observed abnormal AFT was the postural drop in BP test.

The handgrip test was normal in our patients. Ingall et al. reported similar findings [11], whereas Lyu et al. found abnormalities in 33% of their patients[16]. These differences may be due to the insensitivity of the test, especially in CIDP patients with reduced muscle strength [2].

Statistical analysis revealed no significant correlation was found between abnormal AFTs and the clinical course of the disease (remitting–relapsing or slowly progressive) or the age group or gender of the patients. No significant was found between clinical symptoms and age or gender of the patients and the clinical course of the disease. Which may be due to in peripheral demyelinating disease no difference in the pathogenesis of the disease in gender, age group and the clinical course.

CONCLUSION:

this study may suggest a high frequency involvement of ANS in patients with chronic inflammatory Polyneurorediculopathy. The parasympathetic systems are more likely affected than sympathetic system which is involved in CIDP as demonstrated by the higher number of patients with abnormalities on testing. Dysautonomia may be limited either to parasympathetic or sympathetic. There was no significant association found between dysautonomia and age, gender, clinical manifestation and the clinical course of the disease.

Author contributions: Dr. Hasan Azeez Al-Hamadani: drafting/revising the manuscript, study design, study supervision. **Dr. *Muhannad kamil hamid***: acquisition of data, analysis or interpretation of data, statistical analysis. Dr. **Basheer Hussein Salman**: critical revision of the manuscript, study concept.

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List of Abbreviation: Chronic inflammatory demyelinating polyradiculoneuropathy = CIDP and Guillain–Barre´ syndrome = GBS.

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