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RESEARCH PAPER

Pattern of Autonomic Involvement in Adult Patients with Guillain Barre Syndrome in a Tertiary Hospital

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Abstract

Background: Guillain Barre Syndrome (GBS) is an acute post infectious immune mediated peripheral neuropathy with a marked variation in pathology, clinical presentation and prognosis. Autonomic dysfunction is one of the important manifestations of GBS which may lead to significant morbidity and mortality.

Objective: The aim of the study is to assess the autonomic involvement, to determine its frequency and pattern of involvement in adult patients with GBS

Methods: An observational, descriptive, cross sectional study was carried out in the Department of Neurology, BSMMU, Dhaka from March, 2015 to September, 2017. Total 43 patients of GBS and 35 apparently healthy controls were recruited as the study population. On the basis of nerve conduction study patients were classified into different groups: acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and acute motor sensory axonal neuropathy (AMSAN) and other variants. Disability status at the time of autonomic testing was measured by Hughes functional grading scale. The following tests of autonomic nervous system were performed in both patients and controls 1) resting heart rate and heart rate on changing posture (30: 15 ratio) 2) supine blood pressure and blood pressure on changing posture 3) heart rate response to valsalva maneuver 4) heart rate response to deep breathing and E: I ratio 5) sphincter disturbance by symptoms questionnaire.

Results: The mean age of patients was 35±12 years (range18 to 65 years) and 58.1% were male. Around 88.4 % of patients showed some sort of autonomic dysfunction. Variation of heart rate by different maneuver like posture change, deep breathing and valsalva maneuver was found commonly. Among them 30:15 ratio was abnormal in majority of the patients (82.4%) followed by abnormal max-min HR/min (58.1%) and abnormal valsalva ratio (37.2%). Other abnormalities were postural hypotension (38.2%), sinus tachycardia (25.6%), hypertension (16.3%), hypotension (2.7%), sinus arrhythmia (4.7%), constipation (30%), urinary retention (7%) and urinary incontinence (4.7%).

Conclusion: In this study different patterns of autonomic dysfunction was found in 88.4% of patients with GBS involving both sympathetic and parasympathetic components. The present study found no significant association between autonomic dysfunction and motor disability scores. Thus autonomic function assessment is essential in every patient with GBS in addition to motor & sensory function.

Key words: Guillain Barre Syndrome (GBS), autonomic dysfunction, AIDP, AMAN, AMSAN, Hughes functional grading.

Introduction:

Guillain Barre Syndrome (GBS) is an acquired immune mediated disorder of the peripheral nervous system which is assumed to result from aberrant immune responses of the peripheral nerves directed against component of the peripheral nerves. The classic forms of GBS affects persons of all ages, but men are about 1.5 times more likely to be affected than women.[1] The mean annual incidence is1.1 to 1.8 per 100000 population.[2]

GBS is clinically characterized by acute flaccid paralysis, areflexia, mild sensory disturbance and albumino- cytological dissociation in the CSF. Besides motor and sensory deficits, it is often associated with a variety of autonomic involvements including cardiovascular, vasomotor, or sudomotor

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dysfunctions. There is sympathetic hyperactivity in the acute phase which can present as hypertension, hyperhidrosis and tachycardia. Parasympathetic failure occurs during recovery.[3] Clinical symptoms of autonomic disturbances are frequently non-characteristic and therefore in order to identify them it is essential to know the methods of a more detailed assessment of autonomic nervous system.[4]

Autonomic dysfunction of various degree has been reported in 65% of patients admitted to the hospital.[5] Most of the clinically significant autonomic dysfunction occurs with in the first 2-4 weeks of the illness, the peak period of paralysis. Its varied and complex manifestations may be related to either increased or decreased sympathetic – parasympathetic activity resulting in orthostatic hypotension, episodic or sustained hypertension, sinus tachycardia, tachyarrhythmia, bradyarrhythmia, urinary retention, gastrointestinal atony, iridoplegia, anhydrosis or episodic diaphoresis. Potentially serious bradyarrhythmias ranging from bradycardia to asystole were found in 7 to 34 % of patients.[6] Excessive vagal activity accounts for sudden episodes of bradycardia, heart block and asystole. Cardiovascular disturbances were found to be a common feature of patients with GBS who were severely paralyzed, requiring assisted ventilation.[7] Severe autonomic dysfunction is an indication for ICU admission.[8] Approximately 3 to5 percent of patient of do not survive the illness even in best equipped Hospitals. In the early stages, death is most often a result of cardiac arrest, sometimes related to dysautonomia, adult respiratory distress syndrome, pneumo- or hemothorax, or some type of accidental machine failure.[9] Acute autonomic dysfunction develops in the majority of patients with GBS and is a significant cause of death in these patients.[10] Autonomic dysfunction in GBS is usually missed at the time of clinical presentation and therefore it is not treated adequately. This can lead to significant mortality in these individuals. In the view of potentially fatal disturbances of autonomic function that can occur in GBS, it seemed appropriate to assess autonomic function in patients with this condition. However, there are still no clear guidelines regarding whether all GBS patients should be routinely screened for Autonomic Nervous System (ANS) neuropathy. Cardiac autonomic dysfunction is frequently asymptomatic and therefore can be missed on diagnosis. Availability of simple and reliable tests can be used to predict the dangerous manifestations of autonomic function in GBS patients. There is necessity of monitoring autonomic disturbances in all patients with GBS.[6,11]

As far as our knowledge goes, study on autonomic dysfunction in patients with GBS has not been carried out in our population till now. Thus this study was done to know about the frequency and pattern of various autonomic dysfunctions in GBS patients in order to raise the awareness in physicians resulting in an opportunity to avert the sufferings of these patients.

Few previous reports support that autonomic dysfunction is present more often in those with severe motor deficits.[7,13] while others found no significant relationship between them.[12,14] Therefore, there is still debate whether there is any relationship between autonomic dysfunction and the degree of motor disturbances.

Material and Methods

This cross sectional observational study was conducted in the department of Neurology BSMMU, Dhaka from March, 2015 to September, 2017. All patients who were diagnosed as GBS at Neurology ward of BSMMU, Dhaka were taken as study population. Age and sex matched adult apparently healthy attendant of patients or volunteers who did not have any neurological diseases were also taken for comparison. The interval between the onset of weakness and autonomic tests ranged from 10th day to 4th week. Patients with GBS (as cases) and apparently healthy persons (as control) were selected by purposive sampling method.

Disability status of the patients were assessed at the time of autonomic testing based on Hughes functional grading scale. Then the following autonomic tests were performed -1) measurement of heart rate both in supine and on changing posture 2) measurement of blood pressure both in supine and on changing posture 3) heart rate response to valsalva menauver by measuring valsalva ratio 4) heart rate response to deep breathing (maximum- minimum heart rate/min and E: I ratio) and 5) assessment of bowel and bladder dysfunction by symptoms analysis.

At the end of data collection, all the data were rechecked, coded and entered in standard statistical software used in BSMMU, data base using SPSS software. Demographic variables were analyzed by Chi square test. Quantitative data were expressed as mean ±SD and statistical analysis was done by

independent sample t test. Chi- Square test was used to see relationship of autonomic dysfunction with severity of functional disability. The P value <0.05 was considered statistically significant.

Results

In this study mean age of the patients was 35 (±12) years in patient group and 36(±13) years in control group. GBS was slightly prevalent in male (58.1%) than female (41.9%) and male to female ratio was 1.39:1.

All 43 patients presented with variable degree of motor weakness and other presentation was sensory complaints (44.20%), breathing difficulty and dysphagia (7%) and diplopia (4.7%). Regarding symptoms of autonomic dysfunction constipation was found commonly (30.2%) followed by palpitation (14%), urinary retention (7%), Urinary incontinence (4.7%) and dizziness (4.7%). Common cranial nerve palsy was lower motor type facial palsy (27.9%). Bulbar palsy was present in 7% and ophthalmoplegia in 4.7% of cases. Among them one patient (2.3%) had both facial palsy and ophthalmoplegia. Total cranial nerve palsy was present in 34.9% of cases. Based on Hughes functional disability grading score, majority of the patients (41.9%) were in grade 3 followed by grade 4 (39.4%). Grade 1 and 2 constituted 11.6 % of each. None of the patient was in grade 5 (requiring assisted ventilation).

Mean pulse rate of patients was (90±16) whereas control group was (73±10). There is significant difference between two groups (p-value<0.001). Mean systolic blood pressure of both group was (118±15) and (117±8) respectively and there was no significant difference (p-value >0.05). Mean diastolic BP of patients group was (77±11) and that of control group was (76±5), p-value was> 0.05 that is non-significant. Significant difference was seen in almost all autonomic parameter (resting heart rate, heart rate on standing, 30:15 ratio, systolic BP on standing, Valsalva ratio, HR response to deep breathing & E:I ratio) between patient and control group (p-value <0.05) except diastolic BP on standing which was non-significant (Table I).

Valsalva ratio was abnormal in 37.2% of patients. Abnormal 30:15 ratio was found in 82.4% of patients. Maximum –minimum heart rate on deep breathing were abnormal in 58.1% and abnormal fall in systolic blood pressure were found in 26.5% of patients but all the control had normal findings. p-value was significant in all the parameter (Table II).

Other autonomic abnormalities were postural hypotension (38.2%), sinus tachycardia (25.6%), hypertension (16.3%), hypotension (2.7%), sinus arrhythmia (4.7%), constipation (30%), urinary retention (7%) and urinary incontinence (4.7%) (Table III and diagram 1).

Table I: Autonomic parameters of both groups (n=78)

Autonomic	No of patient participating	Patient (n=43) (Mean±SD)	Control (n=35) (Mean±SD)	Total (78) (Mean±SD)	*p*-value
Resting heart rate	43	(91±17)	(73±10)	(83±17)	<0.001^{s}
Heart rate on standing	34	(104±16)	(96±12)	(100±15)	0.026^{s}
30: 15 ratio	34	(1±0.07)	(1.08±0.05)	(1.04±0.07)	<0.001^{s}
Systolic BP on standing	34	(106±15)	(112±7)	(109±12)	0.031^{s}
Diastolic BP on standing	34	(72±11)	(76±5)	(77±9)	0.081^{ns}
Valsalva ratio	43	(1.21±0.23)	(1.44±0.13)	(1.31±0.23)	<0.001^{s}
HR response to deep breathing	43	(10.88±10.47)	(25.29±7.37)	(17.35±11.65)	<0.001^{s}
E:I ratio	43	(1.14±0.15)	(1.4±0.14)	(1.26±0.2)	<0.001^{s}

** *p*-value was derived from Independent sample t- test, s=significant and ns =non-significant

Table II: Autonomic nerve function status of study population (n=78)

	Patient (n=43)			Control (n=35)			
	Normal N (%)	Borderline N (%)	Abnormal N (%)	Normal N (%)	Borderline N (%)	Abnormal N (%)	*p*-value
Valsalva ratio	14 (32.6)	13 (30.2)	16 (37.2)	35 (100)	0 (0)	0(0)	<0.001^{s}
30:15 ratio	6 (17.6)	0 (0)	28 (82.4)	35 (100)	0(0)	0 (0)	<0.001^{s}
Deep breathing (Max-Min HR)	11 (25.6)	7 (16.3)	25 (58.1)	34 (97.1)	1 (2.9)	0 (0)	<0.001^{s}
Fall in systolic BP	20 (58.8)	5 (14.7)	9 (26.5)	35 (100)	0(0)	0 (0)	<0.001^{s}

** *p*-value was derived from Chi-square test, s=significant

Table III: Frequency and pattern of autonomic dysfunction among patients with GBS (n=43)

Autonomic dysfunction	Frequency	Percentage
Tachycardia	11	(25.6)
Sinus Arrhythmia	2	(4.7)
Hypertension	7	(16.3)
Hypotension	2	(4.7)
Postural Hypotension	13	(38.2)
Abnormal 30:15 ratio	28	(82.4)
Abnormal Max-Min HR on deep breathing	25	(58.1)
Abnormal Valsalva ratio	16	(37.2)
Constipation	13	(30)
Urinary retention	3	(7)
Urinary incontinence	2	(4.7)

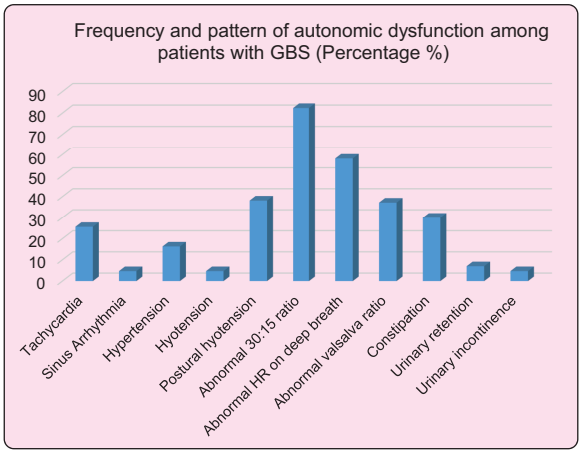

Figure 1:

41.9% of patients had early autonomic involvement. Definite involvement occurred in 32.6% and severe involvement in 14% of patients. None of the control had any form of autonomic involvement. Total autonomic dysfunction was found in 88.4% of patients (Table IV).

No significant relationship was found between autonomic dysfunction & severity of motor disability status according to Hughes functional grading (Table V).

Table IV: Distribution of the study population according to autonomic involvement (n=78)

Autonomic function	Patient (n=43) Frequency (%)	Control (n=35) Frequency (%)	Total Frequency (%)	p-value
Normal	5 (11.6%)	35(100%)	40 (51.3%)	<0.001^{s}
Early Involvement	18 (41.8%)	0(0%)	18 (23.1%)	<0.001^{s}
Definite Involvement	14 (32.6%)	0(0%)	14 (17.9%)	<0.001^{s}
Severe Involvement	6 (14%)	0(0%)	6 (7.7%)	0.021 ^{ns}
Total	43 (100%)	0(0%)	78 (100%)	<0.001^{s}

s = significant, ns = non-significant
*Chi square test was done to measure the level of significance

Table V: Association of autonomic dysfunction with Hughes functional grading (n=43)

	Autonomic nerve function			
Disability	Normal N (%)	Abnormal N (%)	Total N (%)	P-Value
Mild disability	2 (40.0)	8 (21.1)	10 (23.3)	0.346 ^{ns}
Severe disability	3 (60.0)	30 (78.9)	33 (76.7)	
Total	5 (100.0)	38 (100.0)	43 (100.0)	

p-value was derived from Chi-square test, ns =non-significant

Discussion

Autonomic dysfunction is a common and important complication of GBS and may be the cause of significant morbidity and mortality. Incidence of autonomic dysfunction in GBS has been reported to vary considerably. By using cardiovascular reflex test our study revealed autonomic dysfunction in 88.4% of cases though symptoms of autonomic dysfunction like lightheadedness, palpitation, constipation, urinary retention and incontinence were present only in 39.5%. Similar incidence of autonomic dysfunction was found in one previous study.[15] Whereas one study had found higher frequency (83%) of autonomic dysfunction in fisher syndrome.[16,17] Autonomic dysfunction in GBS probably occurs even more frequently than recorded as some of its manifestations are quite transient and require continuous monitoring. Some studies found no relationship between autonomic dysfunction and degree of motor disability.[12,14] Our study also found no significant relationship between them. However one previous study found significant relationship between cardiovascular reflex abnormalities and motor disability.[15]

Autonomic dysfunction in GBS comprises a wide range of cardiac arrhythmias, blood pressure fluctuations, electrocardiographic abnormalities, urinary retention, and gastrointestinal dysfunction. Sustained sinus tachycardia is the most commonly observed manifestation found in 37% and 33.3% of cases. [13,18] Sinus tachycardia was present in 25.6% of cases in our study. Sinus arrhythmia was found in only two of our patients. Though sinus tachycardia is common and usually not require treatment but vagally mediated arrhythmias such as profound bradycardia or cardiac arrest are more ominous and require early recognition for initiation of appropriate preventive therapy. In this study hypertension was found in 16.3% and hypotension in 4.7% of cases.

Postural hypotension is another important and common manifestation in GBS. We had found 38.2% of patients with postural hypotension that coincides the other study.[18] The percentage of postural hypotension may be even higher as it could not evaluated in few patients in our study due to severe weakness. Postural hypotension may lead to syncope and irreversible brain damage in a patient who is inadvertently left in a sitting position. Thus quadriplegic patients should not be left unattended in the upright sitting posture without assessment of postural hypotension.

Common abnormalities were variation of heart rate on changing posture that is 30:15 ratio 82.4%, deep breathing 58.1% and abnormal valsalva ratio in 37.2% of cases reflecting parasympathetic and blood pressure changes in 38.2% of cases reflecting sympathetic dysfunction. So autonomic dysfunction in this study was found abnormal in parasympathetic as well as sympathetic components of ANS.

Regarding bowel and bladder dysfunction we found 30% of patients had constipation. But it was found in 15% of cases as described by another study[13]. Only 3 (7%) of the patient had urinary retention during the course of the illness and two of them had urinary incontinence.

Most of our GBS patients were unable to receive costly treatment due to financial constraint. Autonomic dysfunction, if not discovered and managed early, may be associated with significant mortality.

Conclusion

In this study different patterns of autonomic dysfunction was found in 88.4% of adult patients with GBS involving both sympathetic and parasympathetic components. The present study found no significant association between autonomic dysfunction and motor disability scores. Thus autonomic function assessment is essential in every patient with GBS in addition to motor & sensory function.

Conflict of Interest: There was no conflict of interest.

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