Assessment of Anti-Ganglioside Antibodies in Patients Diagnosed With Guillain Barre Syndrome

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ABSTRACT

Objective: To assess the frequency of patients positive for the presence of anti-ganglioside antibodies and factors related to it among the patients diagnosed with Guillian Barre Syndrome (GBS) at our hospital.

Study Design: Prospective longitudinal study.

Place and Duration of Study: Pak Emirates Military Hospital Rawalpindi, from Jan to Jun 2019.

Methodology: Patients were included in the study once detailed assessment and investigations have been carried out by the consultant neurologist and he has declared the patient suffering from Guillian Barre Syndrome. Anti-ganglioside antibodies were performed on all the patients diagnosed with Guillian Barre Syndrome from the immunology department of the laboratory of our hospital. Factors like age, gender, preceding gastrointestinal infection; sensory involvement and need for mechanical ventilation were related with the presence of Guillian Barre Syndrome in our target population.

Results: A total of 30 patients were enrolled in the study. Out of these 22 (73.3%) were positive for the presence of anti-ganglioside antibodies while 08 (26.4%) did not show the presence of detectable levels of these antibodies in their serum. On fisher exact test preexisting gastrointestinal infection and sensory involvement were statistically significantly related to the presence of anti-ganglioside antibodies among the patients suffering from Guillian Barre Syndrome.

Conclusion: Relationship of presence of anti-ganglioside antibodies was strong with the Guillian Barre Syndrome among the patients enrolled in our study. It was even stronger in among the patients who presented with the sensory involvement or those who had a gastrointestinal infection prior to the onset of symptoms of Guillian Barre Syndrome.

Keywords: Anti-ganglioside antibodies, Guillian barre syndrome, Immuno-neurology.

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INTRODUCTION

Immunological basis of various disorders have been identified after the recent advancement in the field of immunology. Various diseases which were labeled as idiopathic were actually least understood due to the lack of modalities available to diagnose them.[1] Various neurological illnesses were part of that process and were underdiagnosed as well as stigmatized. GBS has been one of those illnesses. Still exact etiology and underlying mechanism is not fully understood; yet there has been a consensus on immunological basis of this illness.[2-4] Response to treatment modalities like steroids, plasmapharesis and intravenous immunoglobulin also strengthens this hypothesis.[5]

A lot of work has been done on the structure, form and link of anti-ganglioside antibodies with various immune based diseases. They have been found in the serum of patients suffering from acute myelitis, chronic inflammatory demyelinating neuropathy, subacute sensory motorneuropathy and various forms of GB syndrome.[6-9]

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Previous studies have shown that antiganglioside antibodies have been commonly found in the serum of patients suffering from GBS. A study done in UK revealed that most of the patients who suffered GB syndrome after the cytomegalovirus infection had these antibodies in their serum,[10] facts highlight the fact that this noninvasive laboratory investigation may play a vital role regarding the screening, diagnosis and prediction of severity and outcome among the patients suffering from this immune based neurological disorder.

Immunology was an under developed field in our part of the world and serum of patients were used to transferred abroad to get the immunological investigations done. In past few years some work has been done in this regard and we are able to carry out a lot of immune based investigations in some centers of our country. Armed forces of Pakistan has also got a well-established immunological laboratory which allowed us to plan this study with the objective to assess the frequency of patients positive for the presence of anti-ganglioside antibodies and factors related to it among the patients diagnosed with Guillian Barre Syndrome (GBS) at neurology department of our hospital.

METHODOLOGY

This prospectivelongitudinalstudy was carried out at the Neurology Unit of Pak Emirates Military Hospital Rawalpindi, from January to June 2019. Sample was gathered by using the non-probability consecutive sampling technique.

Inclusion Criteria: As it is a rare disease and study design was observational so all the patients between the age of 12 and 65 years admitted in the neurology department and diagnosed as GBS by the consultant neurophysician were included in the study. Those patients who were diagnosed elsewhere on same criteria by consultant neurologist but could not be managed and transferred to our hospital were also recruited in the study.

Exclusion Criteria: Patients with unclear medical diagnosis,pregnant patients or those with CSF India ink stain positive for the fungal growth or those with suspected TBM or encephalitis were also not included in the study. Patients with post traumatic meningitis or those with post injection syndrome or poliomyelitis were also the part of exclusion criteria. Patients with diabetes, neoplasia, hypothyroidism, other immunological disorders, renal failure, vasculitis, or history of intoxication those who did not give written informed consent were also excluded from the study.

GBS diagnosis was made according to diagnostic criteria from the National Institute of Neurological Disorders and Stroke from 1990.[11,12] Acute progressive symmetric weakness of the extremities with areflexia or hyporeflexia, Albumino-cytological dissociation in cerebrospinal fluid (raised protein and total cell count of ≤10/mm^3) and demyelinating/axonal neuropathy on electrophysiological studies were the parameters considered in the diagnosis of GBS among the study participants.

All suspected cases of GBS under went electro physiological studies within 48 hours of admission. In our study, the patients were classified into AIDP or AMAN based on the existing electro diagnostic criteria was used to classify the patients into acute inflammatory demyelinating polyneuropathy (AIDP) group, acute motor axonal neuropathy (AMAN) group, acute motor axonal neuropathy (AMSAN) group, miller-Fisher syndrome (MFS) group and cranial nerve variant group (CNV).[13,14]

Neurology department of PEMH Rwp is a tertiary care 140 bed facility with 4 consultants and around 10 residents. Anti-ganglioside antibodies were assessed at immunology department of the laboratory of own hospital by serum samples of patients during the acute stage within 2 weeks of symptom onset. An enzyme-linked immunosorbent assay (ELISA) was used to detect the various types of antiganglioside antibodies, including immunoglobulin G (IgG) and immunoglobulin M (IgM) antibodies against the gang-liosides GM1, GM2, GM3, GD1a, GD1b, GD3, GT1a, GT1b, and GQ1b, as described previously.[11] Although they are not true gangliosides, testing was also performed for galacto-cerebroside and asialo-GM1. The presence and types of anti-ganglioside antibodies were analyzed by researchers who were blinded to the patients' presenting neurological signs and electrophysiological classifications.[15,16]

All statistical analysis was performed by using the SPSS-24.0. Mean and standard deviation for the age of study participants was calculated. Frequency and percentages for gender, variants of GBS and the number of patients positive with the anti-ganglioside antibodies were also calculated. Fisher exact test was applied to see the association of various factors with the presence of anti-ganglioside antibodies among the patients diagnosed with GBS. The *p*-value of ≤0.05 was considered significant

RESULTS

A total of 35 patients were diagnosed as GBS in our department during this time. Three were less than 12 years, one was pregnant and one had history of other immunological disorder as well.

Table-I: Characteristics of patients diagnosed with GBS (n=30).

Age (years)	
Mean ± SD	32.63 (± 4.271)
Range (min-max)	12 - 59 years
Gender	
Male	23 (76.6%)
Female	07 (23.4%)
Clinical Features at Presentation	
Lower limb weakness	08 (26.4%)
Numbness	06 (19.8%)
Depressed reflexes	06 (19.8%)
Facial nerve palsy	05 (16.5%)
dysarthria	03 (9.9%)
Confusion	01(3.3%)
Others	01 (3.3%)
Variants of GBS	
AIDP	15 (50%)
AMAN	07 (23.1%)
AMSAN	04 (13.2%)
MFS	03 (9.9%)
CNV	01 (3.3%)

Out of these 30, 22 (73.3%) showed the presence of anti-ganglioside antibodies while 08 (26.4%) were negative for this antibody on neurological testing. Mean age of the study participants was 32.63 ± 4.271 years. Commonest GBS variant was AIDP followed by AMAN. Characteristics of patients have been described in Table-I.

From the factors studied sensory involvement and preexisting gastrointestinal infection had a significant relationship with presence of anti-gang-lioside antibodies when chi-square was applied (Table-II).

Table-II: Factors Related to the Presence of Anti-Ganglioside Antibodies (Chi-square).

Socio-Demographic Factors	Absent Anti-Ganglioside Antibodies	Presence of Anti-Ganglioside Antibodies	*p*-value
Age			
<18 years	04 (50)	09 (40.9)	0.658
18-60 years	04 (50)	13 (59.1)	
Gender			
Male	05 (62.5)	18 (81.8)	0.284
Female	0337.5	04 (18.2)	
Sensory Involvement			
No	08 (100)	14 (63.6)	0.015
Yes	-	08 (26.4)	
Preexisting Infection			
No	08 (100)	12 (54.5)	0.005
Yes	-	10 (45.5)	
Need for Mechanical Ventilation			
No	07 (87.5)	20 (90.9)	0.787
Yes	01 (12.5)	02 (9.1)	

DISCUSSION

GBS is one of the commonly diagnosed neurological illnesses with immunological basis.[16,17] With the advent of neuro-diagnostic studies and immunological testing, patients receive this diagnosis early and get treatment. This has reduced the mortality and morbidity related to this illness.[18] Even studies from underdeveloped countries shoe a good prognosis of this illness and patients recover well in most of the cases with limited or no disability.[18]

Various treatment options have now been introduced for GBS after understanding the etiological basis. Understanding the etio-pathogenesis of the illness not only helps the physician in early diagnosis but also helps the researchers and pathologist to frame various diagnostic modalities to help the clinicians. Despite adopting modern clinical methods, this aspect lack in our part of the world and research on etiopathogenesis of various illnesses lack in our population so either we have to follow the western studies or limited clinical experience of the senior clinicians. We therefore planned this study with the rationale to look for the immunological basis of this disease in our own population and assess the patients which show the presence of anti-ganglioside antibodies in their serum.

Most of the patients which were included in our study with diagnosis of GBS were positive for the anti-gangloside antibodies. 22 out of 30 patients showed presence of these antibodies in their serum. These results support the results of various studies done in the past on similar subject in 1999 by Khalili *et al* and in 2010 by Meena *et al*,.[10,11] All other investigations related to the diagnosis of GBS are either invasive or expensive or operator dependent. Neurodiagnostic studies involving nerve conduction studies and lumbar puncture for CSF analysis both have their own merits and demerits and patients have to wait and spend a lot for these investigations.[3] If antiganglioside antibodies have a clear link with GBS and it is proved in future studies with more sample size, this can be very useful for the patients as well as the health care providers.

GBS can present in number of ways. Commonest presentation in our patients was lower limb weakness. However sensory problems or numbness was also not an uncommon presentation. Sensory involvement also had a significant link with the presence of antiganglioside antibodies in the serum of the patients. Previously similar results have been produced in studies done in other parts of the world especially study of Kim *et al*, is important in this regard in which sensory involvement patients had mostly positive antibodies.[12] This finding can be helpful segregating the patients for the type of presentation to the treatment options as well as the prognostic significance. Type of neuronal damage may also be linked with the presence or absence of these antibodies in the serum of the patients. More studies in this regard may ascertain these findings.

It has been now believed with evidence that GBS has an immunological basis. Post infectious presentation has been quite common. Upper respiratory tract and GI tract infections have been commonly found in GBS patients in clinical setings. Our study some how provided the link of the infection with the immunological phenomenon. Most of our patients who had preexisting GI infection showed the presence of antignglioside antibodies in their serum. This relationship proved significant on chi-square test as well. Similar results have been generated in the past as well by Meena *et al* in 2010 and Kim *et al* in 2014.[11,12] This links

to the hypothesis that infection modulates the immune system of human body and generates the antibodies which may be responsible for neuronal damage.

Age and gender had no association with presence of antibodies in the serum of patients of GBS. Studies in the past have also not proved this association.[10,12] This reflects that presence of antibodies has nothing to do with the gender or age of the patient. It is the trigger of immune system basically which matters either in the form of infection or some other phenomenon related to it.

This study has few limitations as well. First of all, sample size was very small. Though a tertiary care teaching hospital; still low frequency of GBS allowed us to recruit this much patients only. Moreover, the types and variants of GBS were not separately related to the presence of anti-ganglioside antibodies which might have generated very interesting results. Family history of immunological disorders was also not taken into account which may also account for the presence of these antibodies. More studies with a larger sample size incorporating all the types and addressing the above mentioned limitations may generate more accurate results in this aspect.

CONCLUSION

Relationship of presence of anti-ganglioside antibodies was strong with the GBS among the patients enrolled in our study. It was even stronger in among the patients who presented with the sensory involvement or those who had a gastrointestinal infection prior to the onset of symptoms of GB syndrome.

Conflict of Interest: None.

Authors' Contribution

ZH: Direct contribution, AG:, WA:, KHN:, HU:, SK: Intellectual contribution.

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