Identification of factors affecting outcomes in patients with Guillain Barre syndrome

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Abstract

Background. Guillain Barre syndrome (GBS) is a rare autoimmune neurological disorder resulting in variable clinical course and outcome. Various factors such as age, symptoms and disease form that influence the outcome of GBS have been previously studied.

Aim. This study aimed at identifying factors affecting the outcomes in patients with GBS.

Methods. A retrospective observational study was conducted on GBS (ICD-G61.0) patients admitted to the hospital between 2014 and 2019. Patient information on demographics, medical and medication history, laboratory parameters, electrophysiological data, type of GBS and therapy received were retrieved from medical records. Univariate and multivariate analysis were conducted to identify factors associated with outcome (improved and not improved) and calculate odds ratio (OR).

Results. A total of 212 GBS patients were included in the study, of which 67\% were males and the mean age was 39.9±20.1 years. 168 (79\%) patients showed improvement whereas the remaining 44 (21\%) did not show improvement. Patients with hypertension (OR=4.512; CI=1.309-15.556, p=0.017), alcoholics (OR=5.148; CI=1.234-21.472, p=0.025), sepsis (OR=9.139; CI=1.102-75.760, p=0.040) and cardiac arrest (OR=17.495; CI=1.249-245.027, p=0.034) were associated with risk of no improvement. Whereas those treated with IVIgG plus Physiotherapy/Occupational therapy (OR=0.062; CI=0.016-0.242, p=0.001) and Plasmapheresis plus Physiotherapy/Occupational therapy (OR=0.007; CI=0.000-0.147, p=0.001) were associated with improvement.

Conclusion. Understanding these factors help to further give a more directed and focused management to improve the condition in patients who are at risk of poor outcome. Further follow-up studies could be done to determine and manage the residual disabilities associated with GBS to improve patient’s quality of life.

Keywords: Guillain Barre syndrome, immunoglobulin G, plasmapheresis, physiotherapy/occupational therapy
**Introduction**

Guillain Barre syndrome (GBS) is a rare autoimmune neurological disorder in which the body’s immune system attacks part of its peripheral nervous system resulting in limb and cranial nerve weakness often with respiratory compromise and limitation on physical function [1].

It is composed of 4 main variants including Acute Inflammatory Demyelinating Polyneuropathy (AIDP), Acute Motor Axonal Neuropathy (AMAN), Acute Motor and Sensory Axonal Neuropathy (AMSAN) and Miller-Fisher Syndrome (MFS). The progression of disease is more rapid and recovery is often extended in axonal degeneration compared to demyelinating pattern [2,3] whereas MFS variant is associated with better prognosis and outcome [2,4].

The worldwide incidence of the disease ranges from 0.81 to 1.89 cases per 100,000 person-years [1] with an approximate male to female ratio of 2:1 [5,6]. Although GBS affects all ages, an increase in incidence is observed with increased age, mostly 50 years or above, with a decline after 80 years of age [7]. It is lower in children at 0.34 to 1.34 per 100,000 and increases after 50 years of age from 1.7 to 3.3 per 100000 [8]. However, this may vary based on the quality of surveillance and the geographical prevalence of the causal factors.

GBS may be preceded by gastro-intestinal or respiratory infection (caused by certain bacteria [9] or viruses), weeks prior to its onset or triggered by vaccination, underlying disease, surgery, certain malignancies, pregnancy, trauma, tissue transplant [10] and rarely pesticide exposure [11].

The patients commonly present with areflexia (or hyporeflexia) or quadriparesis, which are required features, along with other features supportive of the diagnosis such as Nerve Conduction Velocity (NCV) findings, electromyography and elevated proteins in cerebrospinal fluid etc. based on National Institute of Neurological Disorders and Stroke (NINDS) diagnostic criteria. The criteria also include features that cast doubt or rule out the diagnosis [2,12-14].

The cornerstone of therapy in GBS is IVIg and plasmapheresis. Although IVIg is preferred over plasmapheresis due to its easy availability and greater convenience of administration [2], both are equally effective. However, IVIgG and plasmapheresis combined are not significantly superior over individual treatment options [2,15]. Also, therapy is selected based on patient related, social and economic factors [2]. Corticosteroids have also been used in the management of the condition however, corticosteroid monotherapy is not effective for the treatment of GBS [2,15], nevertheless short-term benefits, when combined IVIg therapy are noted [2]. Furthermore, small scale studies have shown positive outcomes in terms of strength, endurance, fatigue [16], gait quality and function [17] in patients who underwent physiotherapy.

Several complications may occur due to GBS. Short term complications most commonly include cardiovascular complications (rhythm abnormalities, blood pressure variability and myocardial involvement) and respiratory complications that may require artificial ventilation and close monitoring to improve outcome [18,19]. Long term complications mainly include residual disability and/or psychosocial dysfunction [18]. These may lead to prolonged ICU stay and mortality.

In spite of offering intensive care to patients with progressive form of GBS, the morbidity and mortality remain high. Various factors that may influence the functional recovery of GBS have been previously studied. Early identification of poor outcome predictors and early interventional management helps improve functional outcome and level of disability. This study, therefore seeks additional fundamental knowledge of the factors affecting the poor outcomes in patients with GBS so as to reduce the burden of neurological disorders.

**Methods**

**Study setting and data sources**

The study site is a tertiary care teaching hospital located in South India. Ethical clearance for the disclosure of the records (IEC: 543/2019) was acquired from the Institutional Ethics Committee of Kasturba Hospital, Manipal Academy of Higher Education, Manipal A retrospective descriptive analysis study was performed on the patients admitted between January 2014 to December 2019. This study includes 212 patients with a confirmed clinical and laboratory diagnosis of GBS according to NINDS criteria. These patients were further grouped into either AIDP, AMAN, AMSAN or MFS variant in compliance with NCV findings and clinical presentation to determine the distribution of the types. Demographic data such as age, gender, occupation, social habits and patient outcomes such as improved or not improved were collected. Information on any prior infections, diseases, surgery, vaccination, pesticide exposure, that might have triggered the disease, and any complications faced by the patients were also retrieved. Furthermore, the patients were categorized based on the treatment they received (IVIg, plasmapheresis, physiotherapy/occupational therapy, corticosteroids).

The association between the outcome and the factors: age, gender, occupation, social habits, comorbidities, variants of GBS, possible etiology, complications and treatment, was assessed to determine its effect on the outcome.

**Study population**

The records of 254 patients with a confirmed diagnosis of GBS were recognized using the ICD code G61.0. The data was retrospectively and manually retrieved from medical records. The majority of patients...
were referred from the local hospitals. A total of 212 patients were considered eligible for the study. The rest were not considered either due to exclusion criteria or missing records. The exclusion criterion comprised of all patients with acute myelopathy, vasculitic neuropathy, myasthenia gravis, acute pharyngeal cervicobrachial neuropathy (APCBN), botulism, West Nile encephalomyelitis, amyotrophic lateral sclerosis (ALS), diabetic polyneuropathy (DPN), poliomyelitis and toxic neuropathy (Figure 1).

**Outcomes**

The patients’ outcomes were classified into improved and not improved. These were assessed using the Modified Rankin Scale which is based on symptoms, severity of disability, ability of perform usual activities, need of assistance or death of the patient. Motor power was assessed by MRC grading and respiratory function was monitored by respiratory rate, single breath count, breath holding time and chest expansion. Peak Expiratory Flow Rate (PEFR) was used to monitor respiratory function and was used to intubate and provide assisted ventilation where indicated. Patients were monitored for autonomic system dysfunction especially tachyarrhythmia, bradyarrhythmia and fluctuation in blood pressure.

**Definitions**

Improved category is defined as a Modified Rankin Scale of 0-3. It includes the patients who recovered or whose condition improved, in terms of symptoms/subjective data collected at discharge.

Not improved category is defined as a Modified Rankin Scale of 4-6. It includes the patients who expired, got discharged against medical advice, or whose condition either worsened or remained same (unchanged), in terms of symptoms/subjective data collected at discharge.

Service category under occupation includes company employees, bank employees, teachers, healthcare services etc.

Possible etiology is the suspected cause of the disease, in this case, may be vaccine, surgery, preceding viral or bacterial infection, prior diarrhea or pesticide exposure.

**Statistical analysis**

SPSS 20.0 package (IBM Corp. IBM SPSS Statistics for Windows, Armonk, NY) was used to conduct all statistical analyses. Continuous variables’ values are expressed in terms of mean and standard deviation (SD) whereas categorical variables’ values are expressed in terms of frequency and percentages.

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**Figure 1.** Patient flow diagram.

GBS-Guillain Barre Syndrome, AIDP-Acute Inflammatory Demyelinating Polyneuropathy, AMAN-Acute Motor Axonal Neuropathy, AMSAN-Acute Motor and Sensory Axonal Neuropathy, MFS-Miller-Fisher Syndrome.
Univariate analysis was used for initial identification of risk factors affecting the outcome (not improved) in patients with GBS, and calculation of unadjusted odds ratio. Variables with p<0.25 associated with no improvement in GBS patients in the univariate analysis were selected as independent variables for the multivariate analysis for calculation of p value and adjusted odds ratio. In multivariate analysis, variables with p<0.05 were selected as independent risk factors affecting the outcome.

Results

Patient demographics and clinical features related outcome predictors of GBS patients

Out of 212 patients, 142 (67.0%) were male and 70 (33.0%) were female with an average age of 39.9±20.1 years. The social habits observed in these patients were alcoholism (11.3%, n=24), smoking (6.1%, n=13) and tobacco use (4.2%, n=9). From the comorbidities observed in these patients, the most common were hypertension (n=38, 17.9%) and diabetes (n=32, 15.1%). The patients were grouped into 7 major occupation groups and the no-occupation group, in which most patients belonged to the service category (n=51, 24.1%).

Pesticide exposure (n=28, 13.2%) was found to be the most common etiological factor and AIDP (n=136, 64.2%) was found to be the most common variant among the GBS patients. A total of 40 (18.9%) patients suffered from respiratory paralysis due to the disease. Out of 212 patients, 178 received therapy, of which 157 (88.2%) patients showed improvement whereas the remaining 21 (11.8%) did not show any improvement, with a mortality rate of 3.9% (Table I).

Signs and symptoms of GBS based on Diagnostic criteria

The signs and symptoms were based on Diagnostic criteria for GBS published in Annals of Neurology as requested by NINDS in 1978. Progression of symptoms over days to 4 weeks and Relative symmetry (n=206, 97.2%) were observed in most patients followed by areflexia or hyporeflexia (n=203, 95.8%), typical EMG/nerve conduction velocity studies (characteristic signs of demyelinating process in the peripheral nerves) (n=174, 82.1%) and progressive weakness in both arms and legs (n=161, 75.9%) (Table II).

Table I. Demographics, comorbidities, social characteristics of study population, possible etiologies, types, complications and clinical outcomes of GBS.

| Parameter                      | Frequency (%) | Parameter                      | Frequency (%) |
|--------------------------------|---------------|--------------------------------|---------------|
| Age category                   |               | Social history                 |               |
| <30                            | 68 (32.1%)    | Alcoholism                     | 24 (11.3%)    |
| 30-60                          | 104 (49.1%)   | Smoking                        | 13 (6.1%)     |
| >60                            | 40 (18.9%)    | Tobacco use                    | 9 (4.2%)      |
| Gender                         |               | Possible etiologies            |               |
| Male                           | 142 (67%)     | Viral infection                | 12 (5.7%)     |
| Female                         | 70 (33%)      | Vaccine                        | 26 (12.3%)    |
| Comorbidities                  |               | Bacteria                       | 1 (0.5%)      |
| Hypertension                   | 38 (17.9%)    | Diarrhoea                      | 29 (13.7%)    |
| Diabetes                       | 32 (15.1%)    | Surgery                        | 10 (4.7%)     |
| Ischemic Heart Disease         | 5 (2.4%)      | Pesticide exposure             | 28 (13.2%)    |
| Rheumatoid Heart Disease       | 1 (0.5%)      | Types of GBS                   |               |
| Respiratory Tract Infection    | 3 (1.4%)      | AIDP                           | 136 (64.2%)   |
| Thyroid disorders              | 3 (1.4%)      | AMAN                           | 31 (14.6%)    |
| Bronchial asthma               | 7 (3.3%)      | AMSAN                          | 14 (6.6%)     |
| Dyslipidemia                   | 2 (0.9%)      | MFS                            | 16 (7.5%)     |
| Epilepsy                       | 2 (0.9%)      | Unknown                        | 15 (7.1%)     |
| Tuberculosis                   | 1 (0.5%)      | Complications                  |               |
| Occupation                     |               | Respiratory paralysis          | 40 (18.9%)    |
| Student                        | 41 (19.3%)    | Sepsis                         | 12 (5.7%)     |
| Farmer                         | 30 (14.2%)    | Pulmonary embolism             | 3 (1.4%)      |
| Service                        | 51 (24.1%)    | Cardiac arrest                 | 9 (4.2%)      |
| Housewife                      | 39 (18.4%)    | Others                         | 26 (12.3%)    |
| Cooly                          | 19 (9%)       | Clinical outcome               |               |
| Fishing                        | 4 (1.9%)      | Improved                       | 168 (79.2%)   |
| Labour                         | 4 (1.9%)      | Not improved                   | 44 (20.8%)    |
| No occupation                  | 24 (11.3%)    |                                |               |

AIDP-Acute Inflammatory Demyelinating Polyneuropathy, AMAN-Acute Motor Axonal Neuropathy, AMSAN-Acute Motor and Sensory Axonal Neuropathy, MFS-Miller-Fisher Syndrome.
Table II. Signs and symptoms of GBS based on Diagnostic criteria.

| Signs and symptoms | Frequency (%) |
|--------------------|---------------|
| Progressive weakness in both arms and legs | 161 (75.9%) |
| Areflexia or hyporeflexia | 203 (95.8%) |
| Progression of symptoms over days to 4 weeks | 206 (97.2%) |
| Relative symmetry | 206 (97.2%) |
| Mild sensory signs and symptoms | 73 (34.4%) |
| Cranial nerve involvement, especially bilateral facial weakness | 81 (38.2%) |
| Recovery beginning 2 to 4 weeks after progression ceases | 1 (0.5%) |
| Autonomic dysfunction | 76 (35.8%) |
| Absence of fever at onset | 147 (69.3%) |
| Typical CSF (albuminocytologic dissociation) | 92 (43.4%) |
| EMG/nerve conduction velocity studies (characteristic signs of demyelinating process in the peripheral nerves) | 174 (82.1%) |
| Asymmetrical weakness | 3 (1.4%) |

CSF-Cerebrospinal Fluid, EMG-Electromyography.

Table III. Treatment in GBS.

| Types of treatment | Frequency (%) | IMPROVED | NOT IMPROVED |
|--------------------|---------------|----------|--------------|
| A only             | 12 (5.7%)     | 11 (91.7%) | 1 (8.3%)     |
| A + B              | 79 (37.3%)    | 74 (93.7%) | 5 (6.3%)     |
| A + C              | 3 (1.4%)      | 3 (100%)  | 0            |
| A + B + C          | 18 (8.5%)     | 16 (88.9%) | 2 (11.1%)    |
| D only             | 1 (0.5%)      | 0         | 1 (100%)     |
| D + B              | 13 (6.1%)     | 12 (92.3%) | 1 (7.7%)     |
| D + C              | 1 (0.5%)      | 0         | 1 (100%)     |
| D + B + C          | 4 (1.9%)      | 2 (50%)   | 2 (50%)      |
| B only             | 32 (15.1%)    | 26 (81.3%) | 6 (18.8%)    |
| C only             | 5 (2.4%)      | 3 (60%)   | 2 (40%)      |
| B + C              | 9 (4.2%)      | 9 (100%)  | 0            |
| A + D + B          | 1 (0.5%)      | 1 (100%)  | 0            |
| No therapy         | 34 (16.0%)    | 11 (32.4%) | 23 (67.6%)   |

KEY: A- IV Immunoglobulin G, B- Physiotherapy/Occupational therapy, C- Corticosteroids, D- Plasmapheresis.

Table IV. Identification of factors affecting outcome in GBS patients by univariate analysis.

| Parameter                                      | p value | odd ratio (95% CI) | Percentage not improved |
|------------------------------------------------|---------|--------------------|-------------------------|
| Age category                                   |         |                    |                         |
| <30                                            | 0.003   | 0.270 (0.108-0.675) | 8.8%                    |
| >60                                            | 0.014   | 2.549 (1.192-5.449) | 35%                     |
| AMSAN                                          | 0.035   | 3.158 (1.034-9.640) | 42.9%                   |
| MFS                                            | 0.137   | 0.237 (0.030-1.947) | 6.2%                    |
| Smoking                                        | 0.002   | 5.108 (1.622-16.091)| 53.8%                   |
| Alcohol                                        | 0.001   | 4.875 (2.010-11.823)| 50%                     |
| Hypertension                                   | 0.007   | 2.800 (1.300-6.033) | 36.8%                   |
| Diabetes                                       | 0.112   | 1.952 (0.846-4.501) | 31.2%                   |
| Vaccine                                        | 0.023   | 0.133 (0.018-1.010) | 3.8%                    |
| Respiratory paralysis                          | 0.109   | 1.875 (0.861-4.081) | 30%                     |
| Sepsis                                         | 0.001   | 9.111 (2.602-31.905)| 66.7%                   |
| Pulmonary embolism                             | 0.048   | 7.952 (0.704-89.806)| 66.7%                   |
| Cardiac arrest                                 | 0.001   | 15.703 (3.136-78.664)| 77.8%                   |
| Ventilation                                    | 0.005   | 2.691 (1.337-5.415) | 33.9%                   |
| IVIgG + Physiotherapy/ Occupational therapy    | 0.001   | 0.163 (0.061-0.434) | 6.3%                    |
| Plasmapheresis + Physiotherapy/ Occupational therapy | 0.231 | 0.302 (0.038-2.390) | 7.7%                    |

AMSAN-Acute Motor and Sensory Axonal Neuropathy, MFS-Miller-Fisher Syndrome, IVIgG- IV Immunoglobulin G.
Treatment in GBS

Out of 212 patients, 178 (84%) patients received therapy whereas the remaining 34 (16%) did not receive any therapy. Different treatment regimens were given to the patients who received therapy. The most commonly prescribed regimen was IVIgG + physiotherapy/occupational therapy (n=79, 44.4%) in which 74 (93.7%) patients showed improvement, followed by physiotherapy/occupational therapy only (n=32, 18.0%) in which 26 (81.3%) patients showed improvement and IVIgG + Physiotherapy/occupational therapy + Corticosteroids (n=18, 10.1%) in which 16 (88.9%) patients showed improvement. Most of the patients who did not opt to take any therapy (n=34, 16.0%) were discharged against medical advice (n=22, 64.7%), few of them (n=11, 32.4%) showed improvement in their symptoms with time and 1 (2.9%) showed no change in their symptoms (Table III).

Identification of factors affecting outcome in GBS patients by univariate and multivariate analysis.

Assessment of the relationship between the outcome and variables such as age, gender, occupation, social habits, comorbidities, variants of GBS, possible etiology, complications and treatment was done to determine its effect on the outcome.

The factors that significantly affect the outcomes in GBS are given in table IV along with their odds ratio and p value.

The factors identified in univariate analysis with p<0.25 were selected and included in multiple logistic regression. Variables with p<0.05 were considered significant factors affecting the outcome. The results of multiple logistic regression along with adjusted odds ratio, 95% CI and p values are presented in table V. The association remain intact only with certain variables and rest may have failed to show association, and it may be due to the presence of confounding factors.

Patients who consume alcohol (p=0.025, Adjusted OR=5.148 (1.234-21.472)) were associated with risk of poor outcome in GBS.

Patients who received IVIgG plus physiotherapy/occupational therapy (p=0.001, Adjusted OR= 0.062 95% CI 0.016-0.242) and Plasmapheresis plus physiotherapy/occupational therapy (p=0.001, Adjusted OR= 0.007 95% CI 0.000-0.147) showed better outcome.

The wide confidence intervals may indicate a small sample size.

Discussion

GBS is an autoimmune neurological disorder that results in rapidly progressing limb and cranial nerve weakness that further leads to respiratory compromise and limitation in physical function. Therefore, building the relationship between the outcome and the factors that affect those outcomes helps to futuristically reduce the possibility of poor outcome by identifying and further conducting a focused research on that group to determine treatment and therapy specific to these patients. Furthermore, this helps to reduce the alterations in the statistical power of the study that may occur due to the variations in clinical severity and outcome due to the heterogeneous population [13, 20].

Our study found several such factors that had either positive or negative effect on the outcome. Alcoholism, history of hypertension, development of sepsis and cardiac arrest were potential risk factors for poor outcome in GBS patients. IVIgG + Physiotherapy/ Occupational therapy and Plasmapheresis + Physiotherapy/ Occupational therapy were found to have a protective effect against the same.

One of the factors was age, where initially during univariate analysis, age groups <30 showed to have better improvement and age group >60 had poor outcome. This was supported by a study conducted by Seta et al. where the patients were categorized into two age groups according to the median age. Their results stated that the time taken for one or two functional grade recovery was significantly prolonged in elderly than in the younger group. Hence, they concluded that advanced age resulted

| Parameter                                           | p value | Adjusted odd ratio (95%CI)       | Percentage not improved | Percentage improved |
|-----------------------------------------------------|---------|----------------------------------|-------------------------|---------------------|
| Alcohol                                             | 0.025   | 5.148 (1.234-21.472)            | 50%                     | 50%                 |
| Hypertension                                        | 0.017   | 4.512 (1.309-15.556)            | 36.8%                   | 63.2%               |
| Sepsis                                              | 0.040   | 9.139 (1.102-75.760)            | 66.7%                   | 33.3%               |
| Cardiac arrest                                      | 0.034   | 17.495 (1.249-245.027)          | 77.8%                   | 22.2%               |
| IVIgG + Physiotherapy/ Occupational therapy         | 0.001   | 0.062 (0.016-0.242)             | 6.3%                    | 93.7%               |
| Plasmapheresis + Physiotherapy/ Occupational therapy| 0.001   | 0.007 (0.000-0.147)             | 7.7%                    | 92.3%               |

IVIgG - IV Immunoglobulin G.
in poor short- and long-term outcomes [21]. Since the mean age of our study was similar to their study (39.92 ±20.09 years vs 40.8±17.2 years), the results can be compared. Although, during multivariate analysis, age did not have any significant contribution on the outcomes of these patients.

Smoking as a social habit among the patients was also considered as a risk factor resulting in poor outcome in GBS patients on evaluation by univariate analysis.

Alcohol related peripheral neuropathy is common and marked by deterioration of axons of sensory and motor nerve fibers, with involvement of sensory nerves and lower limb more frequently [22]. It may occur as a result of various factors such as direct toxicity of alcohol [23], malnutrition, family history of alcoholism, duration of alcoholic disease and total life time dose of ethanol (TLDE) [22]. In our study, 11.3% of the patients were alcoholics, and alcoholism was assessed to be a potential risk factor for poor outcome in GBS patients. Ammendola et al. showed an increased duration of alcoholism and higher total life time dose of ethanol in group with neuropathy compared to alcoholics without neuropathy [22]. Thomas et al. also stated that NCS conducted among chronic alcohol abusers had higher rates of neuropathy, with 10% representing polyneuropathies [24].

Among the different variants of GBS, the fraction of the cases of those sub-types relate to the geographical zone in which the disease is reported [4,25,26]. Kasturba Hospital is located in South India, so the sub-type seen will be characteristic of the South Indian population. In our study majority of the population had AIDP variant of GBS which accounted for 64.2% of the patients followed by AMAN in 14.6% of the patients, MFS in 7.5% and lastly AMSAN seen in 6.6% of the patients. From these, MFS showed to have the best prognosis and after further conducting univariate analysis it was proved to result in better outcome, however multivariate analysis did not show significant effect on the outcome. Report by Yitao et al. showed similar results with better prognosis seen in MFS variant of GBS compared to others [4].

On the other hand, on evaluation by univariate analysis, AMSAN variant of GBS was associated with high risk of poor outcome. Among all the variants of GBS, axonal form was associated with poor prognosis and outcome [4,21,27]. Amin et al. supported this observation in his study which confirmed AMSAN variant being linked to worst outcome in GBS [3]. Additionally, Khadilkar et al. also stood by the same observations consistent with the result of this study regarding the sub-types of GBS [28]. However, multivariate analysis proved that there was no significant association between AMSAN variant and outcome in such patients.

Vaccine use has been linked to some cases of GBS, although there is lack of adequate or convincing evidence and most studies do not show any relationship. Combined information from 1992-94 showed a rise in 1 additional GBS case per million following vaccination within 6 weeks, however current data suggests the risk of GBS does not increase following vaccinations against swine flu and influenza [29,30]. Controversial data exists on the same stating Influenza A vaccination following the natural infection with Influenza A helped decreased chances of acquiring the disease [2,26]. In our study vaccination was seen to be a protective factor during univariate analysis, however multivariate analysis proved that there was no significant relationship between vaccination and the outcome in our patient population.

Underlying hypertension along with cardiovascular dysautonomy observed in GBS may result in marked fluctuation of blood pressure. Several theories link hypertension to GBS. It can be explained by sympathetic overactivity supported by high levels of urinary catecholamines [31-33], and plasma norepinephrine [31,32,34] or elevated levels of plasma renin [34]. Other objective evidence reported in GBS patients with autonomic dysfunction include altered levels of plasma cortisol [32,34], 17-hydroxycorticosteroids [32], aldosterone [34], CFS dopamine and serotonin metabolites that may have resulted in hypertension [33]. Evaluation by uni- followed by multi-variante analysis in our study concluded that hypertension was found to be a risk factor for poor outcome in GBS patients. Similarly, hypertension was observed in about 60% of the patients with GBS and it was marked to be a bad prognostic sign leading to poor outcome [35,36]. Gupta et al. through univariate analysis found that cardiovascular complications including hypertension (28.12%) was associated with poor outcome in GBS patients [37]. Yitao et al. also concluded that high blood pressure was demonstrated as poor prognostic factor [4]. However, El-Khayat et al. stated that underlying hypertension did not show any significant statistical difference in their study [27].

Presence of Diabetes Mellitus (DM) can exacerbate the clinical and electrophysiological features of coinciding polyneuropathies including GBS, resulting in poor prognosis and long-term outcome [4,38]. The exact mechanism responsible for DM-induced exacerbation is unclear, but several possibilities are known. First, it may be due to exacerbation or delayed improvement of inflammatory condition in GBS caused by DM, as objective evidence suggest that diabetic patients have chronic low-level inflammation: increased inflammatory markers such as CRP (C-reactive protein), TNF (tumor necrosis factor) and IL-6 (interleukin 6) [39]. Secondly, in subclinical/early DM neuropathy, the axons are partly injured or lost, maybe due to prolonged nerve ischemia [40]. Our study supports the above finding as DM was found to be statistically significant risk factor for poor...
outcome on evaluation by univariate analysis, however, multivariate analysis showed no such association.

Complications associated with the disease, commonly respiratory paralysis, pulmonary embolism, cardiac arrest and sepsis are predictive of poor outcome. Pulmonary embolism was considered as a risk factor resulting in poor outcome in GBS patients on evaluation by univariate analysis, however, no such significant association was observed on evaluation by multivariate analysis.

Approximately 25% of GBS patients have dyspnea and require mechanical ventilation due to the involvement of respiratory muscles [2,18]. This group has been proven to comprise of the largest part of GBS patients with increased disease severity and poor outcome [41] due to various complications associated with ventilation [19,27]. Furthermore, it has been suggested that the outcomes in ventilator dependent group were significantly related to age, duration of ventilation, occurrence of ventilator associated infection, disease progression and ratio of PaO2 to fraction of inspired O2 and pre-intubation maximum inspiratory pressure [41,42]. Our study also confirmed that the requirement of mechanical ventilation is considered as a risk factor associated with poor outcome in GBS patients on evaluation of univariate analysis, however, no significant association was observed on evaluation of multivariate analysis.

In our study, 18.9% of the GBS patients developed respiratory failure and results from univariate analysis suggested that these patients are at risk of poor outcome. Kalita et al. also observed similar results whereby 27.6% of the patients had respiratory compromise, 43% of them needed mechanical ventilation and these patients were associated with poor outcome [19].

In our study, sepsis was found to be a risk factor for poor outcome in patients with GBS. Netto et al. stated that sepsis among other complications significantly caused death (p=0.38), Hughes scale ≤3 (p=0.015), prolonged mechanical ventilation > 21 days (p=0.058) or prolonged hospitalization >36 days (p=0.019) [5].

Two thirds of GBS patients are affected by some cardiovascular abnormalities due to autonomic involvement [43]. According to Gupta et al., cardiovascular complications occurred in 54.2% of patients, and cardiac arrest showed significant association with poor outcome as revealed by the results of univariate analysis [37]. Our study also confirmed that cardiac complications are a risk factor for poor prognosis in patients with GBS.

The cornerstone of therapy in GBS patients is IVIgG and plasmapheresis, and therapy is selected based on patient related, social and economic factors [2]. IVIgG and plasmapheresis combined is not significantly superior over individual treatment options [2,15]. Corticosteroids and Physiotherapy/occupational therapy are also known to be effective in GBS management when combined with the main treatment options [2,15-17]. Out of 212 GBS patients, 178 received therapy. Various treatment options were used for the GBS patients in our study. IVIgG plus physiotherapy/occupational therapy and plasmapheresis plus physiotherapy/occupational therapy showed to have the best prognosis and after further conducting uni- followed by multi-variate analysis, these treatment options were proved to result in better outcome. These combination therapies have not been studied earlier. However, since IVIgG or plasmapheresis have been known to be effective for GBS management, additional benefits of physiotherapy/occupational therapy has led these combinations to result in a better outcome. Small scale studies have shown positive outcomes in terms of strength, endurance, fatigue [16], gait quality and function [17] and in patients who underwent physiotherapy. The remaining 34 patients did not receive any therapy either due to high cost of the treatment or possibly opting to receive treatment at another healthcare center.

The wide confidence intervals may have resulted due to a small sample size.

Limitations
1. The general limitations of a retrospective study apply to this study also. The residual disability associated with GBS cannot be directly assessed.
2. Some clinical parameters that have been concluded as factors affecting outcome in the studies conducted earlier, failed to show statistical difference in our study, such as age, maybe due to confounding factors.
3. Failure to categorize the variant of GBS in some patients due to lack of sufficient data or NCV not conducted for some patients.
4. Our study being retrospective in nature only included information on whether the patients were vaccinated or not. The type of vaccine and time of vaccine was not available to correlate with the onset of GBS.

Conclusion
Guillain Barre syndrome (GBS) is a rare autoimmune neurological disorder in which the body’s immune system attacks part of its peripheral nervous system resulting in limb and cranial nerve weakness often with respiratory compromise and limitation on physical function.

A total of 212 GBS patients were included in the study having a mean age of 39.92±20.09 years with majority being male (n=142, 67%). Out of these 212 patients, 168 (79.2%) showed improvement, whereas the remaining 44 (20.8%) did not show any improvement.

Various factors that may influence the functional recovery of GBS have been previously studied. Our study offers added evidence to the existing literature by providing an insight on the positive and negative factors.
that affect the outcome.

Alcohol intake, medical history of hypertension and complications such as sepsis and cardiac arrest resulted in poor outcome whereas treatment with IVIgG plus Physiotherapy/ Occupational therapy and Plasmapheresis plus Physiotherapy/ Occupational therapy showed better outcome.

Further follow-up studies could be done to determine and manage the residual disabilities associated with GBS to improve patient’s quality of life.

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