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Original Article

Comparison of Intravenous Immunoglobulin (IVIG) and Plasma Exchange in Children with Guillain-Barré Syndrome at a Tertiary Care Hospital in Lahore

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ABSTRACT

Objective: To compare the outcome of IVIG and plasma exchange in treatment of Guillain-Barré Syndrome (GBS) in children.
Study Design: Retrospective Longitudinal Study
Place and Duration of Study: Pediatric Intensive Care Unit (PICU), University of Child Health Sciences and The Children's Hospital, Lahore, Pakistan, from Oct 22 to Sep 23.
Methodology: The study included all pediatric patients aged 1 to 14 years diagnosed with GBS admitted to the ICU. Retrospective data collection was done for the IVIG group, while prospective data collection was done for the plasmapheresis group. Demographics, hospitalization duration, mechanical ventilation period, treatment outcomes, and muscle power improvement were compared between the IVIG and plasmapheresis groups using the Medical Research Council (MRC) Score.
Results: Among 150 patients, 62.7% were male, with mean age 6.19 ± 3.81 years and mean weight 19.75 ± 10.62 kg. The most common EMG/NCS finding was AMAN. Average PICU stay was 33.32 ± 13.79 days, and ventilation duration was 29.22 ± 14.33 days. Both IVIG and plasma groups showed significant muscle power improvement ($p < 0.05$). IVIG patients had shorter PICU stays (27.39 ± 10.50 days) and ventilation durations (23.13 ± 11.56 days) than plasma patients (39.25 ± 14.20 days and 35.31 ± 14.31 days, respectively, $p < 0.05$).
Conclusion: Both IVIG and plasmapheresis are equally effective, but IVIG outperformed plasmapheresis regarding reduced duration of hospitalization and ventilation as well as need for tracheostomy.

Keywords: Guillain-Barré Syndrome, IVIG, Pediatric ICU, Plasmapheresis

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INTRODUCTION

Guillain–Barré syndrome (GBS) is an acute inflammatory polyneuropathy characterized by rapidly progressive, symmetric muscle weakness, absent reflexes, and can involve both demyelination and axonal degeneration.1 It affects approximately 1.[1] to 1.8 per 100,000 people annually, but data specific to Pakistan is lacking.[2] The condition typically begins with weakness in the distal lower extremities and may ascend, potentially involving cranial nerves and leading to symptoms such as ataxia and autonomic dysfunction.[3]

The progression of GBS usually occurs over 4 to 6 weeks, and around 20–30% of patients may experience respiratory failure requiring ICU ventilation.[4] Diagnosis is based on clinical presentation, cerebrospinal fluid analysis, and nerve conduction studies.[5] The primary treatments for GBS are intravenous immunoglobulin (IVIG) and therapeutic plasma exchange. IVIG neutralizes harmful antibodies with a dosage of 0.4g/kg/day for 5 days, while plasma exchange involves removing antibodies from plasma, typically over 5 sessions in 10 days, using 5.0% human albumin solution, 0.9% saline, or fresh frozen plasma.[6]

Research comparing the effectiveness of these treatments has shown mixed results. A study in Egypt found shorter hospital stays and better recovery outcomes with plasma exchange compared to IVIG, which was associated with a higher need for mechanical ventilation and more residual deficits.[7] Conversely, a study in Karachi reported longer pediatric ICU stays and extended ventilation durations with plasma exchange compared to IVIG.[8]

The rationale of the current study is to clarify these conflicting findings and provide data relevant to resource-limited settings like Pakistan. By generating context-specific evidence, it seeks to clarify whether these variations arise from methodological differences, population characteristics, or healthcare system disparities within low- and middle-income countries,

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where clinical resources and diagnostic capacities may be limited.

METHODOLOGY

The study was conducted in Pediatric Intensive Care Unit of The Children's Hospital and The Institute of Child Health, Lahore, Pakistan, from Oct 22 to Sep 23. An ethical letter was obtained from the Institutional Ethical Review Board of The Children's Hospital, Lahore. (No. # 2022-152 CH & ICH). Data from the IVIG cohort were collected retrospectively, and data from Plasmapheresis cohort were collected retrospectively. Sample size was 26, i.e, 13 in each group. It was calculated using the open-epi sample size calculator using a significance level 5%, power 80%, reported incidence of GBS is 1.1/100,000 population/year.[9] But sample size was increased to 150, 75 in each group, as we had a large number of patients presenting with GBS. A non-probability consecutive sampling technique was used.

Inclusion Criteria: All patients diagnosed with GBS from 01 to 14 years of either gender presenting to the Pediatric ICU were included in the study.

Exclusion Criteria: Patients who had expired, patients whose parents did not give consent for treatment, and patients with anoxic brain injury were excluded from the study.

The Medical Research Council (MRC) sum score was used to assess muscle power. It was assessed in 3 muscles of the upper (deltoid, biceps, wrist extensor) and lower limbs (ileopsoas, quadriceps femoris, tibialis anterior) bilaterally. And power was graded according to the following grades: Grade 0 – paralysis, Grade 1 - only a trace or flicker of muscle contraction is seen or felt, Grade 2 - muscle movement is possible with gravity eliminated, Grade 3 - muscle movement is possible against gravity, Grade 4 - muscle strength is reduced, but movement against resistance is possible, and Grade 5 - normal strength. The sum score of 0 is (total paralysis) to 60 (normal strength).[7] Outcome was assessed 14 days after the start of treatment (IVIG and plasmapheresis sessions). An MRC sum score of more than 10 from baseline was labelled as improved.

Data was collected from GBS patients admitted to PICU who met the inclusion criteria. Written, informed consent taken. The collected data was entered and analyzed statistically by using Statistical Package for Social Sciences (SPSS) version 25. Quantitative variables like age, weight and duration of symptoms, duration of PICU stay and duration of mechanical ventilation were presented in the form of mean and standard deviation. Qualitative variables like gender, improvement, residual disability and weaning from respiratory support were presented in the form of frequency and percentage. Effect modifiers like age, duration of symptoms before treatment were controlled through stratification. Plasma exchange and IVIG groups were compared by applying chi-Square test for categorical data. Shapiro-wilk test was used to test normality of numerical data. For non-parametric data e.g., age, weight, duration of PICU stay, duration of mechanical ventilation and MRCS Score before and after treatment were compared in both groups by using Mann-Whitney test. Wilcoxon-signed rank test was applied to compare improvement in muscle power using MRCS Score before and after treatment in each group separately. *p*-value less than or equal to 0.05 was taken as significant.

RESULTS

A total of 150 patients were included in the study. Data on the IVIG cohort were gathered retrospectively, whereas data on the Plasmapheresis cohort were collected prospectively. IVIG was administered to 75 patients, and plasmapheresis was performed on the remaining 75. Electromyography and nerve conduction studies (EMG/NCS) were conducted for all patients, revealing acute motor axonal neuropathy (AMAN) as the most prevalent variant, observed in 75 patients (50%). (Table-I)

About respiratory support, all patients, except one who required continued ventilatory assistance at home upon discharge, were successfully weaned off ventilatory support. Improvement was observed in 107 patients (71.3%). Importantly, there were no recorded instances of mortality among the patients studied. (Table-II)

Table-III demonstrates that in IVIG group, muscle power improved significantly from pre-treatment MRCS Score (Mdn=12) to post-treatment MRCS Score (Mdn=36). Similarly, in Plasmapheresis group, muscle power improved from pre-treatment MRCS Score (Mdn=06) to post-treatment MRCS Score (Mdn=24). All the non-parametric data, including age, weight, duration PICU stay, duration of mechanical ventilation, and MRCS Score before and after treatment, were compared in IVIG and Plasmapheresis groups by using the Mann-Whitney test as shown in the Table-IV.

Table-I: Comparison of Demographics of All Patients, Intravenous Immunoglobulin, and Plasmapheresis Groups (N=150)

Characteristics	All patients	IVIG	Plasmapheresis	*p*-value
Gender Male Female	 94(62.7%) 56 (37.3%)	 44(58.7%) 31(41.3%)	 47(62.7%) 28(37.3%)	1.000
Mean Age (years)	6.19 ±3.81	4.50 ±2.93	7.87±3.86	0.001
Mean weight (kg)	19.75±10.62	14.98±6.66	24.52±11.69	0.001
Residence Urban Rural	 72(48.0%) 78(52.0%)	 34(45.3%) 41(54.7%)	 38(50.7%) 37(49.3%)	0.513
Duration of symptoms at start of treatment <2weeks 2-4weeks >4weeks	 75(50.0%) 58(38.7%) 17(11.3%)	 45(60.0%) 25(33.3%) 05(6.7%)	 30(40.0%) 33(44.0%) 12(16.0%)	0.030
NCS Findings* AIDP AMAN AMSAN CIDP	 34(22.70%) 76(50.70%) 39(26.0%) 01(0.7%)	 24(32.0%) 34(45.3%) 17(22.7%) 00(0.0%)	 10(13.3%) 42(56.0%) 22(29.3%) 01(1.3%)	0.032
Autonomic instability	142 (94.7%)	71(94.7%)	71(94.7%)	1.000
Non-invasive ventilation	07(4.7%)	06(8.0%)	01(1.3%)	0.245
Invasive ventilation	143(95.3%)	69(92.0%)	74(98.7%)	0.116

**IVIG – Intravenous Immunoglobulin,*
NCS- Nerve Conduction Studies; AIDP- Acute Inflammatory Demyelinating Polyradiculoneuropathy;
AMAN-Acute Motor Axonal Neuropathy; AMSAN-Acute Motor Sensory Axonal Neuropathy; CIDP-Chronic Inflammatory Demyelinating Neuropathy

Table-II: Comparison of all patients, Intravenous Immunoglobulin, and Plasmapheresis groups in terms of outcome (n=150)

Characteristics	All patients	IVIG	Plasmapheresis	*p*-Value
Mean duration of PICU stay (days)	33.32 ± 13.79	27.39 ±10.50	39.25±14.20	0.001
Mean duration of Mechanical Ventilation (days)	29.22±14.33	23.13±11.56	35.31±14.31	0.001
Mean MRC Sum Score Before Treatment (range)	10.99±7.63	12.45±7.78	9.53±7.23	0.001
Mean MRC Sum Score After Treatment (range)	30.68±13.36	34.63±12.40	26.59±13.15	0.001
Tracheostomy	63(42.0%)	22(29.3%)	41(54.7%)	0.002
Weaned respiratory support	147(98.0%)	74(98.7%)	73(97.3%)	1.000
Improved	107(71.3%)	57(76.0%)	50(66.7%)	0.206

**IVIG - Intravenous Immunoglobulin, MRC - Medical Research Council, PICU - Pediatric Intensive Care Unit*

It shows that patients in IVIG group differ significantly in age (Mdn=3) and weight (Mdn=12.50) from the plasmapheresis group (Mdn=8, 20, respectively). Duration of PICU stay was significantly higher in the plasmapheresis group (Mdn=38) than in the IVIG group (Mdn=25). Similarly, duration of mechanical ventilation was significantly higher in the plasmapheresis group (Mdn=35)than in the IVIG group (Mdn=22). (Table-IV)

By using the Mann-Whitney test, the MRCS Score before treatment was significantly higher in the IVIG group (Mdn=12) than in the plasmapheresis group (Mdn=6). Similarly, the MRCS Score after treatment was significantly higher in the IVIG group (Mdn=36) than in the plasmapheresis group (Mdn=24).

DISCUSSION

In this study, 62.7% make predominance was aligned with reports of literature. The mean age of participants was 6.19± 3.81 years. Patients treated with IVIG were significantly younger (mean age: 4.50 ± 2.93years) compared to those receiving plasmapheresis (mean age: 7.87± 3.86 years) with significant differences in age. (*p*=0.001). This study found AMAN to be the most common subtype among the participants, aligning with findings from Japan, China, and South America, while contrasting with the more prevalent AIDP seen in Africa, Europe, and North America, potentially due to genetic differences.[10]

In our study, treatment with both IVIG and plasmapheresis was found to be effective. Muscle power, as demonstrated by MRCS score, was considerably improved in both treatment groups. No treatment was found to be statistically superior. Bragazzi *et al.*, reported similar results in their continuum review.[11] However, in this study, the duration of PICU stay was longer for the plasmapheresis group (mean: 39.25± 14.20 days) compared to the IVIG group (mean: 27.39± 10.50days, $p<0.05$), and duration of mechanical ventilation was also found to be longer for the plasmapheresis group (median: 35 days) versus the IVIG group (median: 22 days, *p*=0.001). Abbas *et al.*, assessed the outcome of plasmapheresis in treatment of Guillain-Barré syndrome and factors related to longer hospital duration.[12]

Similarly, Altaf *et al.*, research found that children receiving plasmapheresis had a significantly longer PICU stay (9.45 ± 4.59 days) and prolonged ventilator support (7.33± 3.44 days) compared to those treated with IVIG (4.97± 2.84 days and 2.01± 0.01days, respectively), with both differences being statistically significant ($p < 0.001$).[13] Ali *et al.*, reported significantly shorter ICU stays (20±19.10 days) and earlier weaning from ventilator ($p = 0.002$) for IVIG compared to PE (46.60±30.02 days, $p = 0.001$).[14] Keeping in view of the

Table-III: Comparison of Pre and post-treatment Medical Research Council Sum Score scoring after Intravenous Immunoglobulin and Plasmapheresis treatment by the Wilcoxon signed-rank test

Type of treatment	Median before treatment (ranges)	Median after treatment (ranges)	Test statistic	Z score	*p*-value	Effect size (r)
IVIG	12(0-38)	36(12-56)	2727	7.224	0.001	0.589
Plasma	06(0-40)	24(06-56)	2556	7.329	0.001	0.598

**IVIG – Intravenous Immunoglobulin*

Table-IV: Comparison of Non-Parametric Data Among Intravenous Immunoglobulin and Plasmapheresis Groups by Using Mann-Whitney Test

Parameters		Mean rank	Median	Man Whittney (U)	Z score	*p*-value	Effect size (r)
Age	IVIG	56.41	3	4244	5.400	0.001	0.440
	Plasmapheresis	94.59	8	1381			
Weight	IVIG	54.37	12.50	4397	5.968	0.001	0.487
	Plasmapheresis	96.63	20	1228			
Duration of PICU stay	IVIG	56.84	25	4212	5.265	0.001	0.429
	Plasmapheresis	94.16	38	1413			
Duration of mechanical ventilation	IVIG	56.85	22	4211	5.260	0.001	0.429
	Plasmapheresis	94.15	35	1414			
MRCS before treatment	IVIG	84.13	12	2165	2.555	0.011	0.208
	Plasmapheresis	66.87	6	3460			
MRCS after treatment	IVIG	89.17	36	1787	3.865	0.001	0.315
	Plasmapheresis	61.83	24	3838			

**IVIG - Intravenous Immunoglobulin,*
MRCS - Medical Research Council Score,
PICU - Pediatric Intensive Care Unit,

fact that both PE and IVIG remain the treatment of choice in the management of GBS, yet Nandeesha *et al.*, systematic review also reported that their therapeutic choice remains unclear. But IVIG is considered more user-friendly with a significantly lower patient discontinuation rate than PE. IVIG treatment was found to be significantly more expensive than PE.[15]

In contrast, Mallick et al., found that patients receiving plasmapheresis had significantly shorter hospital stays (15.7± 8 days, p < 0.01) and lower mechanical ventilation rates (12.5%, p < 0.001) compared to those treated with IVIG (29.4 ± 14.7days and 66.66%, respectively). Additionally, plasmapheresis was associated with higher complete recovery rates (59.37%) and fewer residual defects (21.78%) at six-month follow-up, compared to IVIG (recovery23.33%, p < 0.001, and residual deficits 56.66%, p < 0.01).[16]

Beydoun's study noted that plasmapheresis led to longer hospitalizations and increased mortality compared to IVIG.[17] Anwer *et al.* found plasmapheresis had a higher cure rate (100%) compared to IVIG (64%) and steroids (43%).[18] Whereas Zaki *et al.*'s systematic review indicated no significant difference in hospitalization length or ventilation duration between IVIG and PE groups (p = 0.35).19 In our study, tracheostomy was done in 54.7% patients in the plasmapheresis group compared to 29.3% in the IVIG group(p=0.002). Mallick *et al.* showed comparable results.[17]

There was no mortality reported in the index study. In the index study, we observed that both plasmapheresis and IVIg treatments effectively improved muscle power. However, IVIG demonstrated superiority over the plasmapheresis group regarding duration of PICU stay and mechanical ventilation as well as need for tracheostomy. Additional studies need to be done, ensuring the same cohort population for both IVIG and plasmapheresis groups, and the availability of more plasmapheresis machines, reducing the wait time for plasmapheresis so that results can be better compared. Further studies need to be done to include follow-up of patients at 3, 6 months and 1 year interval after treatment.

LIMITATION OF STUDY

The study's limitation stems from the availability of a sole plasmapheresis machine servicing multiple departments. Additionally, age groups and initial disability scores differed between the two groups. Follow-up of these patients at 3-month or 6-month intervals after treatment was not done.

CONCLUSION

Both IVIG and plasmapheresis demonstrate comparable efficacy in ameliorating disability among GBS patients, yet IVIG is associated with reduced duration of hospitalization and ventilation as well as need for tracheostomy.

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Authors' Contribution

Following authors have made substantial contributions to the manuscript as under:

AA & NS: Data acquisition, data analysis, critical review, approval of the final version to be published.

SA & MK: Study design, data interpretation, drafting the manuscript, critical review, approval of the final version to be published.

MP & MS: Conception, data acquisition, drafting the manuscript, approval of the final version to be published.

Authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

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