Pakistan Journal of Neurological Sciences (PJNS)

Volume 13 | Issue 2 Article 10

6-2018

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ASSOCIATION OF SERUM ALBUMIN LEVELS AND GUILLAIN BARRE SYNDROME (GBS) OUTCOME.

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Date of submission: *November 28, 2017* ***Date of revision:*** *February 12, 2018* ***Date of acceptance:*** *February 20, 2018*

ABSTRACT

INTRODUCTION: Guillain-Barre syndrome (GBS) is a polyradiculoneuropathy characterized by a rapidly progressive bilateral paresis of the limbs. Nadir is typically reached within a number of days or weeks, followed by a recovery that is generally much slower and often incomplete. Guillain-Barre syndrome is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots.IVIG and Plasmapheresis are used first line treatments in GBS treatment. For better assessment of treatment response, biomarkers reflecting Plasmapheresis and IVIG efficacy are needed. Aim of this study is to determine serum albumin as an independent biomarker for clinical outcome in plasmapheresis treated-GBS patients.

MATERIAL AND METHODS: This was a descriptive case study conducted in Neurology Department ShaheedZulfiqar Ali Bhutto Medical University Islamabad for the period of six months from July 2017 to December 2017. Serum albumin levels were determined in 70 patients with GBS. Patients were assigned into two groups. One with low albumin level (26 patients, 37.1 %) and other with normal albumin level (44 patients, 62.9%). Every patient underwent same number of sessions of plasmapheresis and assessed clinically by using GBS disability score and Medical Research Council (MRC) sum score for a follow up period of 6 months.

RESULTS: Out of 26 patients with low albumin level 7 patients, 26.9%, had good outcome and 19 patients,73.1%, had poor outcome i.e had significant disability at 6 months follow up with GBS disability scale score of 2 or more.
Out of 44 patients who had normal albumin level 25 patients,45.7%, showed good clinical outcome and 19 patients, 54.3%, showed poor clinical outcome on the basis of GBS disability score and MRC sum score after a period of 6 months. P value was 0.015 and was significant in that higher the albumin levels will be, more chances of having good prognosis.

CONCLUSION: This study determined albumin level as an independent factor for short and long term clinical outcome and prognosis in Guillain Barre Syndrome patients treated with plasmapheresis. However, there is need of prospective studies that should confirm the findings of this study of albumin level as a prognostic biomarker for GBS patient.

Guillain-Barre syndrome (GBS) is a polyradiculoneuropathy characterized by a rapidly progressive bilateral paresis of the limbs. Nadir is typically reached within a number of days or weeks, followed by a recovery that is generally much slower and often incomplete.[1]

The clinical course of GBS follows a typical pattern that can be readily divided into its constituent phases and components (figure-1).[2] Demyelinating and axonal forms of the syndrome occur in varying proportions across different geographical regions.[3]

Guillain-Barre syndrome is usually preceded by infection or other immune stimulation that induces an aberrant autoimmune response targeting peripheral nerves and their spinal roots.[4,5] Despite the positive effect of intravenous immunoglobulin (IVIG) or plasma exchange (PE), about 20% of the patients are unable to walk unaided ('severely affected patients') and remain unable to do so after six months. Moreover, many patients remain otherwise disabled or severely fatigued. Even 3–6 years after onset, GBS had great impact on social life and the ability to perform activities.[6,7] Still, the reasons why some patients respond poorly to IVIG therapy are unknown, and there is an urgent need to find a biomarker that, preferably, can be determined

within the first 2 weeks of onset. Such a biomarker would allow a more personalized approach to monitor treatment efficacy and anticipate outcome.[8,9] Existing prognostic models are based on clinical features, including the extent of muscle weakness and demographic factors, but previous studies failed to identify a serologic biomarker to enhance these models.[10] For better assessment of treatment response, biomarkers reflecting Plasmapheresis and IVIG efficacy are needed. The approach and the measurement of such biomarkers should be easy, accessible, straight forward and accurate, and preferably it should be available with routine diagnostic procedures.

Serum albumin is a protein that binds to the neonatal Fc receptor (FcRn), which transports it back into the circulation and its level is reduced after high-dose IVIG therapy in diseases other than GBS.[11]

Furthermore, serum albumin is identified as an independent factor associated with outcome in amyotrophic lateral sclerosis and failure of IVIG therapy in Kawasaki disease.[12,13] Therefore, serum albumin is an interesting alternative to IgG as a biomarker for assessing the severity of GBS, fitting the profile of a routinely measured protein already established as a prognostic marker in numerous pathologic conditions.[14] Although few studies on serum albumin association with intravenous immunoglobulins-treated guillain barre syndrome are available but no study has been done on serum albumin association with outcome in Plasmapheresis-treated GBS in Pakistan.

In this study, we aimed to find out whether serum albumin levels can serve as a prognostic marker in patients with GBS treated with plasmapheresis. We checked the serumalbumin levels in GBS patients after their initial presentation i.e before plasmapheresis along with routine investigations. Finally, we analyzed whether circulatory albumin levels were associated with disease severity and outcome.

MATERIALS AND METHODS:

This was a descriptive case study conducted in Neurology Department Shaheed Zulfiqar Ali Bhutto Medical University Islamabad for the period of six months from July 2017 to December 2017 after getting permission from ethical committee of the hospital and university. A total of 70 patients of Guillain Barre Syndrome were enrolled using non probability consecutive sampling. Sample size was calculated using WHO sample size calculator. An informed written consent was taken from all patients. All patients of both genders of age 13 to 75 years with Guillain Barre Syndrome were enrolled in this study. GBS was diagnosed on the basis of clinical and electrophysiological criteria. The diagnostic criteria for Guillain Barre Syndrome was defined from National Institute of neurological Disorders and Stroke (NINDS).[15]

For the AXONAL variant of GBS criteria was set not having demyelination and low amplitude of compound muscle action potential (CMAP) in two or more motor nerves in AMAN. For AMSAN no demyelination, low amplitude of compound muscle action potential (CMAP) in two or more nerves as well as low sensory nerve action potentials (SNAP) in two or more nerves. For Miller Fisher variant of GBS reduced or absent SNAPs with evidence of involvement of motor nerves and no demyelination.[16]

Sensory manifestations were determined clinically if patients complained of muscle pain and aches, paresthesias (burning, tingling, pins and needles sensations), numbness in fingers and toes, impaired pin prick, joint position and vibration sensations. Respiratory distress was defined as if patient has single breath count less than twenty.[17]

Patients were divided into two groups i.e patient with low serum albumin levels (3.5mg/dl or below) and patient with normal serum albumin level (3.5-5.5 mg/dl). All 70 patients in both the groups received same number of plasmapheresis. Serum albumin levels were checked before starting plasmapheresis. Patients in both the groups were followed for the period of 6 months and assessed for clinical outcome keeping in mind the association of low and normal albumin levels using Medical Research Council(MRC) sum score, it is a score of six muscles group including shoulder abduction, elbow flexors, wrist extensors, hip flexors, knee extensors and foot dorsiflexors on both sides ranging from 60 (normal) to 0 (quadriplegic), the Modified Rankin Scale (MRS) score of individual muscle ranges from 0 to 5 as shown in figure-1 and GBS disability score ranging from 0 (healthy) to 6 (deceased) as shown in figure-2. Not being able to walk 10 meters independently (GBS disability score >2) at 6 months was regarded as poor outcome.

To assess the possible influence of serum albumin on disease activity and clinical outcome patients were followed and assessed at 0, 1, 2, 4 and 26 weeks interval and GBS disability and MRS sum score was calculated at each stage to determine clinical outcome. Data was entered on a standard performa. Data was analyzed using SPSS version 17. Mean and standard deviations were calculated for numerical variables i.e age. Frequencies and percentages were calculated for categorical variables (gender, outcome).

Chi square test was used to compare the percentages of clinical outcome between two groups. P value of

<0.05 was taken as significant.

Figure-1: GBS disability score

0	A healthy state
1	Minor symptoms and capable of running
2	Able to walk 10 meter or more without assistance but unable to run
3	Able to walk 10 meter across an open space with help
4	Bedridden or chairbound
5	Requiring assisted ventilation for at least part of the day
6	Death

Figure-2: Medical Research Council(MRC) sum score

0	No visible contraction
1	Visible contraction without movement of the limb
2	Active movement of the limb but not against the gravity
3	Active movement against gravity over (almost) the full range
4	Active movement against gravity and resistance
5	Normal power

RESULTS:

Serum albumin levels were determined in 70 patients with GBS with a mean age of 35.3 yeears. Out of 70 patients 45 were males and 25 were females. Patients were assigned into two groups. One with low albumin level (26 patients, 37.1 %) and other with normal albumin level (44 patients, 62.9%) as shown in figure-3. There was no significant age predilection. Albumin levels were obtained on admission. Albumin level with respect to age is shown in figure-4. Every patient underwent same number of sessions of plasmapheresis and assessed clinically by using GBS disability score and MRC sum score. Both axonal and demyelinating variants of GBS were followed and seen for disability. It was noted that the axonal variant of GBS showed poor outcome at the end of follow up period of 6 months.

Figure-3:

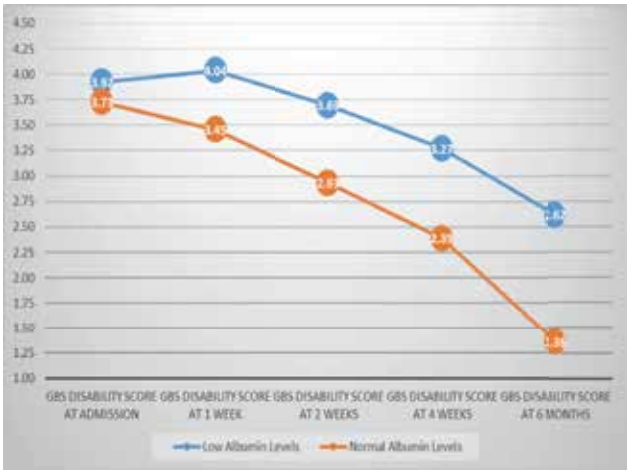
	• Gender					
	Male		Female		Total	
	Count	Column N %	Count	Column N %	Count	Column N %
Albumin Range Low	12	26.7%	14	56.0%	26	37.1%
Normal	33	73.3%	11	44.0%	44	62.9%
Total	45	100.0%	25	100.0%	70	100.0%

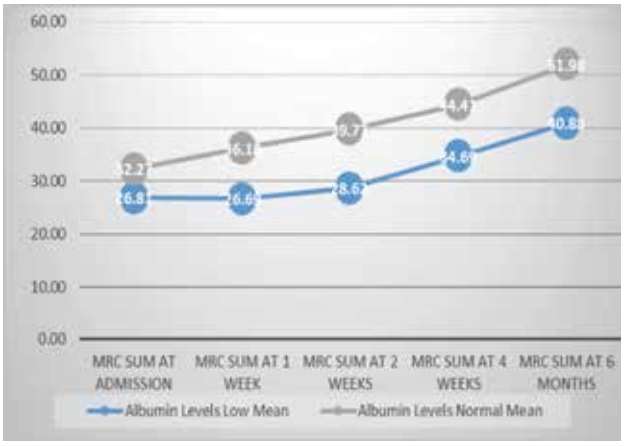
Figure-4:

Count

		Albumin_Range		
		Low	Normal	Total
Age	<20	6	4	10
	20-40	10	23	33
	40-60	8	11	19
	>60	2	6	8
Total		26	44	70

	Albumin Levels	
	Low	Normal
	Mean (SD)	Mean (SD)
GBS disability score at admission	3.92 (0.4)	3.73 (0.8)
GBS disability score at 1 week	4.04 (0.7)	3.45 (0.8)
GBS disability score at 2 weeks	3.69 (0.9)	2.93 (0.9)
GBS disability score at 4 weeks	3.27 (1.0)	2.39 (1.1)
GBS disability score at 6 months	2.62 (1.6)	1.36 (1.5)
MRC sum at admission	26.81 (12.5)	32.27 (13.8)
MRC sum at 1 week	26.69 (13.5)	36.18 (12.4)
MRC sum at 2 weeks	28.62 (14.5)	39.77 (12.9)
MRC sum at 4 weeks	34.69 (14.8)	44.41 (11.2)
MRC sum at 6 months	40.88 (16.3)	51.98 (9.8)





Out of 26 patients with low albumin level 4 patients (15.38%) underwent mechanical ventilation due to respiratory distress. Out of 44 patients with normal albumin 3 patients (6.81%) needed the mechanical ventilation.

Out of 26 patients with low albumin level 7 patients, 26.9%, had good outcome and 19 patients,73.1%,had poor outcome i.e had significant disability at 6 months follow up with GBS disability scale score of 2 or more.

Out of 44 patients who had normal albumin level 25 patients,45.7%, showed good clinical outcome and 19 patients, 54.3%, showed poor clinical outcome on the basis of GBS disability score and MRC sum score after a period of 6 months. These results are showed in figure-5.

P-Value was 0.015 and was significant.

Figure-5:

		Albumin_Range					
		Low		Normal		Total	
		Count	Column N %	Count	Column N %	Count	Column N %
Range_at_6_months	Good Prognosis	7	26.9%	25	56.8%	32	45.7%
	Poor Prognosis	19	73.1%	19	43.2%	38	54.3%
	Total	26	100.0%	44	100.0%	70	100.0%

DISCUSSION:

A positive correlation was observed between serum albumin level and clinical outcome of GBS. With normal albumin level good clinical outcome and low albumin level poor clinical outcome was observed at the end of follow up. In addition, patients not requiring mechanical ventilation also had poor clinical outcome depending upon low albumin levels. Patients who maintained albumin level in normal range showed good clinical improvement indicating albumin level as an independent prognostic factor in GBS. The results of our study are comparable with an international study, Willem-Jan R.et al[18], that established an association of low albumin level with poor outcome in Intravenous Immunoglobulins treated Guillain Barre Syndrome.

The preferable treatment for Guillain Barre Syndrome is Intravenous Immunoglobulins but in resource limited countries like Pakistan affordability is a major issue and plasmapheresis is being done regularly for GBS patients because of its cost effectiveness and easy availability of the procedures at most of the medical centres in Pakistan.

Clinical prognostic models have been developed previously to estimate the chance of respiratory failure and disability at 1, 3 and 6 months.[19-21]

No prognostic biomarkers are available for GBS, an acute and debilitating disease. Biomarkers are of such importance they give an early indication of clinicaloutcome and for optimal care to provide with.

The main causes of a reduction in serum albumin are increased catabolism, decreased

production, and extravasation attributable to increased capillary permeability in the setting of inflammation or severe disease.[14,22,23] In patients with Guillain Barre Syndrome any of the above cause of low albumin level can be found either in isolation or in combination. Regarding prognosis and an indicator for good health albumin has been explored as a marker in numerous diseases.[24]

In a study it was determined that a low serum albumin level is a strong marker of poor outcome in the setting of acute illness.[25,26]

GBS is an also acute illness and needs a prognostic marker to intervene and provide maximum medical care so we tried to find out albumin as an independent model for clinical outcome in Guillain Barre Syndrome. Patients with low albumin levels may also have increased need of ventilatory support and decrease survival ultimately due to disease progression and ventilator associated complications. To prevent such morbidities and mortalities prognostic markers for acute illnesses like GBS are of utmost importance. A study, focusing on ICU and critically ill patients identified serum albumin as a biomarker for survival and the need for mechanical ventilation.[27-29]

Determining the albumin level once and at initial stage also has advantage as its level may change with disease progression and procedure i.e plasmapheresis, related fluctuations of albumin concentrations that may also cause expansion of plasma volume and thereby reducing the albumin levels.

CONCLUSION:

This study determined albumin level, as a part of comprehensive metabolic profile, as an independent factor for short and long term clinical outcome and prognosis in Guillain Barre Syndrome patients treated with plasmapheresis. However, there is need of prospective studies that should confirm the findings of this study of albumin level as a prognostic biomarker for GBS patient.

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Conflict of interest: Author declares no conflict of interest.
Funding disclosure: Nil

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Ghulam Shabbir; data collection, data analysis, manuscript writing, manuscript review
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Danyal Ahmed, data collection, data analysis, manuscript writing, manuscript review