

Original Article

# Guillain-Barre Syndrome and its Prognosis with Hyponatremia

Jerin Romeo<sup>1</sup>, Hemant Mahur<sup>2</sup>, D P Singh<sup>3</sup>, Nitesh Pansari<sup>4</sup>,  
Heeralal Verma<sup>5</sup>, Pavan Kumar KT<sup>6</sup>

<sup>1,5,6</sup>Resident, <sup>2</sup>Associate Professor, <sup>3</sup>Senior Professor, Department of Medicine, RNT Medical College and Associated Group of Hospitals, Udaipur, Rajasthan

## ABSTRACT

**Introduction:** Guillain Barre Syndrome (GBS) can be described as a collection of clinical syndrome that manifest as an acute inflammatory polyradiculopathy with resultant weakness and diminished reflexes. The hyponatremia is a recognized association of GBS and is also known to occur after the administration of intravenous infusion of gamma globulin (IVIG); a treatment often used in management of GBS. Hyponatremia in GBS is very often overlooked entity even though it is well established. The purpose of this study was to document serum sodium concentration in GBS patients before and during management procedures (including IVIG), positive pressure ventilation (PPV) and to assess whether hyponatremia is a predictor of poor outcome.

**Methodology:** All patients (>2 years of age) diagnosed as Guillain-Barre Syndrome (GBS) fulfilling the criteria as modified by Asbury, admitted in the Medicine and Pediatric department of RNT Medical College and Associated Hospital, Udaipur from January 2014 to July 2015 were included in this study. After obtaining clinical history, electrophysiologic studies were performed to determine the GBS subtype. Serum electrolytes were determined at the time of admission of patient and during course of treatment (day 1 and day 3).

**Results:** A total of 50 patients were studied. Male preponderance was observed with the maximum number (38.00%) of patients below 16 years age group and was seen in the months of April to June. All patients received physiotherapy and the nine patients who developed respiratory failure were put on mechanical ventilation. Six

patients required mechanical ventilation inspite of intravenous immunoglobulin (IVIG) therapy. Eight patients received intravenous methylprednisolone (MPS). The mean duration of hospitalization was 8.66 days. Bulbar weakness and need for ventilatory support were higher in GBS with hyponatremia (6 v/s 3).

Serum sodium concentration was low (<135 mmol/L] in 12 out of 50 (24.0%) patients. Eight of them had mild hyponatremia, three patients had moderate hyponatremia, and one patient had severe hyponatremia. Out of 50 patients of GBS, nine patients required mechanical ventilation.

**Conclusion:** Hyponatremia has significant association with severity of GBS and is an indicator of poor prognosis. Hyponatremic patients have a poorer prognosis than eunatremic patients. In GBS, hydroelectrolytic disorders, especially hyponatremia, are processes that mark the prognosis and severity of the disease and must be identified early. Plasma sodium concentrations should be carefully monitored. In the Guillain-Barre syndrome a 'normal' intake of water may prove fatal.

## INTRODUCTION

Guillain-Barre Syndrome (GBS) or acute polyradiculoneuritis is an acute, diffuse post infective disorder of the nervous system involving the spinal roots, the peripheral nerves and occasionally the cranial nerves. It occurs year round at a rate of between 1 and 4 cases per 1,00,000 annually; in the United States, 5000–6000 cases occur per year.<sup>1</sup> Males are at slightly higher risk for GBS than females, and in Western countries adults are more frequently affected than children.<sup>1</sup> It can occur at any age group. The age specific curve seems to show a bimodal distribution, with peaks in young adults and the elderly.<sup>2,3</sup>

There are no consistent geographical variations. However, modest seasonal variations are noted in some series. Syndrome of inappropriate antidiuretic hormone (SIADH) secretion is a common and important electrolyte disorder encountered in GBS.

The hyponatremia is a recognized association of GBS and is also known to occur after the administration of intravenous infusion of gamma globulin (IVIG); a treatment often used in management of GBS. It has significant association with severity of GBS and is an indicator of poor prognosis. It can be symptomatic even though the majority of patients are asymptomatic.<sup>4</sup>

Hyponatremic patients have a poorer prognosis than eunatremic patients; however it is difficult to separate this factor from other poor prognostic factors such as older age and positive pressure ventilation.<sup>5</sup> Hyponatremia in GBS is very often overlooked entity even though it is well established. The purpose of this study was to document serum sodium concentration in GBS patients before and during management procedures (including IVIG), positive pressure ventilation (PPV) and to assess whether hyponatremia is a predictor of poor outcome.

### **METHODS**

All patients (>2 years of age) diagnosed as Guillain Barre Syndrome (GBS) fulfilling the criteria modified by Asbury, admitted in the Medicine and Pediatric department of RNT Medical College and Associated Group of Hospitals, Udaipur from January 2014 to January 2016 were included in this study. 50 patients were prospectively studied in this study. A detailed history with particular attention to the date of onset of neuropathic signs and the tempo of ensuing functional disability was elicited and a clinical examination was performed at admission as per the designed proforma. Repeat examinations of muscle power were performed on alternate days till discharge. Autonomic function tests were performed at the time of admission. Serum electrolytes were determined at the time of admission of patient (within one week of onset of illness) and during course of treatment (day 1 and day 3). During each examination, the following were noted:

- A. Medical Research Council grading of muscle weakness.
- B. Disability grade (0-6) according to the following:
  0. Healthy.
  1. Minor symptoms or signs.
  2. Able to walk 5m without assistance, walking frame, or stick but unable to do manual work including housework, shopping or gardening.
  3. Able to walk 5m with assistance, walking frame, or stick.
  4. Chair/bed bound.
  5. Requiring assisted ventilation (for at least part of day or night).
  6. Dead.

Bedside autonomic function tests were assessed. In addition complaints suggestive of autonomic dysfunction such as excessive sweating, urinary retention and constipation, palpitations, postural giddiness were noted.

Laboratory investigations were performed at the time of admission, including hepatitis B serology and HIV serology, wherever required, cerebrospinal fluid examination was done in most of the patients.

Most of the patients who could afford intravenous immunoglobulin were treated with intravenous immunoglobulin (0.4g/kg for 5 days) and some patients who could not afford intravenous immunoglobulin and progressed clinically were treated with steroids i.e., intravenous methyl prednisolone with informed consent and after explaining the prognosis of disease. Some patients who were not capable to afford intravenous immunoglobulin and who did not progress clinically were treated with supportive therapy only. All patients were treated with physiotherapy and mechanical ventilatory assistance, wherever required. Time taken to reach peak deficit, interval from maximum deficit to onset of improvement (plateau time), duration of ventilatory support required and nature of complications were noted.

SIADH manifests as hyponatremia which can be classified as:

1. Mild Hyponatremia: Sodium (Na) 130-134 mmol/L
2. Moderate Hyponatremia: Sodium (Na) 125-139 mmol/L
3. Severe Hyponatremia: Sodium (Na) <125 mmol/L

**RESULTS**

All 50 patients studied were hospitalized and the average duration of hospital stay was 8.66 days. Thirty five patients (70.00%) were males and fifteen (30.00%) were females. The age of patients ranged from 2 to 65 years (mean age 26.64 years) with the maximum number (38.00%) of patients below 16 years age group. The maximum numbers of cases were seen in the months of April to June. There was higher incidence of GBS from April to September. All patients received physiotherapy and the nine patients who developed respiratory failure were put on mechanical ventilation.

Among these six patients required mechanical ventilation inspite of IVIG therapy. Eight patients received intravenous methylprednisolone(MPS), among this one patient required mechanical ventilation (MV). Patients with intravenous steroids did not show much benefit over supportive treatment. 13 patients received only conservative treatment without any steroid or intravenous immunoglobulins. Among these two patients required mechanical ventilation. On day of admission serum sodium concentration was low (<135 mmol/L) in 12 out of 50 (24%) patients. Eight of them had mild (130-134), three patients had moderate (125-129), and one patient had severe hyponatremia (<125). On third day of admission, mild hyponatremia persisted in seven patients, moderate hyponatremia persisted in two patients and severe hyponatremia persisted in one patient (Table 1).

**Table 1: Serum sodium level of the patients with Guillain-Barre Syndrome**

Serum Sodium (mEq/L)	No. of patients (Day 1)	No. of patients (Day 3)
Severe Hyponatremia (<125)	1	1
Moderate Hyponatremia (125-129)	3	2
Mild Hyponatremia (130-134)	8	7
Eunatremic (>135)	38	40
<b>Total</b>	<b>50</b>	<b>50</b>

Three out of 8 (37.5%) patients with mild hyponatremia required mechanical ventilation whereas 2 out of 3 (66.6%) patients with moderate hyponatremia required mechanical ventilation and one (100%) patient with severe hyponatremia required mechanical ventilation. Three out of 38 eunatremic patients also required mechanical ventilation (Table 1, 2).

**Table 2: Patients on mechanical ventilation with Guillain-Barre Syndrome**

Serum Sodium (mEq/L)	Mechanical Ventilator		
	Not Required	Required	Total
Hyponatremia (<135)	6	6	12
Eunatremia (135-149)	35	3	38
<b>Total</b>	<b>41</b>	<b>9</b>	<b>50</b>

27 patients out of 50 received IVIG in addition to conservative therapy and among them nine patients had hyponatremia (five patients at the time of onset of disease and four new patients developed hyponatremia during or after IVIG therapy) (9 v/s 3; p=0.09) (Table 3).

**Table 3: Patients on intravenous immunoglobulin (IVIG) treatment with Guillain-Barre Syndrome**

Serum Sodium (mEq/L)	Intravenous Immunoglobulin (IVIG) Treatment		
	Not Required	Required	Total
Hyponatremia (<135)	3	9	12
Eunatremia (135-149)	20	18	38
<b>Total</b>	<b>23</b>	<b>27</b>	<b>50</b>

Overall hospital mortality rate in Guillain Barre Syndrome is 2%. One hyponatremic patient died, but none eunatremic patient died. Most of the patients (31 out of 50) remained hospitalized for a period of 5 to 9 days. The mean duration of hospitalization was 8.66 days with a minimum duration of hospitalization of 3 days and maximum duration of hospitalization of 82 days.

**DISCUSSION**

Hyponatremia is a common and important electrolyte disorder encountered in GBS. In this study we correlated the prognosis of hyponatremia in relation with serum sodium concentration and not with other factors. We found that hyponatremia has significant association with severity of GBS and is an indicator of poor prognosis.

Out of all study patients, maximum numbers of patients were of less than 16 years age group (38%) and there was a male preponderance (70%) in the study which is in conformity with the report by Robert M et al.<sup>6</sup> However,

previous study<sup>7</sup> showed an equal incidence in males and females. A higher incidence of GBS during months of April to September is observed in this study in contrast with the majority of studies in literature.<sup>6</sup> However, a few studies have noted a seasonal clustering of cases. Kaur et al<sup>8</sup> reported an increased incidence in summer and autumn. Peter C. Dowling<sup>7</sup> also noted an increase in summer.

Saifudheen K et al<sup>9</sup> found that SIADH was detected in 24 of the 50 patients (48%) at some stage of the illness (median 8.8 days after GBS onset). Six of them had mild SIADH, 12 patients had moderate SIADH, and six patients had severe SIADH. Colls BM<sup>10</sup> found that serum sodium concentration was significantly low (<133 mmol/L) in 26 out of 84 (31%) patients. T Monzón Vázquez, et al<sup>11</sup> found that hyponatremia is often associated with SIADH or salt wasting syndrome in patients with central nervous system disorders.

In the study 12 patients out of total 50 patients had hyponatremia at the initial presentation and six (50%) required mechanical ventilation whereas 6 patients did not develop any significant respiratory difficulty (Table 1 and 3). Bulbar weakness and need for ventilatory support were higher in GBS with hyponatremia (6 v/s 3; p<0.001) in accordance with Saifudheen K et al<sup>9</sup> who noted that bulbar weakness and need for ventilatory support were higher in GBS with SIADH (13 v/s 1, p<0.001).

Colls BM<sup>10</sup> found that in 12 patients, hyponatremia developed during or after IVIG, suggesting that pseudo-hyponatremia was a contributing factor. Kloesel B, Hickson LJ<sup>12</sup> mentioned that although a rare condition, both GBS and its treatment, IVIG, should be considered in the differential diagnosis of hyponatremia. One patient died in this study. This patient developed respiratory failure and required assisted mechanical ventilation. Case fatality in this study was 2%. Mortality in GBS varies from 1.3% to 13% in different series with a mean of about 6%. Winer et al<sup>13</sup> reported 13% mortality in his study of 100 patients. NK Singh et al<sup>14</sup> noted 8% mortality. Colls BM<sup>10</sup> found that six (7%) hyponatremic patients died, but no eunatremic or slightly hyponatremic patient died (p=0.001). In summary, hyponatremia, delayed onset of recovery from paralysis, requirement of mechanical ventilatory support are significant prognostic factors of outcome in GBS.

## CONCLUSION

In GBS, hydroelectrolytic disorders, especially hyponatremia mark the prognosis and severity of the disease and must be identified early. Patients with acute polyradiculitis should, therefore, have their plasma-sodium concentrations carefully monitored and the significance of hyponatremia appreciated. In Guillain-Barre syndrome a 'normal' intake of water may prove fatal.

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**Corresponding Author**

Dr Hemant Mahur, D-6, M B Hospital Campus,  
Udaipur- 313001.  
email:drhemantmahur@yahoo.com

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