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Frequency of Syndrome of Inappropriate Antidiuretic Hormone in Patients with Guillain-Barré Syndrome Presenting at Tertiary Care Hospital, Karachi

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ABSTRACT

Guillain-Barré Syndrome (GBS) is a condition that causes inflammation in the nerves and can sometimes lead to a problem called SIADH. SIADH happens when the body makes too much of a hormone that controls water balance, leading to low sodium levels in the blood. **Objective:** To determine the frequency of SIADH inpatients with GBS presenting at Tertiary Care Hospital, Karachi. **Methods:** This Cross-sectional study was conducted at Department of Neurology, Civil Hospital, Karachi, from 12-07-19 till 12-01-20. Total 119 GBS patients who met the inclusion criteria were included. A brief history was recorded, and demographic details were noted in the form. Numerical data were summarized using simple descriptive statistics.Categorical data were shown as numbers and percentages. **Results:** 71 (59.7%) were male and 48 (40.3%) were female. Mean age in the study was 46.78 ± 2.81 years. Whereas, Mean age, duration of symptoms, serum sodium and GC Sinour study was 46.78 ± 2.81 years, 25 ± 10.78 hours, 128.65 ± 7.52 mmol/L and 11.21 ± 3.14 % respectively. Out of 119 GBS patients, 21% had SIADH. **Conclusions:** This study showed that SIADH is present in significant proportion of patients with GBS. Thus, it is essential to focus on a comprehensive way of management of GBS and its comorbidities rather than primarily treating the neurological symptoms.

INTRODUCTION

Guillain-Barré Syndrome (GBS) is the most common cause of sudden muscle weakness in developed countries [1]. GBS has different types, including AIDP (affects nerve coating), AMAN (affects motor nerves), AMSAN (affects both motor and sensory nerves), and Miller Fisher Syndrome (affects coordination and reflexes) [2]. GBS can cause a range of problems, including sudden weakness that affects both sides of the body, usually starting in the legs and moving upwards. It also leads to the loss of reflexes, changes in sensation, and issues with the autonomic nervous system, which controls functions like blood pressure and heart rate [3]. The condition occurs worldwide and can affect people of all ages and genders. Research suggests that GBS happens when the immune system mistakenly attacks parts of the peripheral nerves. Scientists have found that immune cells (T-lymphocytes) and antibodies target proteins in nerve coverings, such as myelin antigens (P0, P2), glycoproteins, and glycolipids [4]. Other general inflammatory processes also contribute to nerve damage [4]. The exact cause of GBS is still unclear.

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However, it is believed to be triggered by an infection, as about two-thirds of patients experience an infection before developing symptoms [5]. Sodium is the main electrolyte found outside the cells and plays a key role in maintaining the body's fluid balance. Disorders related to sodium levels can lead to serious health complications and even death [6]. Because sodium imbalances are common and can cause neurological problems, it is important to determine the exact cause before starting treatment [7]. Electrolyte imbalances in patients with neurological diseases occur at similar rates as in other medical conditions and are mainly influenced by underlying health problems [8]. The exact cause of SIADH in GBS is not fully understood. One possible explanation is that damage to certain brain cells (in the hypothalamus) causes the inappropriate release of antidiuretic hormone (ADH) into the bloodstream [9, 10]. Another theory suggests that the body's osmoreceptors, which regulate water balance, become misregulated [11]. Recent studies have linked interleukin-6 (IL-6), an inflammatory molecule, to SIADH in GBS. IL-6 can trigger the release of vasopressin (ADH) by stimulating specific brain regions that control thirst and fluid balance [12, 13]. Research has also shown that IL-6-producing immune cells increase early in the acute phase of GBS, further supporting its role in the condition. Elevated IL-6 in acute GBS may trigger inappropriate ADH secretion via the hypothalamic-pituitary axis, contributing to hyponatremia and electrolyte imbalance [14]. Saifudheen et al., found the prevalence of SIADH to be 48 % in patients presenting with GBS [15]. Scarcity of the locally available literature on the frequency of SIADH in patients with GBS is important to determine in order to establish the local perspective. The results of this study will serves as a cornerstone for various healthcare institutions and guidelines for early detection in case of finding positive association in the study. Thus, the patients with GBS can be referred and managed in specialized units. Data from this study would potentially offer new information to clinician that can influence clinical practice of GBS, quality of life, and patient outcomes in the population in light of variable demographic, socioeconomic and co-morbid conditions. Hence the study was designed to aimed in determining the frequency of SIADH in patients with GBS presenting at Tertiary Care Hospital, Karachi.

METHODS

A cross-sectional study was conducted in the Neurology Department of Civil Hospital, Karachi, from July, 2019, to January, 2020, using non-probability consecutive sampling. The study included newly diagnosed GBS patients aged 20-65 years of either gender who presented within 24 hours of symptom onset. Patients who did not consent or had a history of psychiatric disorders such as mania, bipolar disorder, or PTSD, as well as those with lung cancer, thyroid disorders, addison's disease, tuberculosis, asthma, kidney disease, heart conditions (heart failure or myocardial infarction), chronic liver disease, chronic obstructive pulmonary disease (COPD), or central nervous system diseases like head trauma or multiple sclerosis, were excluded from the study. The study was approved by CPSP vide letter no. CPSP/REU/NEU-2017-183-420; dated: July 12, 2019. The required sample size was determined to be 119 patients, based on an estimated SIADH frequency of 48%, [15] a 9% margin of error, and a 95% confidence level, calculated using WHO software. A brief medical history, including illness duration and demographic details, was collected at admission. If the patient had difficulty speaking (aphasia) or a low Glasgow Coma Scale (GCS) score, the information was gathered from their attendants. GBS was diagnosed using Brighton's criteria. within 24 hours followed by a plateau phase, and no other identifiable cause for the weakness [16].SIADH in GBS patients was diagnosed if plasmasodiumconcentration<135mmol/L, plasmaosmolality<280mOsmol/kg, urineosmolality >100mOsmol/kg, urinarysodiumconcentration>30mmol/L, and clinically normal fluid balance (euvolemia) indicated by a supine heartrate≤100bpm and systolic blood pressure ≥100 mmHg.Additionally, patients had to show no signs of adrenal dysfunction (ACTH: 10–60 pg/mL) or thyroid dysfunction and must not have used diuretics in the past three months [17].SPSS version 21.0 was used for data analysis.Chi square was applied to check for the association between SIADH and other categorical variables. P value <0.05 was set as statistically-significant.

RESULTS

Among 19 GBS patients, the mean age of participant was reported to be 46.78 ± 2.81 years with most of the participants belonging to the > 50 years of age group. 71 (59.7%) participants were male and 48 (40.3%) were female. The presence of comorbidities of diabetes mellitus type II was 22.7% (n=27), hypertension was 30.3% (n=36) prevalent and 16.8% (n=20) population were smokers, (Table 1).

Table 1: Sample Description (N=119)

Variables	Value Frequency (%)
Age	
Mean Age of Participants	46.78 ± 2.81
20 - 30 Years	4 (3.36%)
31 - 40 Years	37 (31.09%)
41 - 50 Years	20 (16.81%)
51 - 60 Years	58 (48.74%)
Duration Of Symptoms (Hours)	
Mean Duration of Symptoms	25 ± 10.78
< 48 Hours	56 (47.06%)
> 48 Hours	63 (52.94%)

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Gender	
Male	48 (40.34%)
Female	71 (59.66%)
Diabetes Mellitus	
Present	27 (2.69%)
Absent	92 (771.31%)
Hypertension	
Present	36 (30.25%)
Absent	83 (69.75%)
Smoking Status	
Smoker	20 (16.81%)
Non Smoker	99 (83.19%)

Out of 119 GBS patients, 25 (21%) had and did not have SIADH, as shown in Figure 1.

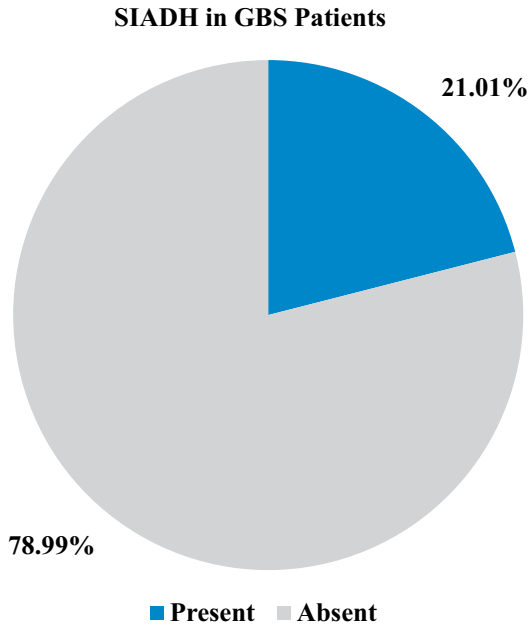

Figure 1: Percentage of Syndrome of Inappropriate Antidiuretic Hormone Secretion among patients of Guillain–Barré Syndrome

The relation between age, gender and duration of symptoms with that of presence of SIADH is showed in Table 2. Age group between 31 to 40 and 51 to 60 has the highest prevalence of SIADH.While 52% (13) of SIADH patients were male.The SIADH was more prevalent in patients who had the duration of symptoms of > 48-hours which was statistically significant (p=0.014).

Table 2: SIADH According To Age, Gender And Duration Of Symptoms Status (N=119)

Groups	Frequency (%)	SIADH		p-Value
		Present Frequency (%)	Absent Frequency (%)	
Age (Years)				
20-30 Years	04 (3.4%)	01 (4%)	03 (3.2%)	0.34
31-40 Years	37 (31.1%)	11 (44%)	26 (27.7%)	
41-50 Years	20 (16.8%)	02 (8%)	18 (19.1%)	
51-60 Years	58 (48.7%)	11 (44%)	47 (50%)	
Gender				
Male	71 (59.7%)	13 (52%)	58 (61.7%)	0.25
Female	48 (40.3%)	12 (48%)	36 (38.3%)	
Duration Of Symptoms				
< 48 Hours	56 (47.1%)	15 (60%)	41 (43.6%)	0.014*
> 48 Hours	63 (52.9%)	10 (40%)	53 (56.4%)	

**Statistically-significant(Chi-square)*

A small portion of patients had the diabetes mellitus along with the SIADH (p=0.28). One-fourth (24%; n=6) patients with SIADH were having comorbidity of hypertension (0.17). A very small portion i.e. 03 (12%) of people with SIADH were smokers. (p=0.09). None of the association was found to be statistically significant (Table 3).

Table 3: SIADH According To Comorbidities (N=119)

Groups	Frequency (%)	SIADH		p-Value
		Present Frequency (%)	Absent Frequency (%)	
Diabetes Mellitus				
Present	27 (22.7%)	07 (28%)	20 (21.3%)	0.28
Negative	92 (77.3%)	18 (72%)	74 (78.7%)	
Hypertension				
Present	36 (30.3%)	06 (24%)	30 (31.9%)	0.17
Negative	83 (69.7%)	19 (76%)	64 (68.1%)	
Smoking Status				
Smokers	20 (16.8%)	03 (12%)	17 (18.1%)	0.09
Non-Smokers	99 (83.2%)	22 (88%)	77 (81.9%)	

DISCUSSION

The results of these study revealed that 21% of the 119 GBS patients had SIADH, consistent with previous literature that indicates SIADH as a recognized but underreported complication of GBS.SIADH is characterized by hyponatremia resulting from excessive antidiuretic hormone (ADH) secretion, leading to impaired water excretion and dilutional hyponatremia. In the present study, the mean serum sodium level among participants was 128.65 ± 7.52 mmol/L, which falls below the normal reference range (135-145 mmol/L), supporting the diagnosis of SIADH in a subset of patients. This finding is comparable to a study conducted by Santoro *et al.*, where hyponatremia was observed in 18.4% of GBS patients, with a mean sodium level of 127.8 ± 6.4 mmol/L [18].The prevalence of SIADH in GBS varies across populations and study designs.For instance, a study conducted in the United Kingdom by James and Jose, reported a SIADH frequency of 25%, slightly higher than these findings [19]. Similarly, a cohort study by Shah PM *et al.*, found that 22% of GBS patients developed SIADH, reinforcing that the frequency observed in this study aligns with global trends [20].These variations can be attributed to differences in patient demographics, severity of GBS, and diagnostic criteria for SIADH across studies.Demographically, this study found that SIADH predominantly affected middle-

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aged and older adults, with most participants being in the 51–60-year age group (48.74%).This is consistent with international studies that indicate older age as a risk factor for SIADH due to decreased renal water excretion and increased sensitivity to ADH [19, 20].The duration of symptoms also appeared to influence the occurrence of SIADH, as more than half of the participants (52.94%) had symptoms lasting longer than 48 hours before presentation.Prolonged illness duration has been associated with increased autonomic dysfunction, which may further contribute to SIADH development [21].The highest prevalence of SIADH was observed in the 31–40 and 51–60 age groups, consistent with international studies that suggest middle-aged and older adults are more susceptible to SIADH due to decreased renal sodium regulation and increased ADH sensitivity [18].A study by James *et al.*, similarly found that SIADH was more frequent in patients above 40 years of age, reinforcing the notion that autonomic dysfunction, a hallmark of GBS, is more pronounced in older populations [19].Gender-wise, this study found that 52% of SIADH patients were male, though the association was not statistically significant.This contrasts with a study by Shah PM *et al.*, which reported a higher prevalence of SIADH in female GBS patients, suggesting potential regional or genetic variations [20]. The non-significant p-value (0.25) in this study indicated that gender alone may not be a decisive factor in SIADH development among GBS patients.A key finding was that SIADH was significantly more prevalent in patients with a symptom duration of more than 48 hours (p=0.014). This aligns with existing literature, as prolonged disease duration is linked to worsening autonomic dysfunction, which may enhance inappropriate ADH secretion [21]. The study also analyzed comorbidities such as diabetes mellitus, hypertension, and smoking. None of these factors showed a significant association with SIADH, consistent with previous research suggesting that autonomic dysfunction rather than metabolic or cardiovascular conditions primarily drives SIADH in GBS [19, 21].

CONCLUSIONS

The study showed that SIADH is present in significant proportion of patients with GBS and is prevalence is associated with longer duration of symptoms (>48-hours). Strategies aimed at preventing hyponatremia in high-risk populations need to be optimized.

Authors Contribution

Conceptualization: MK
Methodology: MK, IA
Formal analysis: MS
Writing, review and editing: MK, SGA, FH, TD, MS, IA

All authors have read and agreed to the published version of the manuscript

Conflicts of Interest

All the authors declare no conflict of interest.

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