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Guillain-Barré Syndrome: Prevalence and Long-Term Factors Impacting Bladder Function in an Australian Community Cohort

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Background and Purpose Urinary dysfunction is associated with significant morbidity in persons with Guillain-Barré Syndrome (GBS). The aim of this study was to describe prevalence and long-term impact of bladder dysfunction on daily activities and quality of life (QoL) in persons in chronic phase of GBS and to examine the relationships between commonly used continence measures in this cohort.

Methods Prospective cohort ($n=66$) following GBS treatment (1996-2009) was recruited from a tertiary hospital and assessed using standardised measures for bladder dysfunction: American Urological Association (AUA) Symptom Index, Incontinence Impact Questionnaire, Urogenital Distress Inventory.

Results Sixty-six participants (64% male, mean age 56 years, median disease duration of 6.1 years) completed the study. Of these more than half reported nocturia and one-third reported urinary urgency and frequency. Urinary problems impacted on participants' daily activities: physical recreation (21%), emotional health and mood (17%), entertainment (14%), participation and mobility (>30 min) (12%), and performance of household chores (8%). Since GBS, 49% reported interference of urinary symptoms with daily life to some extent; and adverse impact on QoL (10.6%). Significant relationship between bladder symptoms; and the level of urogenital distress ($p<0.001$) and the impact of urinary problems ($p<0.001$), was noted. Higher scores on the bladder scales showed significant correlations with psychological, functional and participation scales. The single QoL item (AUA scale) correlated significantly with all other bladder scales ($\rho=0.63-0.86$). This can be a potential 'screening tool' to identify patients for further assessment.

Conclusions Bladder dysfunction in chronic phase of GBS is not well studied. More research in longer-term screening and outcomes for bladder intervention are needed for integrated care and to guide treating clinicians.

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Key Words Guillain-Barré Syndrome, rehabilitation, urinary tract, disability, participation.

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Introduction

Guillain-Barré Syndrome (GBS), an acute demyelinating polyradiculopathy due to inflammation of the peripheral nerves

and nerve roots presents as an evolving acute polyneuritis, and can cause severe motor deficits (symmetrical ascending paralysis), autonomic dysfunction and respiratory failure.^{1,2} Overall, worldwide annual incidence rate of GBS is 1-2 per 100000,³ can occur at any age and with a male preponderance.⁴ Despite available treatment, GBS is associated with significant mortality and morbidity,⁵ and 20% may have residual permanent severe disability.⁶ The distal motor weakness, autonomic disturbances and psychological issues are the key

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features of GBS. Although majority of GBS survivors (75%) have good motor outcomes (i.e., ability to walk independently),⁷ the impact of GBS on activities of daily living, work, social activities and health-related quality of life (QoL) is considerable at 2-6 years after onset and persists beyond this time.⁸⁻¹¹

Autonomic dysfunction in GBS, including the prevalence of urinary dysfunction in up to a quarter of persons with GBS (pwGBS) has been reported.¹²⁻¹⁵ One study ($n=28$) reported 25% of pwGBS had bladder disturbance, characterized by voiding difficulty, urinary retention, nocturnal urinary frequency and occasionally incontinence.¹² Other studies report similar prevalence (27.7%) of urinary dysfunction in pwGBS, including urinary retention (9.2%).¹³ In a study of factors impacting longer-term health-related outcomes in pwGBS ($n=76$), 17% reported ongoing bladder dysfunction (urgency, frequency or nocturia).¹¹ Few studies however, report on the mechanism of bladder dysfunction and/or urodynamic data in this population.¹³ Lower urinary tract dysfunction in pwGBS may include: detrusor acontractility, disturbed bladder sensation and non-relaxing urethral sphincter, causing symptoms (voiding difficulty, urinary retention, frequency, and occasionally overflow incontinence).^{12,13} The underlying mechanisms for urinary dysfunction appear to involve both hypo- and hyper-active lumbosacral nerves with underactive detrusor, overactive detrusor, and to a lesser extent a hyperactive sphincter.¹³

With improved management of GBS and good prognosis generally, issues related to the longer-term health, wellbeing and participation become increasingly important. The pwGBS discharged into the community continue to improve over many months, but may have issues including urinary problems in the transition period, that may limit activity and restrict participation. Various studies suggest longer-term supportive care for pwGBS in the community.^{2,11,16} The existing studies^{12,13,17-21} however, report urinary dysfunction in acute phase of GBS only, while those in the chronic phase in the community have not been studied. The primary aim of this study is to describe the prevalence, disease characteristics and factors impacting bladder dysfunction and impact on QoL in pwGBS in the post-acute phase in the community. A secondary objective is to evaluate relationships between the various common bladder outcome measures in clinical settings in this population.

Methods

Participants and setting

This prospective cross-sectional study was part of a larger research programme examining the effectiveness of rehabilitation in pwGBS at the Royal Melbourne Hospital (RMH), a tertiary referral centre in Victoria, Australia. The RMH GBS programme provides integrated neurological and rehabilita-

tion treatment for inpatients and ambulatory care, 5 days per week for 3-6 weeks. The aim is to reduce patient symptoms (including urinary urgency, frequency, incontinence, pain), and improve activity and participation. The study was approved by RMH ethics committee (HREC no: 2008.171).

The participant selection criteria and methodology have been described previously.^{11,22} Consecutive participants with 'definite' GBS¹⁵ (first admission episode only) treated at the RMH between 1996-2009, were recruited from the RMH Database for this study. The source of these participants was a pool of persons residing in the community, referred to the RMH from public and private medical clinics across greater Melbourne in Victoria. All participants were aged >18 years, able to communicate in English, had confirmed diagnosis of GBS defined by the National Institute of Neurologic Disorders and Stroke clinical criteria,¹⁵ and assessed by an independent neurologist at RMH. Those institutionalised or in care facilities were excluded.

Procedure

All eligible participants ($n=76$) were contacted by mail and invited to participate in the study. A total of 68 who returned signed consent forms were recruited. Of these 66 participants completed the assessment. Two participants were relocated and were unable to be contacted (Fig. 1).

An independent trained researcher (LO), assessed all participants face-to-face (in hospital clinic or in their homes) using a structured format. The participants completed various standardized instruments (see Measures below), and were asked to focus on urinary symptoms experienced over the last 6 months since GBS. Each assessment took approximately 40 minutes. Appropriate rest breaks provided during the assessment. The assessors did not prompt patients, but provided assistance for those who had difficulty completing the questionnaires. All assessments were secured and filed, and opened at the end of data collection at the time of entry into the database by primary researcher (BA).

Measurement

Standardized definitions recommended by the International Continence Society were used for the terminologies related to urinary dysfunction.^{23,24} The International Classification of Functioning, Disability and Health (ICF), a standardised frame work advocated by the World Health Organisation, was used as a conceptual basis for choice of best outcomes for measurement.²⁵

American Urological Association (AUA) Symptom Index²⁶ assessed urinary symptoms (7 questions) and QoL (1 item) (see below). For each urinary symptom the participant chose one of six responses (0-5) indicating severity of the particular

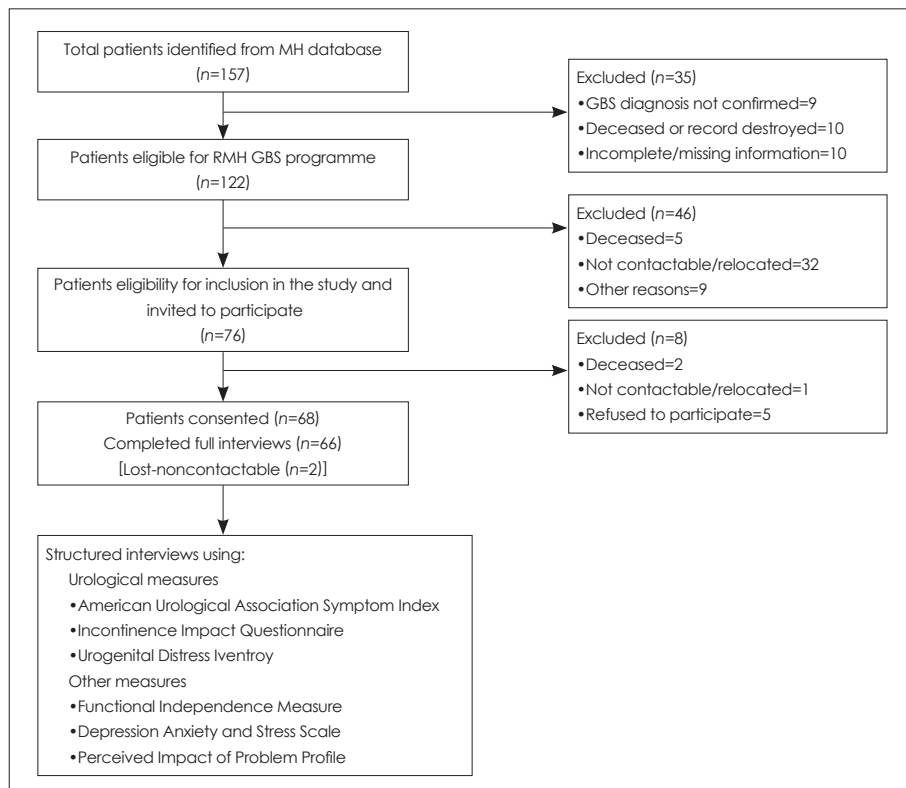


Fig. 1. Flow chart of recruitment process. GBS: Guillain-Barré Syndrome, MH: Melbourne Health, RMH: Royal Melbourne Hospital.

symptom. The total score ranges from 0 to 35 (asymptomatic to very symptomatic).

Incontinence Impact Questionnaire (IIQ7)^{27,28} (abbreviated version) assessed the impact of urinary dysfunction in 4 domains (physical activity, social relationships, travel and emotional health) using a 4-point response scale (0=not at all to 3=greatly).

Urogenital Distress Inventory (UDI6)²⁸ (abbreviated version) assessed three domains (symptoms related to stress urinary incontinence, detrusor overactivity and bladder outlet obstruction) using a 4 point response scale (not at all, slightly, moderately and greatly). UDI6 is designed to complement the IIQ7 by assessing the degree to which the symptoms associated with urinary dysfunction are troubling.

Single QoL question for bladder: a single question of the AUA measure²⁶ (above) assessed QoL of the participants due to urinary symptoms: ‘If you were to spend the rest of your life with your urinary condition, just the way it is now, how would you feel about that?’ The participants rated their responses on a 7-point response scale (ranging from 0=delighted to 6=terrible).

In addition, participants were also asked ‘how much does the urinary problem interfere with your life since your GBS?’ Responses to these were rated on a 4-point Likert scale (1=not at all, 2=a little, 3=somewhat, 4=a great deal).

Other measures

Depression Anxiety Stress Scale-21 (DASS),²⁹ consists of three 7-item self-report scales, measuring the negative emotional states of depression, anxiety and stress. Participants rated the extent to which they experienced each state over the past week on a 4-point Likert rating scale. Subscale scores were derived by totalling the scores, and multiplying by two to ensure consistent interpretation with the longer DASS 42-item version.

Perceived Impact of Problem Profile (PIPP),³⁰ a 23-item scale with five subscales (Mobility, Self-care, Relationships, Participation and Psychological-Wellbeing), assessed the impact associated with a health condition. For each item, respondents were asked to rate ‘how much impact has your current health problem (GBS)’ had on (item of function or activity) using a 6-point scale (‘no impact’ to ‘extreme impact’), with high scores indicating greater impact.

Functional Independence Measure (FIM) (motor),³¹ a 13 item scale with four subscales (Self-care, Transfers, Locomotion, Sphincter control) assessed function (activity) and need for assistance. Each item was rated on a scale of 1 to 7 (1=total assistance, 7=independent). The score reflects burden of care in each area measured.

Statistical analysis

A series of descriptive analyses (n, %) were conducted for

each of the scales to describe the reported bladder symptoms. Cronbach alpha coefficients were calculated for all scales, with values greater than 0.7 indicating sufficient internal consistency and Spearman Rank Order Correlation coefficients were used to explore relationships among the scale scores. Sensitivity and specificity of various cut points were calculated for the single AUA QoL item.

To investigate the potential use of this single item as a screening tool, a binary logistic regression was used assessing its ability to predict scores above and below the AUA severity cut points (mild versus moderate/severe). Given the skewed distributions, continuous predictor variables were split at the median to form approximately equal groups for comparison and non-parametric analyses (Mann-Whitney U tests) were performed to check for age and disease duration (<4 years, ≥4 years) in scores on the bladder scales.

Results

Of 68 eligible pwGBS who returned signed consent forms, 66 participants completed the assessment (Fig. 1). Those who did not participate in the study were not different compared with those who consented in terms of age, gender, GBS duration or median scores for measures used. The mean age of participants was 55.6 years (SD 18.1 years) and median time since diagnosis was 6.1 (IQR 2.7-9.5) years, with 59% with disease duration over 4 years. Sixty-four percent of the participants were male (none had prostate hypertrophy) (Table 1). Participants reporting urinary symptoms did not have a urinary tract infection and were not taking any medications that could affect bladder function.

Impairment and disability

Table 2 shows the presence of urinary symptoms (AUA scores). The most commonly reported symptom was nocturia reported by more than half (59.1%), followed by urgency (39.4%), with 22.8% of participants experiencing this almost or more than half of the time. One third (33.3%) participants

reported frequency. On the AUA severity scale, as expected 46 (69.7%) of participants were rated as 'mild', 16 (24.2%) as 'moderate' and only 4 (6.1%) as 'severe'.

A number of participants (28.8%) reported being bothered 'slightly' or 'moderately' by frequent urination. Other issues reported which bothered the participant 'moderately' or 'greatly', were urine leakage associated with urgency (15.1%), or physical activity (13.5%) (UDI6) (Table 3).

Table 1. Demographic and disease characteristics of the participants (n=66)

Characteristic	Statistic
Gender	
Male (n, %)	42 (63.6)
Age	
Mean (SD)	55.6 (18.1)
Range	19-90
Years since diagnosis	
Median (IQR)	6.1 (2.7, 9.5)
Length of stay-acute (days)	
Median (IQR)	9.0 (7.0, 15.0)
Range	1-123
ICU admission (n, %)	10 (15.1)
ICU length of stay (days) (n=10)	
Median (IQR)	5.0 (3.0, 10.8)
Clinical symptoms and signs (n, %)	
Pain	40 (60.6)
Facial weakness	22 (33.3)
Dysarthria	14 (21.2)
Dysphagia	11 (16.7)
Ophthalmoplegia	10 (15.2)
Treatment received (n, %)	
Plasma exchange	12 (18.2)
Intravenous immunoglobulin	55 (83.3)
Discharge destination (n, %)	
Community (home)	33 (50.0)
Other rehabilitation facility	26 (39.4)

ICU: intensive care unit, IQR: inter quartile range, n: total number, SD: standard deviation.

Table 2. American Urological Association Incontinence Score (AUA) (n=66) showing severity of bladder symptoms in persons with GBS (n, %)

	Not at all	<1 in 5 times	<Half the time	≈Half the time	>Half the time	Almost always
Incomplete emptying	53 (80.3%)	3 (4.5%)	4 (6.1%)	2 (3.0%)	0 (0%)	4 (6.1%)
Frequency	44 (66.7%)	7 (10.6%)	3 (4.5%)	5 (7.6%)	3 (4.5%)	4 (6.1%)
Intermittency	48 (72.7%)	5 (7.6%)	3 (4.5%)	4 (6.1%)	2 (3.0%)	4 (6.1%)
Urgency	40 (60.6%)	7 (10.6%)	4 (6.1%)	5 (7.6%)	4 (6.1%)	6 (9.1%)
Weak stream	44 (66.7%)	6 (9.1%)	3 (4.5%)	8 (12.1%)	2 (3.0%)	3 (4.5%)
Straining	58 (87.9%)	2 (3.0%)	0	3 (4.5%)	2 (3.0%)	1 (1.5%)
Nocturia*	None	1 visit	2 visit	3 visit	4 visit	5 visits
	27 (40.9%)	20 (0.3%)	7 (10.6%)	10 (15.2%)	2 (3.0%)	0

*Visits to toilet per night.

AUA: American Urological Association, GBS: Guillain-Barré Syndrome.

Disability and participation

Participants were rated how much their urinary problems interfered with their lives since GBS. Overall, 15.1% of the participants reported that bladder problems caused ‘some-what’, or ‘a great deal’ of interference with their lives.

A single item AUA scale assessed the impact of urinary symptoms on QoL. Only 7 participants (10.6%) were dissatisfied with their QoL, while a quarter (22.7%) reported their QoL as mixed (i.e., neither delighted nor terrible), due to current urinary symptoms.

A number of pwGBS reported that urinary problems impacted ‘slightly’ or ‘moderately’ or ‘greatly’ (IIQ7) in their various daily activities: physical recreation (21.2%), entertainment activities (13.6%), social activities (12.1%), ability to travel >30 min (12.1%), and to perform household chores (7.6%). A significant portion of pwGBS also reported that urinary problems impacted their emotional health (16.7%), causing feelings of frustration (Table 4).

Relationships amongst the scales

A number of different scales (AUA, UDI6, IIQ7) were used in this study to assess bladder dysfunction. Descriptive statistics and correlations amongst the scale scores are summarised in Table 5. The internal consistency reliability of these scales was adequate (all Cronbach alpha values exceeding 0.85) (Table 5).

Moderately strong, significant relationships was noted between levels of symptoms (AUA) and level of urogenital distress (UDI6 rho=0.79, p<0.001) and the impact of bladder dysfunction (IIQ7 rho=0.56, p<0.001). As expected, partici-

pants with high levels of urogenital distress reported greater impact of bladder dysfunction on their lives (rho=0.79, p<0.001). Scores on these bladder scales showed significant correlations with a number of subscales of the FIM, PIPP and DASS (Table 5). All scales showed significant correlations with the DASS subscales, with high scores on the bladder scales associated with higher levels of anxiety, depression and stress. Low but significant correlations were observed between the bladder scales and the FIM Mobility and Locomotion scales, and the PIPP Participation, Mobility, Relationship and Psychological subscales.

Assessment of screening item for bladder symptoms

A substantial, significant correlations between single AUA item assessing impact of bladder symptoms on QoL and all other bladder scales used in this study (rho=0.63 to 0.86). Logistic regression analyses were used to assess the predictive power of the single QoL item (divided into two groups: 0-2, 3-6) to determine AUA severity (mild vs. moderate/severe). Participants recording scores above 3 on the single QoL item were 23 times more likely than those with scores between 0 and 2 to fall into the moderate/severe AUA group (OR=23.64, 95% CI: 4.63, 120.81). Fig. 2 shows the ability of the single QoL item (AUA scale) to distinguish participants with low versus high urinary symptoms.

Factors impacting on bladder problems

Mann-Whitney U tests revealed significant differences be-

Table 3. Urogenital Distress Inventory (n=66) assessing degree of ‘troubling’ associated with urinary dysfunction in persons with GBS (n, %)

	Not at all	Slightly	Moderately	Greatly
Frequent urination	47 (71.2%)	13 (19.7%)	6 (9.1%)	0
Urine leakage related to urgency	45 (68.2%)	11 (16.7%)	8 (12.1%)	2 (3.0%)
Urine leakage related to activity	46 (69.7%)	11 (16.7%)	8 (12.1%)	1 (1.5%)
Small amounts of urine leakage (drops)	47 (71.2%)	11 (16.7%)	7 (10.6%)	1 (1.5%)
Difficulty emptying your bladder	53 (80.3%)	9 (13.6%)	3 (4.5%)	1 (1.5%)
Pain or discomfort	53 (80.3%)	10 (15.2%)	3 (4.5%)	0

GBS: Guillain-Barré Syndrome.

Table 4. Incontinence Impact Questionnaire (n=66) assessing the impact of urinary dysfunction in everyday life domains in persons with GBS (n, %)

	Not at all	Slightly	Moderately	Greatly
Ability to do household chores	61 (92.4%)	3 (4.5%)	2 (3.0%)	0
Physical recreation	52 (78.8%)	10 (15.2%)	4 (6.1%)	0
Entertainment activities	57 (86.4%)	7 (10.2%)	2 (3.0%)	0
Ability to travel >30 min from home	58 (87.9%)	5 (7.6%)	3 (4.5%)	0
Participation in social activities	58 (87.9%)	5 (7.6%)	3 (4.5%)	0
Emotional health	55 (83.3%)	10 (15.2%)	1 (1.5%)	0
Feeling frustrated	55 (83.3%)	9 (13.6%)	0	2 (3.0%)

GBS: Guillain-Barré Syndrome.

tween males and females in scores on the IIQ7 ($p=0.01$) and UDI6 ($p=0.01$) but no difference in scores on the AUA ($p=0.19$) and the single QOL item ($p=0.08$). Correlation coefficients between scale scores and age and disease duration were very low, with none exceeding 0.30.

Discussion

To our knowledge, this is the first study to report bladder dysfunction and impact on pwGBS in chronic phase in the community (median GBS duration 6.1 years). Urinary dysfunction caused long-term disability in this cohort with more than half participants reporting nocturia, one-third reporting urinary frequency and urinary urgency. Almost one-half reported interference of urinary problems with daily life to some extent over a longer-term. These findings are comparable with the existing literature of reported frequency of bladder dysfunction ranging from 11-28%,^{12,13,18} and suggest that bladder dysfunction should be addressed in symptomatic pwGBS.^{15,32} Bladder dysfunction impacted mainly on participants' physical, recreation/entertainment activities and emotional health and less so, on travel or ability to perform household chores. In contrast with other studies,^{12,13,18} fewer participants (11%) reported dissatisfaction with their QoL due to bladder problems. Many factors impact QoL and there may be 'response shift' phenomenon,³³ this needs further evaluation.

In this study there were weak, but statistically significant relationships between urinary symptoms (AUA), level of urinary distress (UDI6) and impact on participants' lives (IIQ7). The single item QoL for urinary problems (AUA Scale) showed strong significant correlations with all other bladder scales, making it a potential 'screening tool' for routine clinical use to identify patients for further assessment. These findings are consistent with other neurological populations (multiple sclerosis), where self-reported bladder and bowel problems were found to be associated with lower scores on QoL scales.³⁴ Bladder scales also showed significant correlations with the DASS - anxiety, depression and stress subscales, FIM - mobility and locomotion subscales, and PIPP - participation, mobility, relationship and psychological subscales. More research into the correlations between subjective impact reported by the participant and type of bladder dysfunction is needed.

The exact etiology and mechanism of underlying urinary dysfunction in GBS is still uncertain.^{18,20} The urodynamic findings reported in literature include: detrusor areflexia (post-ganglionic, parasympathetic, cholinergic pelvic nerve dysfunction), non-relaxing urethral sphincter during voiding (sphincter dysfunction), impaired bladder sensation (damage to afferent fibres from bladder wall or potential overdistension

injury during initial retention period), and/or detrusor over-activity.^{12,13,17,19,20} Other contributing factors suggested include peripheral nerve lesions and pelvic nerve irritation.²⁰ Urodynamic studies in the chronic phase of GBS for symptomatic patients may help clarify such issues in future patients.

This cross-sectional study was conducted in the 'real world' setting of a busy public hospital with finite resources. There are a number of limitations in this study which may limit generalizability of the findings. This study utilized a relatively small sample from a single tertiary hospital from a metropolitan region. There is a potential of recruitment bias, as the participants were from the larger study programme, listed on a single RMH database who agreed to participate. The participants in this study however are similar to GBS cohorts in other studies in terms of their demographic and disease characteristics. Information on urinary symptoms, duration of indwelling catheterization and/or urodynamic studies conducted during the acute phase for participants were not available. These may have provided a more detailed pattern of symptoms during the course of disease. The high correlations between the 'bladder specific' scales reported may be due to the fact that their items cover overlapping concepts.

It is difficult to compare our findings with other reports due to lack of studies assessing bladder dysfunction in the longer-term. Further studies are needed to replicate these findings in other cohorts and settings. In an attempt to reduce recall bias, all questions were limited in the main to the current situation. We acknowledge that problems not included within the domains of the outcome measures used were not able to be identified; the measures used however were broad and expansive. We were unable to establish causations, as all findings in this study are correlational in nature. Impact of bladder problems on their families/carers and the community; costs associated with these problems and the treatment responses were not assessed as they were beyond the scope of this preliminary study.

Urinary dysfunction in pwGBS in the chronic phase can be associated with significant morbidity and impacts QoL in the longer-term. The clinical implications from these findings support comprehensive evaluation (voiding history, urinalysis, potentially urodynamic studies for symptomatic patients and those with significant abnormalities), early intervention and education for bladder management for pwGBS. The treatment goals include achieving social continence, reduction in symptoms, regular and complete emptying of the bladder at appropriate intervals, infection prevention and preservation of renal function. Although bladder management can occur in the community, many pwGBS with urinary symptoms may require skilled multidisciplinary intervention offered by rehabilitation and continence services. Patient care and clinical research in this area is under-resourced. Improved awareness

and understanding of currently available treatment options can improve patient outcomes. Clinically robust trials are needed to assess the outcomes of bladder intervention in this population to build evidence for integrated care, guide treating clinicians and improve delivery of quality care.

Conflicts of Interest

The authors have no financial conflicts of interest.

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