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Reported fatigue in people after Guillain-Barré Syndrome: a retrospective national survey in the UK

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ABSTRACT

Aim. Despite continuing functional recovery over time, fatigue remains a persistent feature of post-acute Guillain-Barré Syndrome (GBS). The aim of this study was to determine the prevalence of fatigue in people after GBS and investigate its associations with other factors after GBS.

Methods. Validated questionnaires including the SF-36 and fatigue severity scale were sent to members of the GBS support group, a UK wide patient and carer organisation.

Results. A total of 884 questionnaires were returned (58% response rate). Respondents' answers demonstrated that those with severe fatigue following GBS had spent longer in hospital than those who were not severely fatigued ($P=0.003$). Poorer mental health was also associated with more severe fatigue. A strong predictor of prolonged fatigue was discharge from hospital in a wheelchair (OR=2.37, 95% CI 1.52 to 3.71, $P<0.001$) but the severity of fatigue appeared to be independent of recovery of mobility (Kendall's $\tau_b=0.03$, $P=0.2$).

Conclusion. This survey is the largest study of fatigue in people after GBS. Its findings demonstrate that fatigue remains a persistent problem for many people after GBS. More severe fatigue was associated with decreased health related quality of life and increased levels of depression and anxiety in people after GBS. Whilst the severity of fatigue was significantly associated with poorer mobility on discharge, there was no association between the recovery of mobility after discharge and fatigue severity. This indicates that whilst other impairments and activity limitations improved over time, fatigue did not and implies that more severe fatigue is not simply an indicator of a more severe presentation of GBS. Whilst the reasons for persistent severe fatigue remain unclear, this study indicates that further investigations of mobility, mental health and fatigue are warranted so that targeted interventions can be put in place to manage this debilitating complication. (*It J Physiotherapy* 2013;3:154-60)

KEY WORDS: Guillain-Barré Syndrome - Rehabilitation - Fatigue - Mobility.

Guillain-Barré Syndrome (GBS) is an inflammatory peripheral neuropathy affecting 1-2 people per 100,000.¹ In addition to symptoms of weakness, sensory alterations and pain, increased persistent feelings of fatigue are reported to affect up to 80% of people after GBS and which may remain even when other symptoms have improved or disappeared.² The severity of experienced fatigue is more common in women

and those over 50 but appears independent of both the subtype of GBS and antecedent infection.³ Nonetheless, severe feelings of fatigue have a considerable impact upon psychosocial and physical functioning and contribute to persistent activity limitations.^{4, 5} However, the factors precipitating severe fatigue in people after GBS are unclear.^{6, 7} This study aimed to describe the prevalence of feelings of fatigue and identify pos-

sible contributors to the severity of the feelings by undertaking a survey of people after GBS who were members of the GBS Support Group (GBSSG) in the United Kingdom.

Materials and methods

A questionnaire based survey design was utilised. Questionnaires (detailed below) were posted to 1535 members of the GBSSG in January 2007. Only those members with a confirmed diagnosis of GBS were asked to complete the questionnaires and a covering letter asked that those with chronic inflammatory demyelinating polyneuropathy (CIDP) or other forms of peripheral neuropathy should not answer the questionnaire as there was no way of screening out these members. The questionnaires asked for general information (age, gender, time since diagnosis, duration of inpatient stay, mobility on discharge), perceived physical condition (F-Score)⁸ at worst and currently, current health related quality of life (Medical Outcomes Short form 36 questionnaire, SF36),⁹ current mobility, anxiety and depression (Hospital Anxiety and Depression Scale, HADS)¹⁰ and current feelings of fatigue (Fatigue Severity Scale, FSS).¹¹

Once distributed, the investigators had no further direct contact with the volunteers but a notice was placed on the Group's website after six months encouraging suitable members to participate if they had not already so. Data were collected over a one year period.

Ethical approval was granted by the University of Manchester Ethics Committee.

Data analysis

Data were initially analysed to determine respondents with or without severe fatigue using the mean scores on the FSS; if respondents' mean score on the FSS was 5 or over they were considered to demonstrate severe feelings of fatigue.¹² Demographic and clinical characteristics were then analysed according to whether or not the respondent reported severe fatigue. Categorical variables were summarised using numbers and percentages and compared by group using Pearson's chi-square test. Ordinal

and interval/ratio variables were summarised using medians and ranges and compared by group (severe fatigue or not severe fatigue) using Mann-Whitney tests. Level of mobility at discharge and at the time of the survey was determined from the F-score and ranked in terms of the degree to which respondents required support for ambulation: walking independently; using walking aids [stick(s), crutch(es) or frame]; self-propelled in a wheelchair; pushed in a wheelchair.

The association between variables and the FSS score was estimated using Kendall's tau_b correlation which avoids the introduction of a potential artefact when a continuous variable (*e.g.*, the FSS score) is dichotomised.¹³

The association between key predictor variables adjusted for age and gender and whether or not the respondent was currently severely fatigued was estimated using logistic regression; that between key variables and the FSS score was estimated using multiple linear regression. All analysis was undertaken using SPSS Release 15. Residuals from multiple regressions were skewed, so the analysis was repeated using a transformation of FSS scores. However, the same results were obtained and for ease of interpretation, the results for untransformed FSS score are presented here.

Results

The response rate was 58% (N.=884) over the 12 month data collection period. Of the 884 responses, 703 questionnaires were complete for the data of interest and were analysed (Table I).

Three hundred and ninety eight (56.6%) respondents reported severe feelings of fatigue (mean FSS ≥ 5.0). These respondents had significantly worse scores on all SF-36 subscales, HADS anxiety and depression and current F-score ($P < 0.001$; Table II). Poorer SF36 subscale scores also correlated significantly with worsened FSS scores.

Respondents with severe fatigue had experienced a significantly longer inpatient stay (median 70 days v 49 days, $P = 0.003$). However, adjusted for age, gender and mobility on discharge, duration of inpatient stay was not significantly

TABLE I.—*Demographic and mobility characteristics in severely fatigued and not severely fatigued respondents.*

| Characteristic | Severely fatigued ¹ (N.=398) | Not severely fatigued (N.=305) | Difference between severely fatigued and not severely fatigued | Association with FSS ² score | |
|-----------------------------------|--|-----------------------------------|---|---|------------------|
| | Median (range) | Median (range) | P | Kendall's tau _b | P |
| Age (years) | 66 (22 to 96) | 65 (19 to 87) | 0.350 | 0.03 | 0.224 |
| Time since diagnosis (years) | 6.3 (0.2 to 51.4) | 7.2 (0.1 to 58.0) | 0.361 | -0.01 | 0.816 |
| Duration of inpatient stay (days) | 70 (2 to 820) | 49 (2 to 1277) | 0.003 | 0.08 | 0.005 |
| | N (%) | N (%) | | | |
| Female | 206 (51.8) | 149 (48.4) | 0.373 | 0.03 | 0.411 |
| Mobility on discharge | | | <0.001 | | |
| Walking without aids | 47 (12.0) | 53 (17.5) | 0.040 | -0.10 | 0.002 |
| Walking with aids | 202 (51.7) | 168 (55.6) | 0.299 | -0.01 | 0.677 |
| Self-propelled/power wheelchair | 34 (8.7) | 34 (11.3) | 0.261 | -0.01 | 0.646 |
| Pushed in wheelchair | 102 (26.1) | 36 (11.9) | <0.001 | 0.14 | <0.001 |
| Other | 6 (1.5) | 11 (3.6) | 0.075 | -0.07 | 0.022 |

¹ FSS ≥5, ² FSS: Fatigue Severity Scale.TABLE II.—*Anxiety, depression and function in severely fatigued and not severely fatigued respondents.*

| Characteristic | Severely fatigued ¹ (n=398) | Not severely fatigued (n=305) | Difference between severely fatigued and not severely fatigued | Association with FSS ² score | |
|-------------------------------|---|----------------------------------|---|---|------------------|
| | Median (range) | Median (range) | p | Kendall's tau _b | P |
| HADS ³ Anxiety | 8 (0 to 21) | 4 (0 to 18) | <0.001 | 0.24 | <0.001 |
| HADS Depression | 7 (0 to 21) | 2 (0 to 20) | <0.001 | 0.43 | <0.001 |
| F-score ⁴ at worst | 5 (1 to 6) | 5 (1 to 6) | 0.247 | 0.02 | 0.596 |
| Current F-score | 3 (1 to 5) | 2 (1 to 5) | <0.001 | 0.37 | <0.001 |

¹ FSS ≥5, ² FSS: Fatigue Severity Scale, ³ HADS: Hospital Anxiety and Depression Scale, ⁴ F-score: perceived physical condition.

associated with being severely fatigued (Odds Ratio, OR=1.00, 95% Confidence Interval, CI: 0.999 to 1.001, P=0.89) or the FSS score (B=0.00, 95% CI -0.001 to 0.001, P=0.76).

The F score at nadir was not significantly different for gender, age or the time since diagnosis. However, mobility at discharge from hospital was significantly poorer in respondents who reported severe fatigue (Table I) and severely fatigued respondents appeared more dependent at discharge. There was a significant improvement in mobility level from discharge to the point of the survey (P<0.001; N.=453 improved, N.=91 declined from discharge). Although there was a significant association between greater fatigue and poorer mobility on discharge (Table I), the change in the level of mobility from discharge to the respondents' current mobility was not sig-

nificantly associated with their severity of fatigue (Kendall's tau_b=0.03, P=0.2).

The regression analyses (Table III) showed that being pushed in a wheelchair at discharge was the only mobility category significantly associated with being severely fatigued (OR=2.37, 95% CI 1.52 to 3.71, P<0.001) and it was positively and moderately associated with a higher FSS score (B=-0.55, 95% CI 0.21 to 0.89, P=0.001). Walking without aids at discharge was significantly associated with lower fatigue levels (FSS scores, B=-0.57, 95% CI -0.96 to -0.19, P=0.004).

Discussion

Feelings of fatigue are common in people after GBS.¹⁴ This study is the largest survey of feelings of fatigue in people after GBS and provides im-

TABLE III.—*Adjusted associations between key predictors and being severely fatigued and Fatigue Severity Scale (FSS) score (N.=645).*

| Predictor | Being severely fatigued ¹ using logistic regression ² | | | FSS score using linear regression ³ | | |
|--|--|--------------|------------------|---|-----------------|--------------|
| | Odds ratio | 95% CI | P | B | 95% CI | P |
| Age | 1.01 | 0.99 to 1.02 | 0.384 | 0.01 | -0.002 to 0.02 | 0.138 |
| Female | 1.23 | 0.90 to 1.70 | 0.197 | 0.14 | -0.12 to 0.39 | 0.305 |
| Duration of inpatient stay (days) | 1.00 | 0.99 to 1.01 | 0.886 | 0.000 | -0.001 to 0.001 | 0.755 |
| Walking without aids at discharge | 0.74 | 0.46 to 1.18 | 0.210 | -0.57 | -0.96 to -0.19 | 0.004 |
| Self-propelled/powered wheelchair at discharge | 0.86 | 0.48 to 1.55 | 0.620 | 0.09 | -0.40 to 0.57 | 0.727 |
| Pushed in wheelchair at discharge | 2.37 | 1.52 to 3.71 | <0.001 | 0.55 | 0.21 to 0.89 | 0.001 |
| Other mobility at discharge | 0.49 | 0.16 to 1.52 | 0.218 | -0.74 | -1.63 to 0.16 | 0.105 |

¹ FSS ≥ 5 , ² model $\chi^2=27.20$; df: 7, $P<0.001$; Nagelkerke $R^2=0.06$, ³ ANOVA $F=4.74$, df=7 and 637, $P<0.001$; adjusted $R^2=0.04$.

portant indications of the nature and prevalence of fatigue many years after nadir.

The response rate of the survey was moderate (58%) and was similar to a postal survey of fatigue conducted in Norway (60%⁷). All members of the GBSSG were sent the survey but members with other conditions, such as CIPD, or members who were a relative of someone with GBS were asked not to complete the questionnaire, reducing the response rate. As such, the response rate of 58% should be considered as a conservative estimate. The proportion of those in the group with CIPD and other associated conditions is unknown as such the true rate of response is likely to have been much higher than 58%.

This study found that severe fatigue was present in over half of all respondents (57%; $N=398$). This indicates that fatigue is a persistent symptom of GBS and agrees with the findings of others. However, levels in the current study were somewhat lower than a survey from the Netherlands (80% of 113 patients, 83 with GBS)¹⁵ but higher than the proportion of patients reporting severe fatigue in a similar survey in a smaller sample in Norway (38% of 50 patients).⁷ Two recent studies which examined the presence of severe fatigue many years after GBS reported slightly lower levels of severe fatigue (42% and 35% of 24 and 29 patients respectively), although their samples were much smaller than the current study which may account for this difference.¹⁶

Respondents were an average over six years after nadir which indicates that fatigue continues

to be a significant problem for people many years after the onset of GBS. However, the relatively long time since nadir challenges the accuracy of the recall of symptoms. The results of this study are also limited as some respondents could have been more motivated to complete and return the questionnaire if they felt that they had not fully recovered, which may have inevitably biased the sample.

The findings demonstrated that respondents with severe fatigue had poorer health related quality of life. This finding is supported by others who have reported that greater fatigue was significantly associated with poorer functioning and quality of life in people with peripheral neuropathy.^{6, 17} However, the severity of fatigue was not significantly associated with age or gender which contradicts the findings from one study of 100 people that found fatigue was significantly more severe in women and those over 50 years.¹⁷

As shown in Table II, scores of anxiety and depression were still within or just above normal levels in the current study¹⁰ but respondents with more severe fatigue demonstrated higher levels of anxiety and depression when compared to those with little or no fatigue. This is a novel finding as others have reported few differences in anxiety and depression between people with and without severe fatigue after GBS.^{7, 17} Furthermore, anti-depressant medication has shown little benefit on fatigue in people after GBS, suggesting that mood and fatigue are unconnected.¹⁸ However, the current study could not determine if a greater severity of fatigue is symptomatic of poorer mood or if

increased anxiety and depression occurred secondary to greater feelings of fatigue. It is also possible that the tools used to measure mood had items which could also represent fatigue or the physical symptoms of GBS (*e.g.*, “I feel as if I am slowed down”) which could have artificially increased scores and associations with the FSS. Future work could utilise tools that do not include physical symptoms of mood in order to reduce this potential limitation.

Mobility at discharge was strongly associated with current levels of fatigue, despite many respondents being many years after the onset of their illness. This initially suggested that worsened fatigue was an indicator of a more severe condition, and as the patient recovered, the severity of fatigue would also improve. However, whilst mobility had significantly improved since discharge (N.=453 improved, N.=91 declined, median mobility at discharge: 3.5, median mobility at time of survey: 1, $P<0.001$) implying significant recovery of impairments and activity limitations, the current levels of fatigue were not associated with this change. This finding indicates the severity of fatigue cannot be assumed to change alongside other symptoms after GBS and that severe fatigue may be present despite relatively good recovery of other impairments. However, others have argued that greater feelings of fatigue are simply another symptom of a worsened condition,⁷ contradicting the findings of the current study. Rekand *et al.* (2009) also reported that people after GBS with severe fatigue had a two-fold risk of having significant muscle weakness, suggesting that greater fatigue was directly associated with a more severe presentation of GBS and/or incomplete recovery. Conversely, others have found that the level of fatigue was not linked to the severity of GBS at nadir or the course of recovery in 100 people at least one year after the onset of GBS.¹⁷ Similarly, there were no associations between fatigue severity and nerve conduction velocity distributions in 13 “neurologically well recovered” participants one year after GBS and 2 people with CIDP, implying that the severity of fatigue was independent of neurological and other impairments.¹⁹

One potential explanation for this finding is

that people who were most limited in their mobility at discharge are likely to have taken longer to become more mobile and increase their independence. In turn, this longer duration of recovery may have meant that, over time, some respondents became less motivated to return to their pre-morbid hobbies and occupations or no longer had access to rehabilitation services and support to enable them to return to activities such as sport. Indeed, people several years after the nadir of GBS are recognised to have difficulty returning to sports²⁰ and employment²¹ despite substantial clinical recovery. In the current study, despite becoming ambulant over time and returning to some activities, some respondents could have undergone cardiovascular de-conditioning. A reduction in daily activities brought about by the physical sequelae of GBS and/or by feelings of severe fatigue could elicit considerable de-conditioning so that even simple activities are perceived as effortful, tiring and increase the severity of fatigue. Conversely, it is equally possible that severe feelings of fatigue reduced participation and activity in some respondents, which would also result in reduced cardiovascular fitness.²² The link between fitness and fatigue is unclear but others have found significantly reduced feelings of fatigue in people several years after the nadir of GBS after their participation in an exercise programme, suggesting there is some association.²³⁻²⁵ The finding of the present study suggests that poorer mobility at discharge increased the likelihood of developing more severe fatigue, despite recovery of mobility. This highlights that people who are discharged from hospital using a wheelchair after GBS could benefit from further targeted and possibly prolonged interventions. Further research is warranted to determine if a greater duration of, and/or more intensive rehabilitation, could decrease the severity of fatigue in people who are less mobile after GBS.

However, it is acknowledged that there are many reasons that influence the duration of inpatient stay, in addition to the level of physical functioning. Social, personal and psychological factors such as the desire for patients to return to their family and loved ones, social circumstances or simply pressure on hospital beds which pre-

cipitates discharge of patients for whom little more can be offered other than continued therapy (which can be conducted in the community) and natural recovery are all likely to influence discharge planning. However, it is clear that discharge is likely to precipitate a reduction in the amount of therapy offered to patients²⁶ which could slow functional recovery. Future work could seek to identify factors that influence the timing of hospital discharge for people after GBS and investigate the provision of rehabilitation services for this patient group.

Conclusions

This is the largest study of fatigue in people after GBS. Although tempered by the effect of recall and the self-selected sample, the findings show that people with more severe levels of fatigue have greater levels of anxiety and depression and poorer quality of life. They also show that severe fatigue several years after nadir may be associated with the level of mobility at discharge. However, whilst mobility significantly improved over time, the severity of fatigue was not associated with this improvement, suggesting that other factors may influence fatigue and that greater fatigue is not simply an indicator of a more severe disease course. Further work is now needed to investigate other factors that may contribute to severe fatigue including cardiovascular fitness and mental health and to devise targeted rehabilitation programmes to manage fatigue in people after GBS. However, the results of this study indicate that persistent fatigue is a problem for many people several years after nadir and suggest that longer follow up and monitoring of fatigue could be indicated particularly for those who have the greatest limitations in mobility on discharge from inpatient care.

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