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Pain determinants and quality of life in Guillain-Barre syndrome: a prospective cohort study

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ABSTRACT

Background Pain is a serious manifestation in both the acute and chronic stages of Guillain-Barre syndrome (GBS). We evaluated the frequency, characteristics and associated factors of pain and its impact on quality of life (QoL) among patients with GBS.

Methods We enrolled 644 patients with GBS from prospective cohort studies in Bangladesh conducted between 2010 and 2024. Data were collected at enrolment and at standard follow-up time points up to 26 weeks. Pain intensity was measured by a pain numeric rating scale. Group differences were tested using the χ^2 or Fisher's exact test, longitudinal changes were analysed with repeated-measures analysis of variance and correlations were analysed with Spearman's rank test.

Results The median age of the patients was 31 years, with 70% men. During enrolment, 71% of patients reported pain, which persisted among 38% at week 13 and 26% at week 26. Pain was significantly associated with disease severity, muscle weakness and treatment with intravenous immunoglobulin in both the acute and chronic stages. Patients with acute pain had a higher proportion of axonal GBS (p=0.000) than those without pain. Chronic pain was associated with higher age (p=0.006), male sex (p=0.000), preceding diarrhoea (p=0.033) and dysautonomia (p=0.000). Higher pain intensity was reported among women (p=0.027), patients with higher age (p=0.029) and severe form of GBS (p=0.038) compared with counter groups. Acute pain was significantly associated with the 'self-care' (p=0.023), 'usual activities' (p=0.049) and 'anxiety/depression' (p=0.048) domains of QoL, whereas chronic pain was associated with the 'anxiety/depression' (p=0.005) domain.

Conclusions Pain presented as a serious symptom negatively affecting the QoL in GBS. Systematic evaluation of pain is recommended to ensure a personalised treatment approach for GBS.

WHAT IS ALREADY KNOWN ON THIS TOPIC

⇒ Pain in Guillain-Barré Syndrome (GBS) is a common and severe symptom but is often underemphasized in clinical practices, despite its significant impact on patients' quality of life (QoL).

WHAT THIS STUDY ADDS

⇒ This research sheds light on the prevalence and characteristics of both acute and chronic pain in GBS, evaluating the factors associated with pain and its correlation with disease severity and QoL using one of the largest prospective GBS cohorts from Bangladesh.

HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

⇒ The findings emphasise the importance of systematic pain evaluation in clinical settings, which could lead to more personalised treatment approaches. These findings could potentially aid in the development of clinical guidelines and future research on pain management in GBS.

INTRODUCTION

Guillain-Barré syndrome (GBS) is an immune-mediated peripheral neuropathy characterised by an acute onset of symmetrical muscle weakness, with a variable disease course, severity and outcome.[1–3] GBS is predominantly regarded as motor neuropathy, and most attention is given on muscle weakness. Pain is a frequent and severe complaint among patients with GBS, but it often receives less attention from healthcare providers.[4] The prevalence of pain in patients with GBS varies widely, ranging from approximately 3% to 89% at different stages of the disease.[5–7] Pain can be the first presenting symptom even before the onset of muscle weakness in one third of patients with GBS.[8] During the acute stage, ~85% reported pain as moderate to severe.[9] Long-term follow-up studies indicated that 35%–40% of patients with GBS continue to experience persistent pain 1–2 years after disease onset.[2 6] Patients with GBS may experience various types of pain, including muscle pain, low back pain, joint pain, radicular pain and painful paresthesia. Additionally, multiple pain patterns can coexist and overlap which further complicates systematic assessments.[4] Pain has been

reported in all subtypes of GBS, including acute inflammatory demyelinating polyneuropathy (AIDP), acute motor axonal neuropathy (AMAN) and Miller Fisher syndrome.[10–12] The relationship between disease severity and pain is controversial, as pain has been reported even in mild forms of the disease.[10] The residual pain symptoms have a considerable impact on the physical and mental health of the patients and are negatively correlated with quality of life (QoL).[13]

Despite the significant burden of pain in GBS, it has not been systematically evaluated in routine clinical practice, and only a few studies have evaluated the profile of pain in GBS. Majority of these studies were conducted in western countries with relatively small sample size.[5 11 14 15] In addition, longitudinal evaluation of pain throughout the disease course has rarely been addressed. We aimed to describe the frequency and characteristics of pain and evaluate the factors associated with pain in both the acute and chronic stages of the disease, using prospective longitudinal data from Bangladesh using one of the largest GBS cohorts worldwide. We also assessed the impact of pain on the QoL of patients with GBS.

METHODS AND MATERIALS

Study design and study subjects

A total of 644 patients with GBS were included from prospective observational cohort studies conducted in Bangladesh between February 2010 and February 2024.[16–19] All patients were recruited within 2 weeks of the onset of weakness and met the National Institute of Neurological Disorders and Stroke criteria for GBS.[20]

Sociodemographic and clinical data collection

During enrolment, detailed data were collected on sociodemographics, history of preceding infections and clinical and neurological features, including GBS disability score (GBS-DS), Medical Research Council (MRC) sum score and treatment (figure 1). The GBS-DS measured the functional state of patients with GBS and ranges from 0 (healthy) to 6 (death).[21] The MRC sum score measured the sum of individual MRC scores for the six muscles in the upper and lower limbs on both sides and ranges from 0 (quadriplegic) to 60 (normal).[22] After enrolment, patients underwent follow-ups at 2 weeks, 4 weeks, 13 weeks and 26 weeks according to a predefined protocol. Disease severity was categorised as mild (GBS-DS ≤2) and severe (GBS-DS >2). Poor outcome at week 4 and week 26 was defined as GBS-DS >2 at that time points.

Pain data collection

Detailed data on pain were collected at study inclusion and during all follow-up time points. These included information on pain locations, types and characteristics like muscular pain (muscle cramps and twitching), joint pain (pain/discomfort in the joint) and paresthesia (sensation of tingling, burning, pricking or prickling, skin-crawling, itching, 'pins and needles' or numbness). The locations of each type of pain were collected, for example, upper limb pain, lower limb pain, neck pain and back pain. Pain intensity was measured using the pain numeric rating scale (NRS), which ranges from 0 to 10, with 0 indicating no pain and 10 representing the most extreme pain imaginable.[23] Pain intensity was categorised as mild (pain NRS 1–3), moderate (pain NRS 4–6) and severe (pain NRS 7–10) as described earlier.[24] For further analysis, we combined the mild and moderate

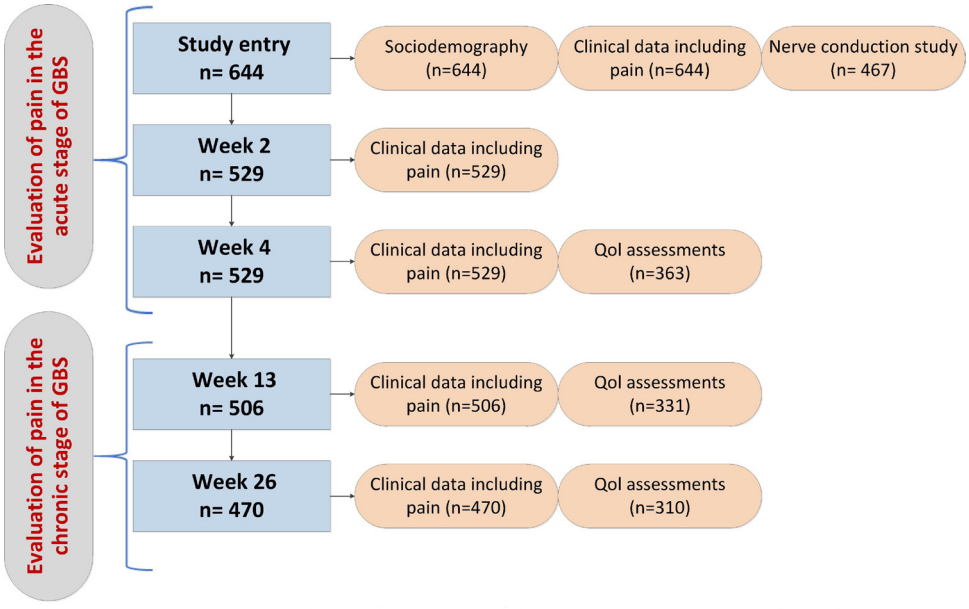

Figure 1 Study population and schedule of data collection. Flowchart describing study population included in the analysis and the schedule of data collection at different timepoints.

pain into one group (pain NRS 1–6) and compared it with the severe pain group (pain NRS 7–10). Acute pain was defined as pain occurring at any point from study entry to week 4, while chronic pain was defined as pain that persisted or appeared after 4 weeks of study entry until week 26. The maximum pain NRS reported by the patient at any time points had been considered for measuring the pain intensity, for example, maximum NRS from study entry till week 4 for acute pain intensity and maximum NRS after week 4 till week 26 for chronic pain intensity.

QoL assessment

QoL was assessed using Euroqol-5D-5L (EQ-5D-5L) questionnaire at week 4, week 13 and week 26. EQ-5D-5L was a standardised self-reported instrument that contained two parts to measure different health profiles. The descriptive part included five dimensions (mobility, self-care, usual activities, pain/discomfort and anxiety/depression). Each dimensions of the descriptive part had five levels: 'no problems' (level 1), 'slight problems' (level 2), 'moderate problems' (level 3), 'severe problems' (level 4) and 'extreme problems'/'unable to perform' (level 5).[25] For categorical analysis, we combined the responses 'no problems' and 'slight problems' into one group (no/slight problems) and moderate to extreme problems into another group (moderate/severe/extreme problems). Depending on the level of responses of the patients, a number was assigned to each dimension; so that a 5-digit number combination was obtained. By using a special algorithm, this 5-digit score was converted into a single score called EQ-5D index value that represented patient's health status or QoL. The EQ-5D index ranges from −0.594 to 1.0 with 1.0 indicating 'perfect health' and 0.0 indicating 'death'. Negative values represented health states perceived as worse than dead, which was considered equal to 0.[26] For computing EQ-5D index values for the current study, we have used the Indian value set as country-specific preference weighting was not available for the Bangladeshi population.[27] The visual analogue scale (VAS) of EQ-5D-5L provided a 20 cm vertical scale starting from '0' (the worst imaginable health status) to '100' (the best health status).

Electrophysiological examination

Nerve conduction study (NCS) was performed during study enrolment or within 1 week by an experienced neurologist following a standardised protocol and using a Viking Select EMG system (CareFusion, San Diego, California, USA).[28] NCS was classified according to the GBS criteria proposed by Hadden *et al*.[29]

Data management and statistical analysis

All questionnaires were double checked by two independent study physicians to ensure accuracy and completeness. All data were entered and analysed using SPSS V.20 (SPSS, Chicago, Illinois, USA) and GraphPad Prism 5. There were missing data at different follow-ups due to either patient was lost during any follow-up time points, or patient was dead. All data analysis was performed with complete cases for each follow-ups.

Quantitative data were presented as percentages and means with SD if normally distributed. The median with IQRs were used if the distribution was not normal. Differences in proportion between groups (patients with or without pain) were assessed by χ^2 test or Fisher's exact test as appropriate. Longitudinal analysis of pain NRS at different time points was performed using repeated-measurement analysis of variance (ANOVA). For ANOVA, patients were divided into different subgroups, such as by age (using the median value as cut-off), sex (male and female), NCS (axonal and AIDP) and disease severity at study entry (mild and severe). Correlation between pain NRS and disease severity (MRC sum score and GBS-DS), and QoL (EQ-5D index score and EuroQol-5D-5L VAS), was analysed using the Spearman's rank correlation test (r_s).

Patient and public involvement

There was no direct patient and public involvement in the design, conduct or reporting of this study.

RESULTS

Study population

The median age of the patients was 31 years (IQR 20–44), and 70% was men (table 1). Gastroenteritis was the predominant antecedent event (41%), followed by respiratory tract infection (12%). During enrolment, majority of the patients (55%) were bedbound with GBS-DS=4, and 22% of patients required mechanical ventilation. NCS was performed on 467 patients, revealing that 53% had the axonal variant of GBS, followed by 33% with AIDP. Majority of the patients (67%) received only supportive care for GBS, while 21% received intravenous immunoglobulin (IVIg) and 10% underwent plasma exchange. Poor outcomes were observed in 62% of patients at week 4 and in 24% of patients at week 26.

Characteristics of pain

During enrolment, 460 patients (71%) reported different types of pain (figure 2A). After the acute phase, pain persisted among 38% at week 13 and 26% at week 26. In all follow-ups, patients mostly had muscle pain (77% in acute stage and 56%–67% in chronic stage). After muscular pain, the proportion of painful paresthesia (34%–41%) was found more than joint pain (17%–20%) in the acute stage, whereas in the chronic stage, the frequency of joint pain (33%–40%) was found higher than painful paresthesia (21%–23%) (figure 2B). Regarding the location, pain was mostly located in lower limb (77%–89% in the acute stage and 64%–78% in the chronic stage) followed by upper limb (67%–44% in acute stage and 51%–58% in chronic stage of the disease). Back pain was observed among 29%–39% of patients in different time point of follow-ups (figure 2C).

Table 1 Characteristics of patients with and without acute and chronic pain

Variables at study entry	All patients, N (%)	Acute pain*			Chronic pain†		
		Patients with acute pain, N (%)	Patients without acute pain, N (%)	P value‡	Patients with chronic pain, N (%)	Patients without chronic pain, N (%)	P value§
Age (years)	31 (20, 44)¶	32 (20, 44)¶	27 (17, 43)¶	0.547	35 (23, 48)¶	26 (18, 39)¶	**0.006**‡‡
≤40	453/644 (70)	359/511 (70)	60/85 (71)		149/231 (65)	206/266 (77)	
41–60	171/644 (27)	135/511 (26)	24/85 (28)		75/231 (32)	55/266 (21)	
>60	20/644 (3)	17/511 (4)	1/85 (1)		7/231 (3)	5/266 (2)	
Sex				0.134			**0.000**‡‡
Male	448/644 (70)	343/511 (67)	64/85 (75)		139/231 (60)	203/266 (76)	
Female	196/644 (30)	168/511 (33)	21/85 (25)		92/231 (40)	63/231 (24)	
Preceding diarrhoea**	259/639 (41)	199/509 (39)	38/84 (45)	0.287	85/228 (37)	124/265 (47)	**0.033**‡‡
Preceding RTI**	76/639 (12)	60/509 (12)	11/84 (13)	0.732	25/228 (11)	37/265 (14)	0.317
MRC sum score Total							
41–60	83/644 (13)	57/511 (11)	21/85 (25)	**0.001**‡‡	21/231 (9)	47/266 (18)	**0.011**‡‡
21–40	264/644 (41)	208/511 (41)	36/85 (42)		97/231 (42)	113/266 (43)	
0–20	297/644 (46)	246/511 (48)	28/85 (33)		113/231 (49)	106/266 (40)	
GBS disability score							
1	3/644 (1)	1/511 (0)	2/85 (2)	**0.003**‡‡	0/231 (0)	3/266 (1)	**0.003**‡‡
2	53/644 (8)	37/511 (7)	12/85 (14)		22/231 (10)	24/266 (9)	
3	90/644 (14)	71/511 (14)	13/85 (15)		30/231 (13)	34/266 (13)	
4	354/644 (55)	281/511 (55)	48/85 (57)		123/231 (53)	173/266 (65)	
5	144/644 (22)	121/511 (24)	10/85 (12)		56/231 (24)	32/266 (12)	
Sensory deficits	80/638 (13)	57/505 (11)	15/85 (18)	0.097	30/230 (13)	30/262 (12)	0.590
Cranial nerve involvement	345/644 (54)	270/511 (53)	41/85 (48)	0.432	110/231 (48)	144/266 (54)	0.087
Facial involvement	157/644 (24)	122/511 (24)	17/85 (20)	0.434	54/231 (23)	65/266 (24)	0.433
Bulbar involvement	282/644 (44)	225/511 (44)	30/85 (35)	0.132	91/231 (39)	113/266 (43)	0.272
Autonomic dysfunction	146/637 (23)	121/506 (24)	12/84 (14)	0.051	61/230 (27)	36/261 (14)	**0.000**‡‡
Treatment							
IVIg	134/644 (21)	122/511 (24)	7/85 (8)	**0.003**‡‡	64/231 (28)	32/266 (12)	**0.000**‡‡
Plasma exchange	67/644 (10)	57/511 (11)	10/85 (12)		37/231 (16)	19/266 (7)	
SVPE	12/644 (2)	12/511 (2)	0/85 (0)		7/231 (3)	5/266 (2)	
Supportive care only	431/644 (67)	320/511 (63)	68/85 (80)		123/231 (53)	210/266 (79)	
Nerve conduction study							
Axonal	249/402 (62)	216/334 (65)	17/48 (35)	**0.000**‡‡	96/163 (59)	102/163 (63)	0.496
AIDP	153/402 (38)	118/334 (35)	31/48 (65)		67/163 (41)	61/163 (37)	

Continued

Table 1 Continued

Variables at study entry	All patients, N (%)	Acute pain*			Chronic pain†		
		Patients with acute pain, N (%)	Patients without acute pain, N (%)	P value‡	Patients with chronic pain, N (%)	Patients without chronic pain, N (%)	P value§
Poor outcome†† week 4	366/591 (62)	304/472 (64)	35/85 (41)	**0.000‡‡**	150/230 (65)	149/259 (58)	0.082
Poor outcome†† week 26	132/540 (24)	105/424 (25)	3/80 (4)	**0.000‡‡**	47/215 (22)	35/257 (14)	**0.019‡‡**

*Pain at any time points from entry to week 4.
†Pain persisted/appeared after week 4 and onwards till week 26.
‡P value between patients with and without acute pain.
§P value between patients with and without chronic pain.
¶Median with IQR.
**Within 4 weeks prior to the onset of weakness.
††Defined as GBS disability score >2.
‡‡Statistically significant.
AIDP, acute inflammatory demyelinating polyradiculopathy; GBS, Guillain-Barre syndrome; IVIg, intravenous immunoglobulin; MRC, Medical Research Council; RTI, respiratory tract infection; SVPE, small volume plasma exchange.

Pain severity was maximum at study entry where 37% of patients reported severe pain that subsequently decreased to 13% at week 4 and 4% at week 13 (figure 2D). None of the patients had severe pain at week 26. However, 11%–13% of patients reported moderate pain at week 13 and week 26. Mean pain intensity was 6.31 at enrolment, which gradually decreased in subsequent follow-ups and became 3.71 at week 26 (figure 2D).

Characteristics of patients with acute pain

The characteristics of patients with and without pain in the acute and chronic phases of GBS are summarised in table 1.

Acute pain was significantly associated with disease severity as defined by MRC sum score (p=0.001) and GBS-DS (p=0.003). Higher proportion of patients with acute pain received IVIg (24% vs 8%; p=0.003) and had

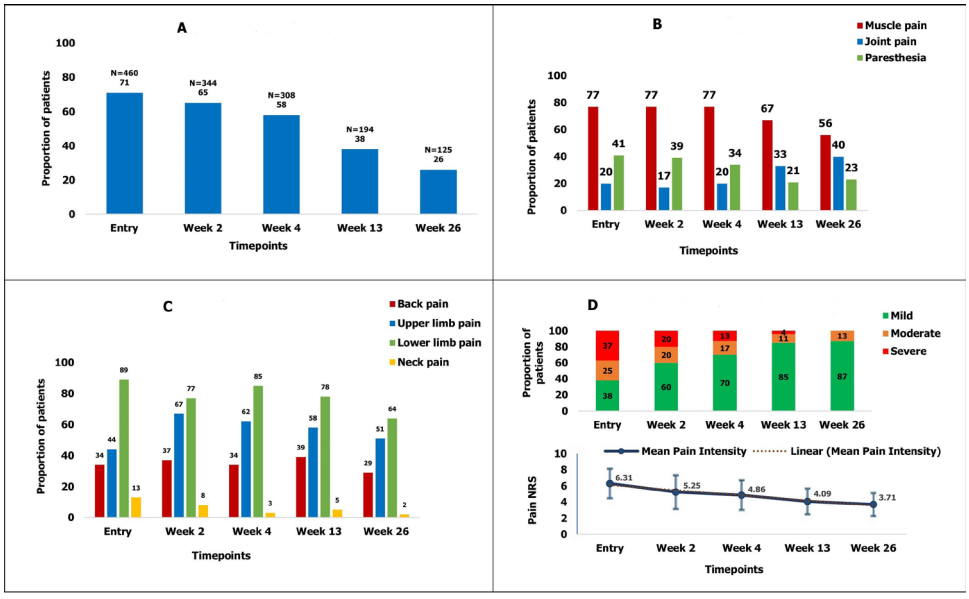

Figure 2 Prevalence and characteristics of pain at different time points. Bar diagram showing the prevalence and characteristics of pain at different time points where X-axis represented time points of follow-up, and Y-axis represented proportion of patients. (A) Prevalence of pain, (B) types of pain, (C) location of pain and (D) severity of pain and mean pain intensity.

Table 2 Correlation between GBS disability score and MRC sum score with pain intensity (numeric rating scale) at different timepoints

	GBS disability score		MRC sum score	
Time points	r_s	P value	r_s	P value
Entry	0.139	**0.000***	−0.181	**0.000***
Week 2	0.149	**0.001***	−0.116	**0.046***
Week 4	0.213	**0.000***	−0.231	**0.000***
Week 13	0.145	**0.002***	−0.208	**0.000***
Week 26	0.130	**0.006***	−0.192	**0.001***

GBS, Guillain-Barre syndrome; MRC, Medical Research Council; rs, Spearman's rank correlation coefficient.

axonal GBS (65% vs 35%; p=0.000) compared with the patients without acute pain. Poor outcomes at week 4 and week 26 were more prevalent among the patients with acute pain than those without acute pain.

Characteristics of patients with chronic pain

Chronic pain was significantly associated with higher age (p=0.006), male sex (p=0.000), preceding diarrhoea (p=0.033), muscle weakness at study entry (p=0.011), higher GBS-DS (p=0.003), presence of autonomic dysfunction (p=0.000) and treatment with IVIg (p=0.000).

Poor outcome at week 26 was more prevalent among the patients with chronic pain compared with those without chronic pain (22% vs 14%; p=0.019).

Factors correlated with pain intensity

The correlation between pain intensity with GBS-DS and MRC sum score at different time points of follow-ups are listed in table 2. Pain NRS was positively correlated with GBS-DS and negatively correlated with MRC sum score at all time points of follow-ups.

Longitudinal analysis of pain NRS showed higher mean pain intensity among women (3.25 vs 2.59; p=0.027), patients with higher age (2.99 vs 2.58; p=0.029) and severe form of the disease (2.84 vs 2.23; p=0.038) compared with the counter groups (figure 3). However, there was no significant difference of mean pain intensity among the patients with axonal GBS and AIDP.

Pain and QoL

Patients with acute pain had significantly higher proportion of 'moderate/severe/extreme problems' in the following domains of EQ-5D-5L questionnaire: 'self-care' (p=0.023), 'usual activities' (p=0.049), 'pain/discomfort' (p=0.000) and 'anxiety/depression' (p=0.048) (table 3). Apart from pain/discomfort domain, chronic pain was significantly associated with long-term anxiety/depression (p=0.005) of the patients.

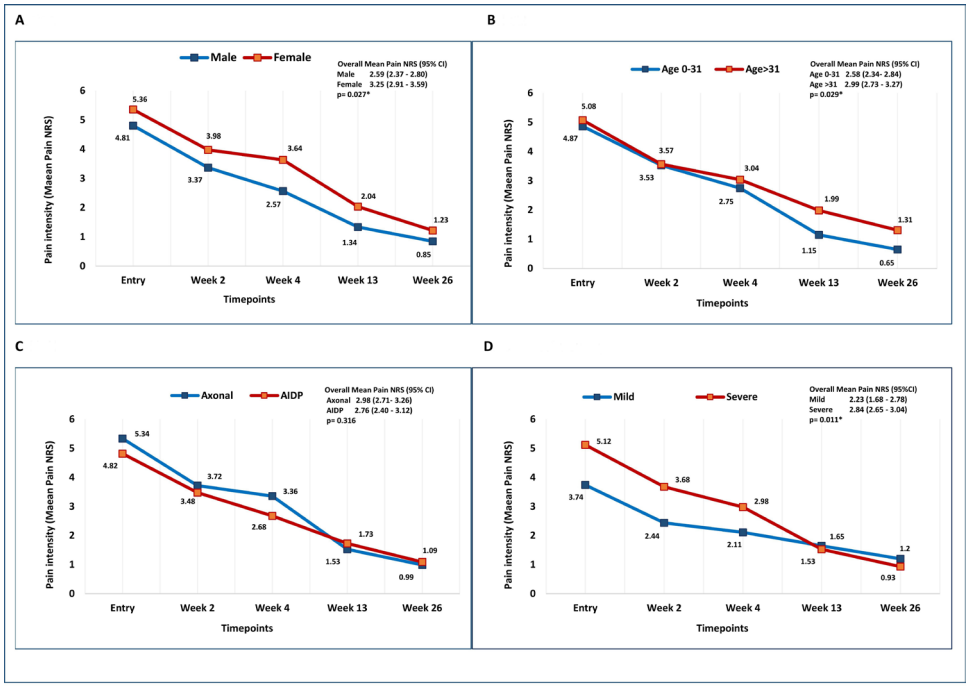

Figure 3 Mean pain intensity among GBS subgroups. This figure showed longitudinal analysis of pain numeric rating scale (NRS) starting from study inclusion up to week 26 using repeated-measurement analysis of variance (ANOVA). For subgroup analysis, patients were divided into different subgroups: (A) Sex (male and female), (B) age (using the median value as cut-off), (C) nerve conduction study (Axonal and AIDP) and (D) disease severity (severe[1] and mild[2]). [1]GBS disability score >2; [2]GBS disability score ≤2. AIDP, acute inflammatory demyelinating polyneuropathy; GBS, Guillain-Barre syndrome; NCS, nerve conduction study.

Table 3 Impact of pain on the quality of life (QoL) of the patients

	Acute pain*		
Euroqol-5D-5L at week 4	**Patients with acute pain**	**Patient without acute pain**	**P value**
Mobility			
No/slight problem	98/320 (30.6)	17/43 (39.5)	0.238
Moderate/severe/extreme problem	222/320 (69.4)	26/43 (60.5)	
Selfcare			
No/slight problem	90/320 (28.1)	19/42 (45.2)	**0.023‡**
Moderate/severe/extreme problem	230/320 (71.9)	23/42 (54.8)	
Usual activities			
No/slight problem	81/320 (25.3)	17/43 (39.5)	**0.049‡**
Moderate/severe/extreme problem	239/320 (74.7)	26/43 (60.5)	
Pain/discomfort			
No/slight problem	197/319 (61.8)	40/43 (93.0)	**0.000‡**
Moderate/severe/extreme problem	122/319 (38.2)	3/43 (7.0)	
Anxiety/depression			
No/slight problem	192/320 (60.0)	19/43 (44.2)	**0.048‡**
Moderate/severe/extreme problem	128/320 (40.0)	24/43 (55.8)	
	Chronic pain†		
Euroqol-5D-5L at week 26	**Patients with chronic pain**	**Patient without chronic pain**	**P value**
Mobility			
No/slight problem	124/175 (70.9)	102/135 (75.6)	0.356
Moderate/severe/extreme problem	51/175 (29.1)	33/135 (24.4)	
Self-care			
No/slight problem	139/175 (79.4)	114/135 (84.4)	0.258
Moderate/severe/extreme problem	36/175 (20.6)	21/135 (15.6)	
Usual activities			
No/slight problem	132/175 (75.4)	112/135 (83.0)	0.108‡
Moderate/severe/extreme problem	43/175 (24.6)	23/135 (17.0)	
Pain/discomfort			
No/slight problem	139/175 (79.4)	135/135 (100.0)	**0.000‡**
Moderate/severe/extreme problem	36/175 (20.6)	0/135 (0.0)	
Anxiety/depression			
No/slight problem	134/175 (76.6)	120/135 (88.9)	**0.005‡**
Moderate/severe/extreme problem	41/175 (23.4)	15/135 (11.1)	

*Pain at any timepoints from entry to week 4.
†Pain persisted/appeared after week four and onwards till week 26.
‡Statistically significant.

In both the acute and chronic stages of the disease, pain intensity was negatively correlated with EQ-5D-5L VAS (r_s=–0.118, p=0.029 at week 4; r_s=–0.174, p=0.003 at week 26) and EQ-5D index score (r_s=–0.248, p=0.000 at week 4; r_s=–0.360, p=0.000 at week 26) (figure 4).

DISCUSSION

Pain has been found to be a common symptom in approximately 70% of patients during study enrolment and persisted in about one-fourth of patients after 26 weeks of disease onset. Both acute and chronic pain were significantly associated with muscle weakness, disease severity, treatment with IVIg and poor outcome. Patients with acute pain had a higher proportion of axonal GBS; whereas patients with chronic pain had higher age, male sex, preceding diarrhoea and autonomic dysfunction compared with those without pain. Pain intensity was found higher among women, patients with higher age

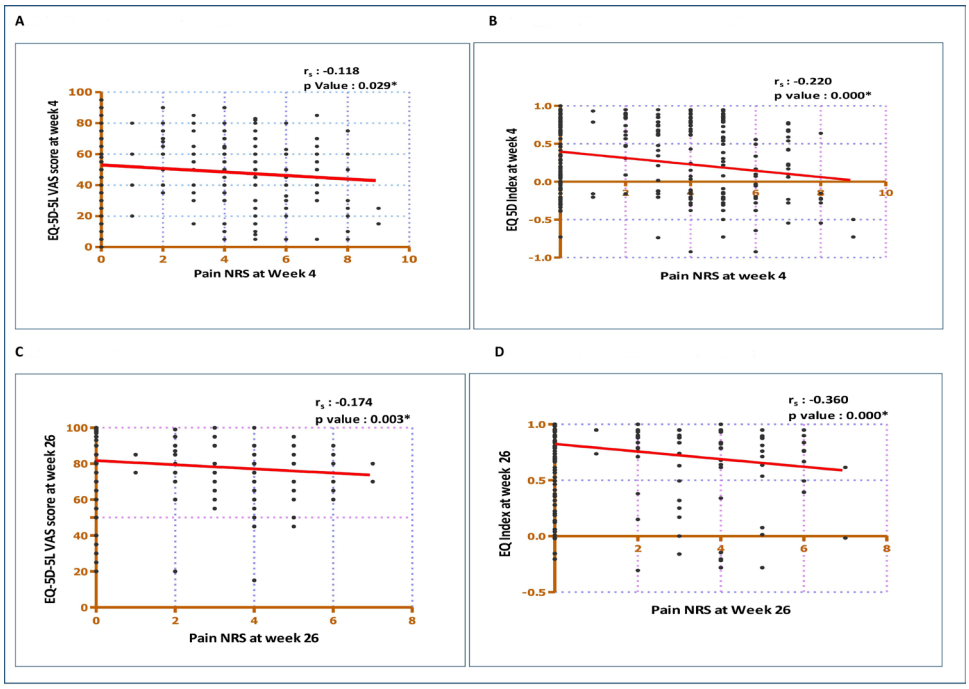

Figure 4 Correlation with pain intensity (numeric rating scale) and quality of life. Scatter diagram showing the correlation between the pain intensity measured by pain numeric rating scale (NRS) in X-axis, and quality of life measured by the EQ-5D-5L visual analogue scale (VAS) and EQ-5D index score in Y-axis. (A) Pain NRS vs EQ-5D-5L VAS at week 4, (B) Pain NRS vs EQ-5D index score at week 4, (C) Pain NRS vs EQ-5D-5L VAS at week 26 and (D) pain NRS vs EQ-5D index score at week 26.

and severe form of the disease compared with the counter groups. Acute pain was significantly associated with 'self-care', 'usual activities' and 'anxiety/depression' domains of QoL, whereas chronic pain was only associated with long-term 'anxiety/depression'.

The incidence of pain in the acute phase varied widely between 33% and 90% in different studies throughout the world.[5–7 11 14 15] The variation might be due to small sample size in most of the studies. In addition, the median duration between disease onset and study enrolment might also influence this proportion. For instance, in the Netherlands, 50%–57% of patients reported pain during study enrolment which increased to 79% after 2 weeks.[5 14] Several studies showed that a considerable proportion of patients (36%–70%) reported pain even before the onset of weakness.[5 9 15 30] Pain presented as the initial symptom for GBS, especially among children, which may cause a diagnostic dilemma.[4 31] In addition, pain might also induce movement restriction, resulting in interference with the assessment of the severity of muscle weakness. This was reflected in the study where they reported misdiagnosis at the early stage of the disease among 69% of patients with GBS under 6 years who initially presented only with pain.[15] This emphasises that pain should be considered as an initial manifestation of GBS especially in young children.

Pain prevalence was found maximal during the early phase of the disease (first 3–4 weeks of the illness) which gradually decreased both in prevalence and pain severity.[9 30] The findings were consistent with the current study. Long-term follow-up studies showed that pain persisted in 38%–48% of patients after 1–5 years from disease onset.[9 32] The prevalence of persistent pain after 26 weeks was found to be lower in the current study (26%). Multiple reasons might have contributed to the lower prevalence of chronic pain among the GBS population in Bangladesh. For instance, in Bangladesh, 30%–40% of patients with GBS had residual weakness and movement difficulties 6 months to 1 year after disease onset, which was much higher compared with the Western world (~20%).[33–36] Therefore, pain might be considered as a secondary complaint, leading to under-reporting by many patients, as most attention was provided to the motor function. Moreover, the incidence of pain might also differ among patients of different age groups and subtypes of GBS. For example, in Bangladesh, most of the patients with GBS were young and had the axonal variant of GBS, whereas in Europe/America, the majority of the patients were elderly and had AIDP.[35 36] Pain tolerance may also differ among different ethnic groups, especially between developed and low- and middle-income countries.[37]

In the current study, both acute and chronic pain had been found to be significantly associated with disease severity, which was consistent with the findings from patients with GBS in the Netherlands.[9] However, the relationship between pain intensity with muscle weakness and disability remains controversial in different studies. Some studies reported no correlation; some reported negative correlation

between pain and disease severity in the acute stage of disease; whereas another study reported significant correlation in the chronic stage of the disease.[7 9 38] In our study, pain intensity was found to correlate with disease severity and muscle weakness in both the acute and chronic stages of the disease. These variable findings from different studies could be partially explained by the variability of sample size or study design. Therefore, this needs further evaluation with long-term prospective multi-country studies.

We found that acute pain was more prevalent among the axonal patients with GBS compared with AIDP. However, although non-significant, chronic pain was more frequent among patients with AIDP than axonal GBS in Bangladesh. A study from China also showed that pain was more prevalent in AMAN than in AIDP in the acute stage of GBS.[38] In contrast, another retrospective study conducted in China reported that 34.5% of patients with GBS had pain, and among them, 97.7% of the patients had AIDP.[14] However, very limited studies evaluated the detailed NCS parameters associated with neuropathic pain but none of these studies focused on pain in GBS.[39] Therefore, future research is warranted to evaluate the value of individual NCS parameters to understand and predict the development, severity and persistence of pain in GBS.

In the current study, pain has been reported significantly associated with poor outcome and reduced QoL in both acute and chronic stages. In the acute phase, pain was associated with physical (self-care and daily activities) and emotional (anxiety/depression) domains of QoL. A study from India also found significant impairment in emotional, social and vitality components of SF-36 in patients with GBS with neuropathic pain compared with those without pain.[39] The same study also found a higher occurrence of psychological stress such as anxiety and depression, during the acute stage, which subsequently improved at the time of hospital discharge. In contrast, the current study showed significant levels of anxiety and depression among the patients with pain during the chronic stage of the disease. One of the major dissimilarities between these two studies was that the Indian population received psycho-social interventions which was mostly lacked in Bangladesh population. This emphasised the importance of rehabilitation and psychosocial counselling from the early stage of the disease to prevent long-term mental health consequences of GBS.

We acknowledge some limitations of the current study. First, the exact starting time of pain was missing in the current study, and therefore, the proportion of patients reporting pain preceding weakness could not be explored among patients with GBS in Bangladesh. Second, the complex nature of pain in GBS, including co-occurrence of one or more pain type, intensity and location, might have impacted the study results. To resolve this, we stratified the patients based on the time of onset of pain and pain intensity and conducted a subgroup analysis. Third, in most cases, the treatment of pain symptom was inconsistent. Thus, we were unable to evaluate the treatment effects on pain among patients with GBS in Bangladesh. Fourth, we did not evaluate the impact of other physical comorbidities, for example, diabetes, arthritis, nutritional and inflammatory factors, fatigue, etc, which might affect the incidence and nature of pain.

In conclusion, the current study evaluated the prevalence and characteristics of pain along with the factors associated with pain in both the acute and chronic stages of GBS using the largest prospective GBS cohort from Bangladesh. Pain presented as a noteworthy cardinal feature among patients with GBS in Bangladesh, which persisted even after years of disease onset and had a negative correlation with QoL of the patients. This signified the necessity for routine pain assessment and personalised pain management strategies to ensure physical, social and emotional well-being of the patients with GBS. Future research is required to explore the pathophysiology of pain, identify biomarkers, develop predictive models for the development and persistence of pain and develop targeted therapy for pain in GBS.

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