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JNNP Online First, published on January 11, 2018 as 10.1136/jnnp-2017-316930

RESEARCH PAPER

Guillain-Barré syndrome in southern China: retrospective analysis of hospitalised patients from 14 provinces in the area south of the Huaihe River

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► Additional material is published online only. To view please visit the journal online (http://dx.doi.org/10.1136/jnnp-2017-316930).

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Received 23 July 2017
Revised 2 November 2017
Accepted 22 November 2017

ABSTRACT

Objectives The clinical and epidemiological profiles of Guillain-Barré syndrome (GBS) in southern China have yet to be fully recognised. We aimed to investigate the subtypes of GBS in southern China, compare the clinical features of demyelinating form with that of axonal form and test whether preceding infections and age have influence on the clinical phenotype, disease course and severity of GBS.

Methods Medical records of patients with a diagnosis of GBS admitted to 31 tertiary hospitals, located in 14 provinces in southern China, from 1 January 2013 to 30 September 2016, were collected and retrospectively reviewed.

Results Finally. 1056 patients, including 887 classic GBS and 169 variants, were enrolled. The 661 classic patients with available electromyographic data were grouped as having acute inflammatory demyelinating polyneuropathy (AIDP, 49.0%), acute motor axonal neuropathy (AMAN, 18.8%), inexcitable (0.9%) and equivocal (31.3%). In contrast to AIDP, patients with AMAN were characterised by earlier nadir (P=0.000), higher Hughes score at nadir (P=0.003) and at discharge (P=0.000). Preceding upper respiratory infections were identified in 369 (34.9%) patients, who were more inclined to develop AIDP (P=0.000) and Miller-Fisher syndrome (P=0.027), whereas gastrointestinal infection were found in 89 (8.4%) patients, who were more prone to develop AMAN (P=0.000), with more severe illness (P=0.001) and longer hospital stay (P=0.009). Children (≤15 years) and the elderly (≥56 years) were more severe at nadir, the elderly had the longest hospital stay (P=0.023).

Conclusion AIDP is the predominant form in southern China, which is different from data of northern China. The different subtypes, preceding infection and age of onset can partially determine the disease progression, severity and short-term recovery speed of GBS.

Clinical trial registration ChiCTR-RRC-17014152.

INTRODUCTION

Guillain-Barré syndrome (GBS) is the leading cause of acute flaccid paralysis, with about 100 000 people developing this disorder every year worldwide. Relatively higher rates of disability and mortality in low/middle-income countries bring heavy economic burden to the state and society.[1–3]

Acute inflammatory demyelinating polyneuropathy (AIDP) and acute motor axonal neuropathy (AMAN) are the two main phenotypes of GBS with different pathogenesis, pathological characteristics and may be different prognosis.[1–4] As the primary subtype of GBS in northern China, AMAN has received worldwide attention.[5–8] Reports suggested that AMAN accounted for approximately 65% of patients with GBS in northern China and predicted a more serious condition,[5–8] whereas AMAN constituted only 1–3% of GBS in Europe and North America.[9–11] Since the clinical and electrophysiological patterns of GBS in southern China have yet to be fully recognised, neurologists always use data from northern China to estimate the profiles of Chinese patients. However, these kinds of generalisations may ignore regional differences, particularly the genetic and environmental differences between South China and North China, and thus lead to somewhat incorrect assessments.[12] For example, unlike the data from northern China, a single-centre research conducted in southwest China has revealed that AIDP was the most common subtype (up to 57%).[13] In addition to affecting an individual's susceptibility to develop a specific subtype of GBS, regional differences may also influence the course and severity of disease.[3] Under this circumstance, we performed this large multicentre retrospective study, in order to increase our understanding of the clinical features and electrophysiological profiles of GBS in southern China, aid in patient counselling and in the design of clinical trials.

To cite: Liu S, Xiao Z, Lou M, *et al*. *J Neurol Neurosurg Psychiatry* Epub ahead of print: [*please include* Day Month Year]. doi:10.1136/jnnp-2017-316930

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METHODS

Patient ascertainment

The medical records of consecutive hospitalised patients (children and adults) with a diagnosis of GBS and its variants in 31 representative tertiary hospitals, located in 14 provinces in southern China, that is, the area south of the Huaihe River, between 1 January 2013 and 30 September 2016, were collected. The neurologists (ZL, ZX, JG) and 12 well-trained GBS team members (SL, YL, JY, YY, MZ, XF, GG, HZ, MD, SF, QC, JL) at the Department of Neurology, Renmin Hospital of Wuhan University, validated the GBS diagnosis for each patient. Patients who fulfilled the established clinical criteria of Asbury and Cornblath (1990) were enrolled.[14] In addition, the patients whose clinical presentation and ancillary data were typical of GBS except for preservation or exaggeration of reflexes were also included.[15 16] GBS variants were identified according to new diagnostic classification proposed by Wakerley *et al*.[17] Cranial nerve variant was diagnosed when patients showed pure cranial nerve palsies in the absence of ataxia and prominent limb weakness.[13] Patients who abandoned examination and treatment within 5 days after admission and those with an alternative diagnosis for weakness were excluded. The detailed flow chart is shown in figure 1.

Information extraction

Information on age, sex, season, preceding events, initial symptoms, concomitant symptoms, severity at admission, at nadir, at

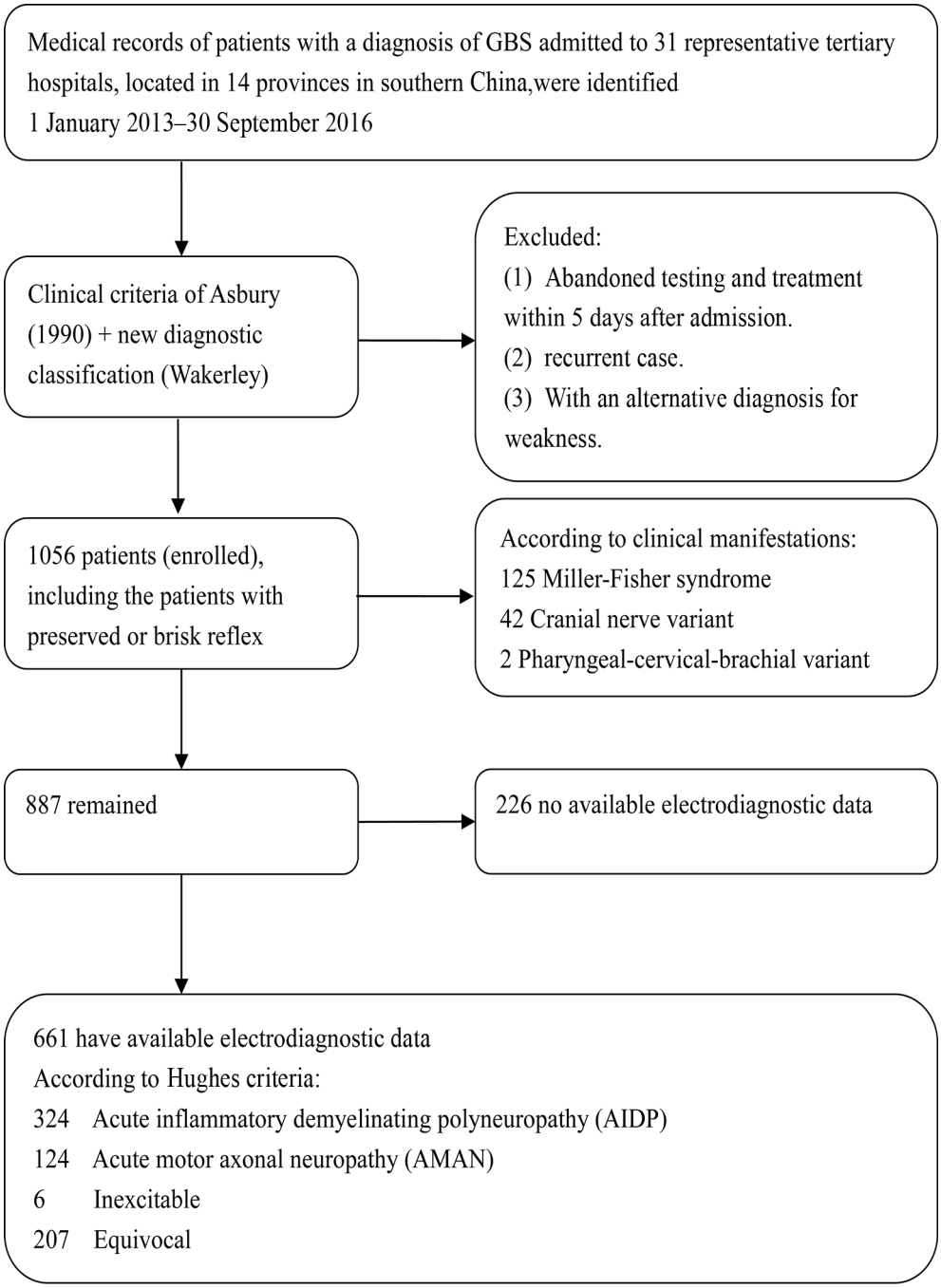

Figure 1 Flow chart of patient ascertainment. GBS, Guillain-Barré syndrome.

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discharge, time from onset to nadir, length of hospitalisation, findings of electrodiagnosis (EDX), treatment regime, cerebrospinal fluid investigations and other laboratory reports were extracted by our team members after strict training. The strict training included: (1) validating the diagnosis of GBS and its variants; (2) analysing the electrodiagnostic reports and classifying subtypes and (3) some details encountered in information extraction (online supplemental material). The motor function deficits of included patients were assessed by the Hughes Functional Grading Scale (HFGS), a widely accepted scale of disability for GBS (grade 6, dead; grade 5, requiring assisted respiration; grade 4, bed bound; grade 3, able to walk with aid; grade 2, able to walk independently; grade 1, minimal signs and symptoms, able to run; grade 0, normal). The peak time was defined as the time when the HFGS reached nadir, but for patients with no lower extremities, weakness and respiratory insufficiency, it referred to the time when the symptoms were no longer progressing. Only in cases in which a patient developed symptoms of autonomic nerve dysfunction after the onset of GBS, and we could find no other coexisting disease to explain these symptoms, could we say that the patient with GBS suffered from autonomic dysfunction. The autonomic symptoms included instability of systemic blood pressure (hypertension/hypotension), heart rate (tachycardia/bradycardia) and sweating (hyperhidrosis/anhidrosis); bowel and bladder incontinence or retention and vasomotor instability. When there was uncertainty in the process of data extraction, consensus was reached though discussion. Three members (SL, YL, JY) typed the data in table and verified all the information.

Electrophysiological classification

The available EDX should include data from nerve conduction study (NCS) and F-wave study in at least three motor nerves (median, ulnar, peroneal and/or tibial, bilaterally) and data from NCS in at least three sensory nerves (median, ulnar and sural, bilaterally). The parameters of motor nerve included distal motor latency, motor conduction velocity, amplitudes of distal and proximal compound muscle action potentials and minimal F-wave latency. Patients with available EDX were subclassified into AIDP, AMAN, inexcitable and unequivocal according to the eletrodiagnostic criteria summarised by Hughes (online supplementary table).[1] If serial NCSs were conducted, we distinguished subtypes mainly by the second results. In order to reduce the bias as much as possible, a unified parameter standard (local data) was adopted in the analysis of NCS for patients older than 15 years (table 1). For the children younger than 15 years, the results of NCS were compared with the age-matched and gender-matched controls.

Age grouping of patients with GBS

The patients with GBS were divided into four groups according to their ages: group 1: ≤15 years; group 2: 16–35 years; group 3: 36–55 years and group 4: ≥56 years.

Statistical analysis

Statistical analysis was performed with SPSS V.17.0 software (IBM, West Grove, Pennsylvania, USA). Categorical data were presented as proportions, and continuous data were presented as means and SDs. Differences in proportions were tested by the χ^2 tests. The continuous variables with a normal distribution were tested using Student's t-test or analysis of variance test, and the continuous variables with a skewed distribution were tested using Mann-Whitney U test or the Kruskal-Wallis analysis. For all statistical tests, $P<0.05$ was considered to be significant.

RESULTS

Baseline clinical characteristics

Finally, 1056 patients with a diagnosis of GBS and its variants were included, among whom 634 (60.0%) were men and 422 (40.0%) were women. The mean age was 47.2 years (age range 2–82 years). Upper respiratory infection (URI) was identified in 369 (34.9%) patients, gastrointestinal (GI) infection in 89 (8.4%) patients and both infections in 15 (1.4%) patients. Other preceding events included surgery, overfatigue, pesticide exposure, trauma, herpes virus infection and vaccine. No any antecedent event was documented in 326 patients. The common autonomic symptoms of our patients included cardiac arrhythmia, hypertension, hypotension, orthostatic hypotension, sweating, bowel and bladder incontinence or retention. Seventeen patients died during hospitalisation.

Distribution of GBS subtypes and variants

A total of 169 GBS variants, including 125 cases with Miller-Fisher syndrome (MFS, including 36 MFS/GBS), 42 cases with cranial nerve variant (including 16 facial diplegia variant, 9 pharyngeal variant and 17 polycranial neuritis) and 2 pharyngeal-cervical-brachial form were identified. Of the 887 patients with classic GBS, 661 cases with available EDX were categorised into AIDP (324, 49.0%), AMAN (124, 18.8%), inexcitable (6, 0.9%) and equivocal (207, 31.3%). Among the patients with AMAN, 29 had sensory and motor forms. Serial EDX tests were completed in 169 cases (25.6%), the number of patients with AMAN increased from 22 to 37 (13.0% to 21.9%) and AIDP was still the main subtype (48.5%) in subsequent analysis although a shift occurred from AIDP to AMAN (n=10) (figure 2). The proportion of each EDX form has no significant differences at different timings after onset of weakness (table 2).

Clinical features of different subtypes (AIDP vs AMAN)

There were no significant between-group differences in terms of age, gender, frequency of mechanical ventilation (MV) and hospital stay. In contrast to the patients with AIDP, patients with AMAN were characterised by higher proportion of severe patients (HFGS ≥3) on admission (59.9 vs 86.3, P=0.000), higher HFGS score at nadir (3.19±1.16 vs 3.59±0.75, P=0.003) and at discharge (1.75±1.26 vs 2.66±1.13, P=0.000). Additionally,

Table 1 The unified parameter standard for electrophysiological classification

	DML (ms)			CMAP (mV)				MCV (m/s)			F-response latency (ms)	
Motor nerve	ULN	110%	120%	LLN	50%	20%	10%	LLN	90%	85%	ULN	120%
Median	4	4.4	4.8	6	3	1.2	0.6	50	45	42.5	31	37.2
Lunar	4	4.4	4.8	6	3	1.2	0.6	50	45	42.5	31	37.2
Tibial	5	5.5	6	6	3	1.2	0.6	40	36	34	55	66
Peroneal	5	5.5	6	2.5	1.25	0.5	0.25	40	36	34	55	66

CMAP, compound muscle action potential; DML, distal motor latency; LLN, lower limit of normal; MCV, motor conduction velocity; ULN, upper limit of normal.

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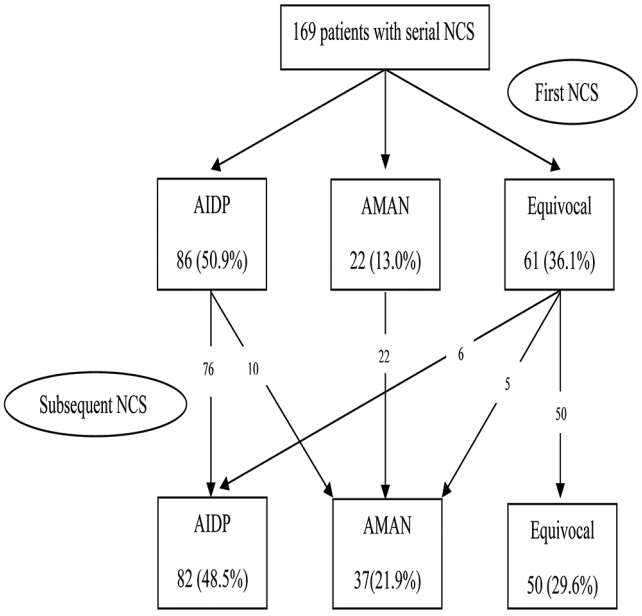

Figure 2 Proportions of subtypes and changes in the electrodiagnosis from the first to subsequent study. AIDP , acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; NCS, nerve conduction study.

79.8% of the patients with AMAN (but only 42.5% of patients with AIDP) progressed to its nadir within 7 days (P=0.000). However, patients with AIDP had a significantly higher frequency of facial/bulbar paralysis (42.6 vs 21.0, P=0.001), oculomotor paralysis (7.4 vs 2.4, P=0.048), dyspnoea (22.5 vs 12.2, P=0.012), pneumonia (17.3 vs 8.1, P=0.016) and autonomic dysfunction (25.9 vs 8.1, P=0.001). Note that hyperreflexia was more frequent in patients with AMAN (5.9 vs 16.1, P=0.002), in whom paresthesia occurred less frequently (54.6 vs 33.9, P=0.001) (table 3).

Clinical features of GBS with different preceding infections (URI vs GI infection)

Patients with URI were more inclined to develop AIDP (49.1 vs 17.9, P=0.000) and MFS (16.3 vs 6.8, P=0.027), had a higher frequency of cranial nerve paralysis (51.5 vs 28.1, P=0.000), paresthesia (51.8 vs 31.5, P=0.001), dyspnoea (18.7 vs 9.0, P=0.027) and autonomic dysfunction (24.9 vs 11.2, P=0.004), whereas patients with GI infection were more frequently to develop AMAN (11.7 vs 47.8, P=0.000), had higher HFGS at nadir (2.57±1.48 vs 3.13±1.19, P=0.001) and longer hospital stay (17.86±13.13 vs 21.85±11.40, P=0.009) (table 4).

Table 2 Classification of subtypes in relation to timings of NCSs*

	1–7 days	8–14 days	15–21 days	>21 days	P value
AIDP	33 (51.6%)	71 (49.6%)	99 (48.3%)	121 (48.6%)	0.96
AMAN	8 (12.5%)	24 (16.7%)	38 (18.5%)	54 (21.7%)	0.33
Inexcitable	0	0	2 (1.0%)	4 (1.6%)	0.43
Equivocal	23 (35.9%)	48 (33.7%)	66 (32.2%)	70 (28.1%)	0.52
Total (n=661)	64 (9.7%)	143 (21.6%)	205 (31.0%)	249 (37.7%)	

*For the patients with serial electrodiagnosis tests, only the results from the last time of NCSs were adopted for statistical analysis.
AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; NCSs, nerve conduction studies.

Table 3 Clinical features of different subtypes

Parameters	AIDP (n=324)	AMAN (n=124)	Two-tailed P value
Age (mean, years)	50.23±18.44	47.67±21.19	0.238
Male, n (%)	221 (68.2)	81 (65.3)	0.574
Hughes score on admission, n (%)			
≥ 3	194 (59.9)	107 (86.3)	**0.000**
<3	130	17	
Onset to nadir, n (%)			
≤ 7 days	138 (42.5)	99 (79.8)	**0.000**
>7 days	186	25	
Hughes score at nadir (mean, g)	3.19±1.16	3.59±0.75	**0.003**
Treatment, no. (%)			
IVIg	147 (45.4)	53 (42.8)	0.671
Plasmapheresis	50 (15.4)	28 (22.6)	0.094
Concomitant symptoms, n (%)			
Neurological symptoms			
Facial/bulbar paralysis	138 (42.6)	26 (21.0)	**0.001**
Oculomotor paralysis	24 (7.4)	3 (2.4)	**0.048**
Hyperreflexia	19 (5.9)	20 (16.1)	**0.002**
Paresthesia	177 (54.6)	42 (33.9)	**0.001**
Complications			
Autonomic dysfunction	84 (25.9)	10 (8.1)	**0.001**
Deep venous thrombosis	4 (1.2)	5 (4.0)	**0.123**
Pneumonia	56 (17.3)	10 (8.1)	**0.016**
Dyspnoea	73 (22.5)	15 (12.2)	**0.012**
Gastrointestinal bleeding	2	0	—
Acute pancreatitis	1	0	—
Laboratory abnormalitis, n (%)			
Hyponatraemia	87 (26.9)	29 (23.5)	0.473
Hypoalbuminaemia	71 (22.9)	30 (24.2)	0.615
Mechanical ventilation, n (%)	39 (12.0)	7 (5.6)	0.055
Death in hospital stay, n (%)	1 (0.3)	2 (1.6)	0.187
Hospital stay (mean, days)	17.74±10.90	19.20±9.73	0.190
Hughes score at discharge (mean, g)	1.75±1.26	2.66±1.13	**0.000**

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; IVIg, intravenous immunoglobulin.
Statistically significant results are in bold.

Clinical features of GBS in different age periods

There were no significant differences between the four groups in terms of gender. A strikingly higher incidence of AMAN was found in patients younger than 15 years (P=0.034), while an obviously higher incidence of AIDP was found in patients older than 36 years (P=0.030). As to MFS, the relatively higher incidence was found in patients aged 16–55 years (P=0.009). The proportion of patients unable to walk independently on admission (HFGS ≥3) (P=0.000) and HFGS at nadir (P=0.000) were significantly higher in patients younger than 15 years and patients older than 56 years (see also in figure 3A). The percentage of patients progress to nadir within 7 days was significantly smaller in the elderly (≥56 years)(P=0.000), indicating that the elder would progress slowly. The hospital stay, an indicator of short-term recovery speed, was longest in the elderly (≥56 years) (P=0.023) (see also in figure 3B). The elderly had a higher frequency of MV (P=0.005), and they were more likely to suffer from autonomic dysfunction (P=0.001), dyspnoea (P=0.000), pneumonia (P=0.000), hypoalbuminaemia (P=0.000) and hyponatraemia (P=0.000) (table 5).

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Table 4 Clinical features of GBS with different preceding infections

Parameters	URI (n=369)	GI tract infection (n=89)	Two-tailed P value
Age (mean, years)	44.12±19.39	43.62±20.67	0.832
Male, n (%)	223 (60.4)	49 (55.1)	0.400
Clinical subtypes, n (%)			
MFS	60 (16.3)	6 (6.8)	**0.027**
CNV	20 (5.4)	1 (1.2)	0.094
PCB	2 (0.5)	0	>0.9
Electrodiagnostic subtypes, n (%)	230	67	
AIDP	113 (49.1)	12 (17.9)	**0.000**
AMAN	27 (11.7)	32 (47.8)	**0.000**
Inexcitable	2 (8.7)	0	> 0.9
Equivocal	88 (38.3)	23 (34.3)	**0.667**
Hughes score at nadir (mean, g)	2.57±1.48	3.13±1.19	**0.001**
Treatment, n (%)			
IVIg	135 (36.6)	31 (34.9)	0.807
Plasmapheresis	51 (15.4)	10 (11.2)	0.403
Concomitant symptoms, n (%)			
Neurological symptoms			
Cranial nerve paralysis	190 (51.4)	25 (28.1)	**0.000**
Hyperreflexia	23 (6.2)	9 (10.1)	0.244
Paresthesia	191 (51.8)	28 (31.5)	**0.001**
Complications			
Autonomic dysfunction	92 (24.9)	10 (11.2)	**0.004**
Deep venous thrombosis	6 (1.6)	0	0.602
Dyspnoea	69 (18.7)	8 (9.0)	**0.027**
Laboratory abnormalities, n (%)			
Hyponatraemia	56 (15.2)	19 (21.6)	0.201
Hypoalbuminaemia	72 (19.5)	22 (24.7)	0.306
Mechanical ventilation (MV), n (%)	24 (6.5)	3 (3.4)	0.324
MV (mean, days)	19.87±14.71	18.66±7.37	0.914
Death in hospital stay, n (%)	1 (0.3)	2 (2.2)	0.098
Hospital stay (mean, days)	17.86±13.13	21.85±11.40	**0.009**

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; CNV, cranial nerve variant; GBS, Guillain-Barré syndrome; GI tract infection, gastrointestinal tract infection; IVIg, intravenous immunoglobulin.; MFS, Miller-Fisher syndrome; PCB, pharyngeal-cervical-brachial variants; URI, upper respiratory infection. Statistically significant results are in bold.

DISCUSSION

Our study revealed that the predominant subtype of GBS in southern China was AIDP (49.0%), with AMAN constituting a smaller proportion of subjects (18.8%), whereas, according to the well-known studies in northern China in the 1990s, axonal form made up approximately 65–70% of patients.[5–8] It is worth noting that although AMAN is much less frequent in southern China, the proportion (18.8%) is still higher than data from Europe and North America (1–3%).[9–11] We believe geographical differences in phenotype are the results of various factors interacting with each other, such as environmental characters, geographical differences in genetic polymorphisms of *Campylobacter jejuni* strains and varying genetic polymorphisms between populations living in different regions or countries.[3 18] The strikingly different proportion of subtypes between North and South China can be partially explained by the different probability of exposure to certain infectious organisms. In northern China, the infection of *C. jejuni*, which is expected to invariably induce AMAN,[19] was reported to be predominant,[5–8] whereas our data showed that URI was the most common preceding event in southern China. In addition, we cannot rule out the possibility that the disease spectrum changes over time. Well-known studies conducted in northern China in the 1990s revealed that AMAN predominated in the yearly summer outbreak of GBS among children and youngsters. Considering that people who lived in the past 20 years (especially the children and youngsters) always swam in river and drank unboiled well water in summer,[6] we have reasons to believe that AMAN was the main subtype of GBS in China in the 1990s, but in recent years, AIDP has become dominant, since the majority of people have access to clean domestic water and foods with the improvement of living standard. Recent data (2013) from northeast China showed that AIDP was the main subtype[20]; although the preceding infection was unavailable, this study still tends to support our hypothesis and suggests that we need to focus on the changes in disease spectrum. As for the reason why the proportion of AMAN in southern China is lower when compared with data from other east Asian countries (Japan, Korea),[21 22] we consider it has a lot to do with the food culture; Japanese and Koreans are fond of eating raw meat, such as sashimi, torisashi and yukhoe, which may increase the probability of infection with *Campylobacter*.[23]

Then, our results revealed that the speed of progression, severity and the incidence of some concomitant symptoms differed in the two main subtypes. In contrast to AIDP, patients with AMAN were marked by an earlier nadir, more severe condition, relative sparing of the cranial nerves and autonomic nerve. However, patients with AIDP were at heightened risk of MV, dyspnoea and pneumonia, although the difference in the frequency of MV did not reach statistical significance. These above-mentioned features remind us that although patients with AIDP are less severe than patients with axonal forms, active monitoring must be performed in each patient with AIDP in case of respiratory insufficiency, even those with mild disability at admission. As to the reasons for heterogeneity in subtypes, we have some thoughts. First, in terms of the higher frequency of MV, dyspnoea and pneumonia in AIDP, the robust association between phrenic nerve conduction block and respiratory insufficiency may be one explanation[24]; an alternative explanation can be the higher ratio of facial/bulbar paralysis in patients with AIDP, which is reportedly the independent risk factor for respiratory insufficiency.[25 26] Of course, the mechanism of respiratory failure might vary in different populations because of various factors, such as pathogenic agents and genetic susceptibility.[24] The second question relates to the higher rate of hyperreflexia in patients with AMAN; inhibitory interneuron damage caused by the neurotoxic effects of internalised and retrogradely transported antiganglioside antibodies, as seen in tetanus toxicity, may be implicated in the hyperreflexia observed in AMAN.[15 16] The last question concerns the higher incidence of autonomic dysfunction in AIDP. The common autonomic symptoms of our patient included cardiac arrhythmia, hypertension, hypotension, orthostatic hypotension, sweating, bowel and bladder incontinence or retention; these symptoms were the patterns of autonomic dysfunction of AIDP according to a previous study, which revealed that the patterns of autonomic involvement were qualitatively different between AIDP and AMAN, and that AMAN was marked by hypoactivity in sudomotor or skin vasomotor function.[27] Given the absence of skin vasomotor examination in our study, the higher incidence of autonomic dysfunction in AIDP is conceivable. We should perform more autonomic function tests in future and pay more attention to the different patterns of autonomic involvement between different subtypes to improve the care and treatment of individual patients.

In our study, the URI-related group was more prone to develop AIDP and MFS, while GI infection-related group more frequently developed AMAN and had higher HFGS scores at

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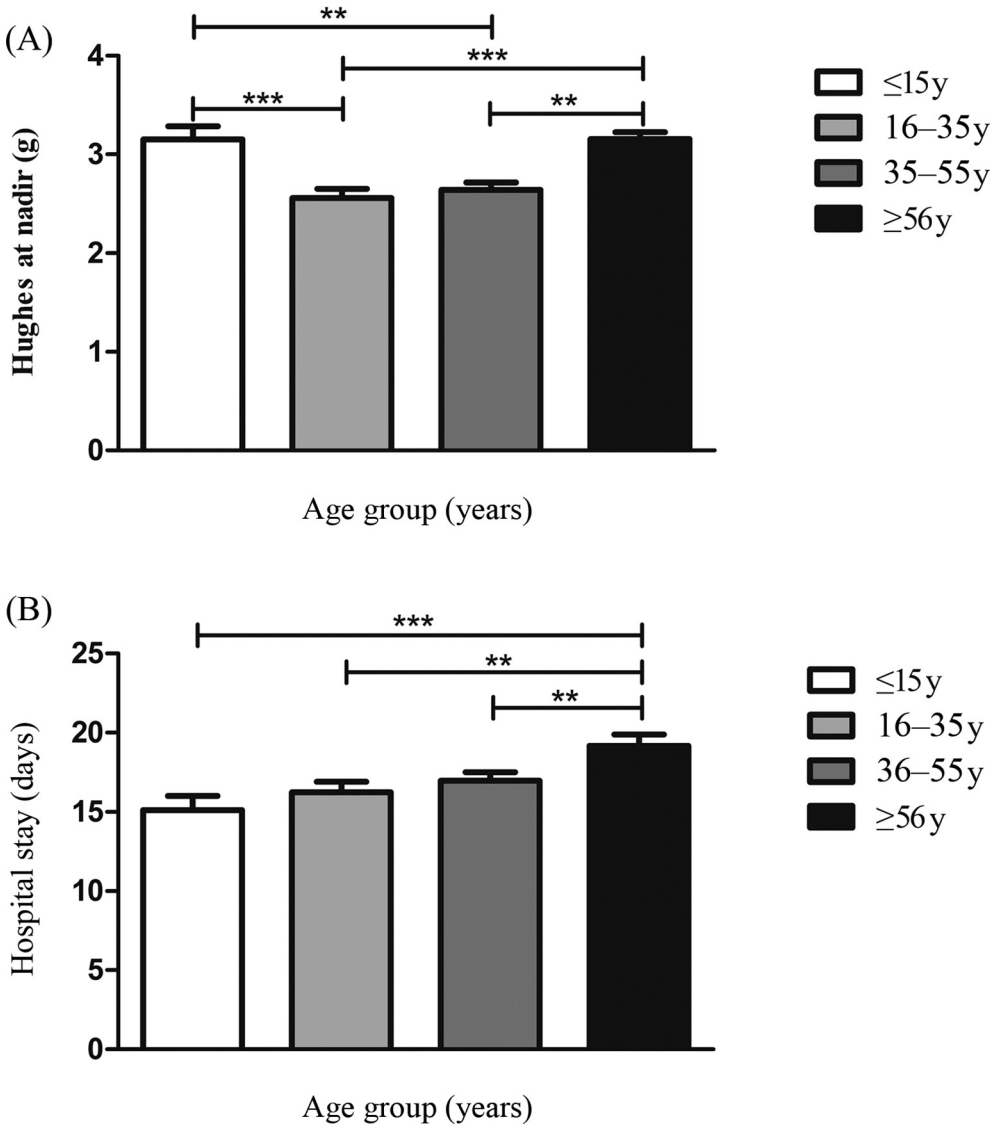

Figure 3 The Hughes score at nadir (A) and the hospital stay (B) of the four age groups. **P<0.01; ***P<0.001.

nadir and longer hospital stay. These results are consistent with a previous study, which revealed preceding infections influence the neurophysiological classification and clinical features of GBS.[28] Furthermore, these results confirm our supposition that geographical variations in preceding infections may be important in explaining why each subtype occurs in varying proportions across different regions. However, the limited microbiological data in the current study make it difficult to demonstrate the relationship between specific microorganisms and subtypes; thus, further research is urgently needed.

Few studies have compared the clinical features among different age groups. In our study, a relatively higher incidence of MFS was found in patients aged 16–55 years. As for the electrodiagnostic subtypes, we found that AMAN was more common in patients aged ≤15 years. The reason for different subtype distributions in different age groups is unknown. The relatively weak awareness of hand washing after defecation and before meals is probably enough to explain the high frequency of AMAN in children.[29 30] The patients aged ≤15 years and ≥56 years showed worst disability at nadir than others and the elderly (≥56 years) recovered most slowly; the fact further confirms the finding that age influences the capacity to recover.[31 32] Taking the higher incidence of abnormal laboratory tests (hyponatraemia and hypoalbuminaemia) and complex concomitant symptoms (autonomic dysfunction, deep venous thrombolysis and pneumonia) in the elderly into consideration, the slow recovery is not difficult to understand, because emerging evidence reveals that hyponatraemia, hypoalbuminaemia and autonomic dysfunction are independent risk factors for slow recovery of patients with GBS.[33–35] Somewhat unexpectedly, the elderly progressed more slowly than other patients, as indicated by the small percentage of elderly patients reaching nadir within 7 days, the exact reason for this result must be further researched; however, it might be a peculiar feature of elderly patients with GBS in southern China.

Our results also revealed a higher frequency of MV, pneumonia and dyspnoea in the elderly. We ascribe these findings to the overall state of old people, who are more vulnerable to a variety of diseases, particularly the infectious complications caused by low immunity.[36] What's more, the reduced compensatory function of neuroendocrine system and viscera makes the elder more likely to develop electrolyte and acid-based disturbances, such as hyponatraemia, hypokalaemia and acidosis, which will definitely worsen respiratory problems and weakness.[2 37] These

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Table 5 Clinical features of GBS in different age groups

Parameters	≤15 years (n=66)	16–35 years (n=211)	36–55 years (n=381)	≥56 years (n=398)	Two-tailed P value
Male, n (%)	43 (65.2)	132 (62.6)	231 (60.6)	228 (57.3)	0.459
Clinical subtypes, n (%)					
MFS	2 (3.0)	30 (14.2)	56 (14.7)	37 (9.2)	**0.009**
CNV	0	11 (5.2)	17 (4.5)	14 (3.5)	0.258
PCB	0	0	1	1	—
Electrodiagnostic subtypes, n (%)	46	120	218	277	
AIDP	18 (39.1)	47 (39.2)	111 (50.9)	148 (53.4)	**0.030**
AMAN	16 (34.8)	20 (16.7)	41 (18.8)	47 (17.0)	**0.034**
Inexcitable	0	1	0	5	—
Equivocal	12 (26.1)	52 (43.3)	66 (30.3)	77 (27.8)	**0.016**
Hughes score on admission, n (%)					
≥ 3	45 (68.2)	97 (46.0)	168 (44.1)	252 (63.3)	**0.000**
<3	21	114	213	146	
Onset to nadir, n (%)					
≤ 7 days	44 (66.7)	134 (63.5)	233 (61.2)	194 (47.0)	**0.000**
>7 days	22	77	148	204	
Hughes score at nadir (mean, g)	3.16±1.07	2.55±1.35	2.64±1.43	3.15±1.37	**0.000**
Treatment, n (%)					
IVIg	30 (45.5)	81 (38.4)	158 (41.5)	179 (45.0)	0.414
Plasmapheresis	9 (13.6)	25 (11.8)	36 (9.4)	61 (15.3)	0.096
Concomitant symptoms, n (%)					
Neurological symptoms					
Cranial nerve paralysis	14 (21.2)	87 (41.2)	165 (43.3)	169 (42.5)	**0.008**
Paresthesia	19 (28.8)	97 (46.0)	174 (45.7)	216 (54.4)	**0.001**
Complications					
Autonomic dysfunction	7 (10.6)	30 (14.2)	53 (13.9)	94 (23.6)	**0.001**
Deep venous thrombosis	0	0	1	10	—
Dyspnoea	10 (15.2)	21 (10.4)	47 (12.3)	86 (21.6)	**0.000**
Intestinal obstruction	0	0	4	4	—
Pneumonia	9 (13.6)	16 (7.6)	50 (13.1)	84 (21.1)	**0.000**
Gastrointestinal bleeding	1	0	3	3	—
Acute pancreatitis	0	0	0	1	—
Laboratory abnormalitis, n (%)					
Hyponatraemia	10 (15.2)	26 (12.3)	62 (16.3)	115 (28.9)	**0.000**
Hypoalbuminaemia	3 (4.5)	12 (5.7)	36 (9.4)	97 (24.4)	**0.000**
Mechanical ventilation (MV), n (%)	3 (4.5)	10 (4.7)	24 (6.3)	46 (11.6)	**0.005**
MV (mean, days)	10.50±2.12	22.30±10.03	19.17±10.05	22.06±15.64	**0.220**
Death in hospital stay, n (%)	0	2 (0.9)	2 (0.5)	13 (3.3)	**0.010**
Hospital stay (mean, days)	15.53±7.57	16.34±9.98	17.01±10.76	18.86±13.22	**0.023**

AIDP, acute inflammatory demyelinating polyneuropathy; AMAN, acute motor axonal neuropathy; CNV, cranial nerve variant; GBS, Guillain-Barré syndrome; IVIg, intravenous immunoglobulin.; MFS, Miller-Fisher syndrome; PCB, pharyngeal-cervical-brachial variants.
Statistically significant results are in bold.

results deliver us explicit information: paying close attention to the overall condition of old people and identifying factors that predict deterioration are the important priorities, except for immunotherapy.

Our study is also subject to some limitations. First, as a retrospective study, we got insufficient information on long-term follow-up, and thus further studies would be done to explore the prognosis of different subgroups. Second, because the study was a retrospective review of medical records and database, extracting bias was anticipated. However, in order to reduce the bias as much as possible, a unified parameter standard in the analysis of NCS was adopted and data were extracted by our team members through strict training; when there was uncertainty, consensus was reached though discussion. Third, it has become apparent that the optimal diagnosis of AMAN requires serial electrophysiological testing, combined with assessment for the presence of antiganglioside antibodies.[38 39] However, as it currently stands, the incidence of axonal GBS was probably underestimated, because the specific antibody tests and serial electrophysiological examination are not widely available in southern China. Nonetheless, about 70% of patients in our study completed NCS after 2 weeks from onset, and we compared the ratio of each form in different timings after onset of weakness and found that there were no significant differences. What's more, although the ratio of AMAN has increased after serial NCSs, AIDP was still the predominant subtype. We suppose that the underestimation of AMAN is not sufficient to affect our entire subtype distribution.

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In conclusion, as the first large-scale study performed in southern China, this study substantially advances the understanding of the clinical features and epidemiology of GBS in southern China. AIDP is the predominant subtype in southern China and URI is the most frequent preceding event. The different subtypes, preceding infection types and age of onset can partially determine the disease progression, severity and short-term recovery speed of GBS. Future efforts should focus on the model predicting the clinical course and severity to provide further insight in determining appropriate care for patients with GBS. In addition, regional difference should be taken into account in formulating these prediction models.

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Funding This work was supported by grants from Wuhan Science and Technology Bureau scientific research project (2015060101010047). The sponsors played no role in the study design, data collection and analysis or decision to submit the article for publication.

Competing interests None declared.

Ethics approval This retrospective study was approved by the ethics committee of the Remin Hospital of Wuhan University, Wuhan, China. The informed consent was waived.

Provenance and peer review Not commissioned; externally peer reviewed.

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Guillain-Barré syndrome in southern China: retrospective analysis of hospitalised patients from 14 provinces in the area south of the Huaihe River

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J Neurol Neurosurg Psychiatry published online January 11, 2018

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