# Guillain-Barre Syndrome: A Clinical Study in King Chulalongkorn Memorial Hospital

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***Background:*** *Guillain-Barre Syndrome (GBS) is an acute, fatal, but treatable polyradiculopathy. Clinical data concerning this entity is scarce in Thailand. The purpose of the present study was to describe clinical profiles and management of GBS as well as to determine prognostic factors in GBS.*

***Material and Method:*** *Clinical data of GBS in King Chulalongkorn Memorial Hospital during 2002-2007 were searched by using in-patients hospital database. Asbury and Cornblath's criteria were applied for the diagnosis of GBS. Clinical data, electrophysiological data, management, and clinical prognostic factors were collected and analyzed by SPSS version 16.*

***Results:*** *Fifty-five patients with GBS were recruited, 26 were male and 29 were female. Mean age was 43 $\pm$ 17 years. History of antecedent infection included: respiratory tract 29%, gastrointestinal tract 7%, ear 2%, and non-specific infection 14%. Initial presentations were limb weakness 87%, limb numbness 78%, bulbar weakness 31%, and facial weakness 18%. Electrodiagnostic study revealed demyelinating process in 54% and axonopathy in 46%. Twenty-nine patients received intravenous immunoglobulin while 13 patients underwent plasmapheresis. Clinical outcomes were satisfactory in most of the patients and only two patients died from sepsis and pneumonia. On discharge, the status of the patients were Hughes grade 1-4 in 73%, 14%, 5%, and 4% respectively. Bulbar paresis as the presenting symptom was the only clinical prognostic factor that significantly determined airway compromised and subsequently respiratory failure.*

***Conclusion:*** *Clinical features of GBS in the present series were characterized by generalized muscle weakness with mild numbness in combination with facial and bulbar paresis in nearly half of patients. Respiratory failure was encountered in 9% of cases. Clinical outcomes were satisfactory in most of the patients with or without specific treatment. The most significant predictor for adverse clinical course was the bulbar paresis as a presenting symptom and patients who presented with less disability score had a better recovery.*

***Keywords:*** *Guillain-Barre syndrome, Clinical features, Prognostic factors*

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Almost a century ago, Guillain, Barre, and Strohl described an acute paralysis with areflexia that had a spontaneously recovered course[1]. A combination of normal cell count with increased protein concentration in the cerebrospinal fluid (CSF) or albuminocytological dissociation could differentiate the condition from poliomyelitis[2,3]. Since the worldwide elimination of poliomyelitis, Guillain-Barre Syndrome (GBS) has been the leading cause of acute flaccid paralysis in medical practice[2,3]. Clinical data concerning this important entity is scarce in Thailand. The purpose of the present study was to describe clinical profiles and management as well as to determine prognostic factors in GBS in a tertiary care center. Comparison with other series from East Asian countries was also performed.

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## Material and Method

Clinical recordings were searched from databases of King Chulalongkorn Memorial Hospital between 2002 and 2007. Keywords were Guillain-Barre Syndrome, acute polyradiculopathy, and acute neuropathy. GBS was diagnosed according to Asbury and Cornblath's criteria[4]. The criteria included presence of progressive bilateral muscle weakness with deep tendon areflexia or severe hyporeflexia, absence of sharp sensory level, and absence of conditions known to cause acute polyneuropathy. Patients were excluded from the present study if: (i) they had marked,

persistent asymmetry of neurological signs, (ii) cerebrospinal fluid (CSF) pleocytosis with > 100 mononuclear leucocytes, (iii) conditions such as diabetic or alcohol neuropathy, neuropathy associated with industrial agent, metals, and drugs, poliomyelitis or porphyria. The clinical status was graded by Hughes's disability scale[5] as follows: grade 1-minor signs or symptoms; grade 2-able to walk 5 m across an open space without assistance; grade 3-able to walk 5 m across an open space with the help of one person and walking frame-stick; grade 4-wheelchair, bed-bound and unable to walk; grade 5-requiring assisted ventilation and grade 6-death. For the purposes of analysis, patients with grades 4-6 were defined as poor outcome whilst patients with grades 1-3 were defined as good outcomes. Data included age, sex, history of antecedent infection, initial presenting symptoms, clinical manifestations, CSF profiles, electrodiagnostic tests, treatments and clinical course of the patients were collected and analyzed by SPSS version 16. The authors also compared the present results with other series from East Asian countries that have a close ethnic relationship *i.e.* Taiwan[6], Hong Kong[7], and China[8].

## Results

Fifty-five patients were recruited, 26 (48%) were male and 29 (52%) were female with the sex ratio of 1:1.12. The age of patients ranged from 15 to79 years with the mean of 43 $\pm$ 17 years. Twenty-five patients (45%) were admitted during the cold season (October to January). Seventeen patients (31%) and 13 patients (24%) were admitted during the summer and the rainy season respectively. Preceding events included respiratory tract infection in 16 patients (29%), gastrointestinal tract infection in four patients (7%), ear infection in one patient (2%), and non-specific infection in eight patients (14%). Twenty-six patients (48%) did not report any infection prior to paralytic illness.

All patients had generalized flaccid paralysis during the course. The most frequent presenting symptoms were limb weakness and numbness followed by bulbar and facial paresis. The presenting symptoms are summarized in Table 1. The combined patterns of syndromes were varied. Weakness of both legs with or without numbness was the most frequent symptom presented in 30 patients (54%). Weakness of both feet and hands with or without sensory abnormalities were detected in 18 patients (33%). Seventeen patients (31%) had dysarthria and/or dysphagia in combination with limbs weakness and 10 patients (18%) had facial paresis and weakness of the limbs. The degree of legs weakness was worse than arms in 35 patients (64%) and was equal in 13 patients (24%). Grading of motor weakness (MRC) ranged from grade II to grade IV in which grade III was the most frequent finding. Hughes's disability data on admission and discharge are summarized in Table 2. During the admission, five patients (9%) developed respiratory failure. The duration from presenting symptom to the nadir of the symptoms ranged from 2 days to12 days with the mean of 5 $\pm$ 2.5 days.

Lumbar puncture was performed in all 55 patients. Initial CSF profiles revealed albumino-cytological dissociation in 40 patients (73%). Subsequent CSF profiles in 15 patients (27%) who had normal initial CSF protein showed increased protein level on the follow-up. The mean CSF total protein was 96 $\pm$ 10.7 mg/dl with the maximum of 295 mg/dl. The white blood cell (wbc) count in CSF ranged from 0-29 cells/mm$^3$. The CSF cell count < 10 cells/mm$^3$ was found in 42 patients (76%) and CSF cell count ranged from 14-29 cells/mm$^3$ was detected in five patients (9%). Electrodiagnostic test was performed in 22 patients

**Table 1.** Presenting clinical syndrome (n = 55)

| Clinical presentation | n (%) |
|---|---|
| Limb weakness | 48 (87) |
| Limb numbness | 43 (78) |
| Bulbar paresis | 17 (31) |
| Facial paresis | 10 (18) |
| Back and leg pain | 7 (13) |
| Headache | 4 (7) |
| Ataxia | 2 (4) |
| Bladder dysfunction | 2 (4) |

**Table 2.** Hughes's disability data on admission and discharge

| Disability grading | Admission n (%) | Discharge n (%) |
|---|---|---|
| Hughes grade 1 | 32 (58%) | 40 (73%) |
| Hughes grade 2 | 16 (29%) | 8 (14%) |
| Hughes grade 3 | 5 (9%) | 3 (5%) |
| Hughes grade 4 | 2 (4%) | 2 (4%) |
| Hughes grade 5 | 0 (0%) | 0 (0%) |
| Hughes grade 6 | 0 (0%) | 2 (4%) |
| Mean disability grade | 1.72 $\pm$ 0.02 | 1.54 $\pm$ 0.04 |

**Table 3.** Comparison among East Asian countries

| Clinical series | Taiwan Lyu et al[6] | Hong Kong Hui et al[7] | Harbin, China Cheng et al[8] | KCMH Areeyapinan et al |
|---|---|---|---|---|
| Number | 167 | 20 | 71 | 55 |
| Mean age(year) | 37 | 45 | 20 ± 17 | 43 ± 17 |
| Male | 68% | 45% | 61% | 48% |
| Female | 32% | 55% | 39% | 52% |
| Season | Spring | NM | Summer | Cold summer |
| Respiratory infection | 56% | NM | 68% | 29% |
| Gastrointestinal tract infection | 2% | 25% | 11% | 7% |
| Initial presentation | | | | |
| Limb weakness | 41% | 100% | 82% | 87% |
| Limb numbness | 38% | 100% | 17% | 78% |
| Bulbar palsy | 10% | NM | 14% | 31% |
| Facial paresis | 0.5% | 35% | 32% | 18% |
| Back and leg pain | 7% | 45% | NM | 13% |
| Headache | 4% | NM | NM | 7% |
| Ptosis | 1.3% | 20% | NM | 0% |
| Ataxia | 8% | NM | NM | 4% |
| Electrophysiologic test | 71 (100%) | 20 (100%) | 25 (35%) | 22 (40%) |
| AIDP | 49% | 100% | 96% | 54% |
| Axonopathy | 4%* | 0% | 4% | 46% |

NM = not mention; GI = gastrointestinal tract; AIDP = acute inflammatory demyelinating polyneuropathy
* 47% in this series were not classified as AIDP or axonopathy

(40%). The test showed demyelination predominant in 12 patients (54%) and axonopathy predominant in 10 patients (46%).

The clinical course was not deteriorated in 43 patients (78%) and 12 patients (22%) developed respiratory insufficiency in which five patients (9%) subsequently needed intubation. Intravenous immunoglobulin (IVIg) was prescribed in 29 patients (52%) whereas plasmapheresis was performed in 13 patients (24%). Thirteen patients (24%) received neither IVIg nor plasmapheresis. The hospital stay ranged from 6 to 63 days with the mean of 15 ± 4.5 days. The clinical outcomes on discharge were satisfactory in most of the patients (Table 2). There were two deaths (4%) due to severe sepsis and severe pneumonia. Regarding the prognostic factors, the odds ratio using Pearson Chi-square test for bulbar palsy, age > 40, antecedent infection and time to maximal symptom < 7 days, revealed bulbar paresis as the only prognostic factor for adverse complication *i.e.* respiratory failure with odds ratio of 26.5 (95% CI 3.2-220) $p < 0.0002$. Comparison with the other series in East Asian countries was demonstrated in Table 3.

## Discussion

Although Asbury and Cornblath's clinical criteria[4] are very helpful for clinical diagnosis of GBS, variation in clinical presentations especially in the early clinical course may be problems in the diagnosis. As demonstrated in the present series, the onset of weakness may begin in either lower or upper extremities or cranial nerves and these may mimic myopathy, anterior horn cell disease, or myasthenia gravis. Symmetrical weakness with hypo or areflexia is an important clue to differentiate GBS from these conditions. History of antecedent infection, which was detected in nearly half of the presented cases, was also helpful for the diagnosis. Apart from weakness, some GBS patients can present with muscle pain, ataxia, and headache[2,3].

CSF examination in GBS typically shows albuminocytological dissociation. However, CSF protein may be normal in the first week, and gradually elevated in more than 90% of the patients at the end of the second week[2,3]. The typical course of CSF protein elevation was demonstrated in the present series. Electrophysiological testing is an important confirmatory test in the diagnosis of GBS and it is

very useful in differentiating subtypes of GBS *e.g.* demyelinating or axonal neuropathy which may be subclassified into: acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN)[2,3]. In this series, demyelinating process and axonopathy was encountered in 54% and 46% of the patients. Moreover, electrophysiological testing can be used to follow-up and predict the outcomes of the syndrome[9].

Weakness in GBS may be maximal and reach a nadir by 2 weeks[2,3]. The patients in the present series followed this rule. Poor prognostic factors which have been studied in the literatures included advanced age, duration from onset to nadir of the disease less than 7 days, bulbar dysfunction, axonal involvement, previous diarrheal illness, *C. jejuni* infection, cytomegalovirus infection, and anti-GM1 antibodies[10,11]. In the present study, bulbar paresis significantly correlated with poor clinical outcome with the odds ratio of 26.5 (95% CI 3.2-220) while other potential prognostic factors did not demonstrated any statistically significant association with the prognosis. However, *C. jejuni* infection, cytomegalovirus infection, and anti-GM1 antibodies had not been studied in the present series.

Advances in immunotherapy *i.e.* plasmapheresis or plasma exchange (PE) and intravenous immunoglobulin (IVIg) have dramatically changed the clinical course and prognosis of GBS especially in the severe cases. However, supportive care is still the most important component of management[2,3]. Large randomized controlled trials and meta-analysis have shown the efficacy of PE and IVIg in management of GBS[12-18]. Largest beneficial effect was seen when started within the first two weeks[13-15]. However, PE still has a beneficial effect when applied within the first four weeks of onset[15,16,18]. IVIg is shown as effective as PE[16,18]. The decision of which regimens would be applied in the present series depended on clinical status and judgment of attending physicians. The clinical disability outcome in the present series was dramatically improved after both treatments. However, the predictors for good or poor outcomes depended on the regimen used as well as on the clinical presentation and disability grade. The present series disclosed that all patients with Hughes grade 1-3 had a good outcome while patients of Hughes grade 4-6 had been improved partially and two patients died.

Comparisons with other East Asian countries had been probed. Two of the studies[6,7] as well as the present study recruited only adults and one study[8] recruited children and adults. There was some variation in sex distribution among these series, which may be due to number of the studied population. Age-specific curve in GBS seems to have a bimodal distribution, with peaks in young adults and the elderly[19]. Age distributions of GBS in the present study, Taiwan[6] and Hong Kong[7] series were around 40 years and was less frequent in the old age group. In, the China series[8] which included children, the highest GBS incidence was found in the younger age group and the incidence among the elderly was remarkably low. In most series, non-specific upper respiratory tract infection was the most common preceding event followed by acute gastrointestinal illness[20]. Most studies have failed to identify the relationship between incidence of GBS and season[20]. Lack of seasonal association may be due to the fact that most frequent antecedent infections *i.e.* respiratory and enteric infections have opposite seasonality. In the present study, the authors found seasonal clustering in cold months, which may be correlated with respiratory tract infection that has a high incidence during this period of the year in Thailand. The study from China found a seasonal predominance in the summer months and in children[8]. The possible explanations for this pattern of age-specific incidence, summer season, and high percentage of gastrointestinal tract infection may be due to infection with *C. jejuni* and poor personal hygiene among children[21]. Electrodiagnostic test showed acute inflammatory demyelinating process (AIDP) in about half of the patients in the present study and in the Taiwan study[6] which contrasted with the study from Hong Kong[7] and China[8], which revealed AIDP in most cases of GBS. The clinical manifestations in the four studies showed diverse patterns. The variations in electrophysiological subtypes of GBS and clinical manifestations in these series may reflect the difference in pathophysiology of GBS, which may be related to the preceding infections and may be related to the difference in the number of the patients in various series.

**References**


1. Guillain G, Barre J, Strohl A. Sur un syndrome de radiculo nevrite avec hyperalbuminose du liquide cephalorachidien sans reaction cellulaire. Remarques sur les caracteres cliniques et graphiques des reflexes tendineux. Bull Soc Med Hop Paris 1916; 28: 1462-70.
2. Ropper AH, Wijicks EFM, Truax BT. Guillain-Barre

syndrome. Philadelphia: FA Davis; 1991.
3. Hughes RA, Cornblath DR. Guillain-Barre syndrome. Lancet 2005; 366: 1653-66.
4. Asbury AK, Cornblath DR. Assessment of current diagnostic criteria for Guillain-Barre syndrome. Ann Neurol 1990; 27(Suppl): S21-4.
5. Hughes RA, Newsom-Davis JM, Perkin GD, Pierce JM. Controlled trial prednisolone in acute polyneuropathy. Lancet 1978; 2: 750-3.
6. Lyu RK, Tang LM, Cheng SY, Hsu WC, Chen ST. Guillain-Barre syndrome in Taiwan: a clinical study of 167 patients. J Neurol Neurosurg Psychiatry 1997; 63: 494-500.
7. Hui AC, Chow KM, Tang AS, Fu M, Kay R, Wong KS. Electrophysiological, clinical and epidemiological study of Guillain-Barre Syndrome in Hong Kong Chinese. J Clin Neurosci 2005; 12: 134-6.
8. Cheng Q, Wang DS, Jiang GX, Han H, Zhang Y, Wang WZ, et al. Distinct pattern of age-specific incidence of Guillain-Barre syndrome in Harbin, China. J Neurol 2002; 249: 25-32.
9. Miller RG, Peterson GW, Daube JR, Albers JW. Prognostic value of electrodiagnosis in Guillain-Barre syndrome. Muscle Nerve 1988; 11: 769-74.
10. van Koningsveld R, Steyerberg EW, Hughes RA, Swan AV, van Doorn PA, Jacobs BC. A clinical prognostic scoring system for Guillain-Barre syndrome. Lancet Neurol 2007; 6: 589-94.
11. Hiraga A, Kuwabara S. Early prediction of prognosis in Guillain-Barre syndrome. Lancet Neurol 2007; 6: 572-3.
12. The Guillain-Barre syndrome Study Group. Plasmapheresis and acute Guillain-Barre syndrome. Neurology 1985; 35: 1096-104.
13. French Cooperative Group on Plasma Exchange in Guillain-Barre syndrome. Efficiency of plasma exchange in Guillain-Barre syndrome: role of replacement fluids. Ann Neurol 1987; 22: 753-61.
14. French Cooperative Group on Plasma Exchange in Guillain-Barre Syndrome. Plasma exchange in Guillain-Barre syndrome: one-year follow-up. Ann Neurol 1992; 32: 94-7.
15. Raphael JC, Chevret S, Hughes RA, Annane D. Plasma exchange for Guillain-Barre syndrome. Cochrane Database Syst Rev 2002; (2): CD001798.
16. van der Meche FG, Schmitz PI. A randomized trial comparing intravenous immune globulin and plasma exchange in Guillain-Barre syndrome. Dutch Guillain-Barre Study Group. N Engl J Med 1992; 326: 1123-9.
17. Hughes RA, Raphael JC, Swan AV, van Doorn PA. Intravenous immunoglobulin for Guillain-Barre syndrome. Cochrane Database Syst Rev 2006; (1): CD002063.
18. Plasma Exchange/Sandoglobulin Guillain-Barre Syndrome Trial Group. Randomized trial of plasma exchange, intravenous immunoglobulin, and combined treatments in Guillain-Barre syndrome. Lancet 1997; 349: 225-30.
19. Chio A, Cocito D, Leone M, Giordana MT, Mora G, Mutani R. Guillain-Barre syndrome: a prospective, population-based incidence and outcome survey. Neurology 2003; 60: 1146-50.
20. Hughes RA, Rees JH. Clinical and epidemiologic features of Guillain-Barre syndrome. J Infect Dis 1997; 176(Suppl 2): S92-8.
21. Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR, Griffin JW, et al. Guillain-Barre syndrome in northern China. Relationship to Campylobacter jejuni infection and anti-glycolipid antibodies. Brain 1995; 118(Pt 3): 597-605.

# การศึกษาลักษณะทางคลินิกของกลุ่มอาการ Guillain-Barre ในโรงพยาบาลจุฬาลงกรณ์

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***ภูมิหลัง:*** *กลุ่มอาการ Guillain-Barre (GBS) เป็นกลุ่มอาการรากประสาทอักเสบที่เป็นอย่างเฉียบพลัน และอาจรุนแรงถึงแก่ชีวิตแต่เป็นภาวะที่สามารถรักษาได้ข้อมูลการศึกษาทางคลินิกของกลุ่มอาการนี้มีน้อยในประเทศไทย*

***วัตถุประสงค์:*** *เพื่อศึกษาลักษณะอาการทางคลินิก การดูแลรักษากลุ่มอาการ GBS และประเมินปัจจัยชี้วัดการพยากรณ์โรคในกลุ่มอาการ GBS*

***วัสดุและวิธีการ:*** *ได้ทำการรวบรวมบันทึกข้อมูลทางคลินิกของกลุ่มอาการ GBS ในโรงพยาบาลจุฬาลงกรณ์ ระหว่างปี พ.ศ. 2545 ถึง พ.ศ. 2550 โดยการรวบรวมจากข้อมูลของผู้ป่วยที่เข้ารับการรักษาในโรงพยาบาล การวินิจฉัยกลุ่มอาการ GBS ใช้เกณฑ์การวินิจฉัยของ Asbury และ Cornblath's ข้อมูลทางคลินิก, ข้อมูลการตรวจทางประสาทสรีรวิทยาข้อมูลการดูแลรักษา และปัจจัยการทำนายโรคได้ถูกรวบรวม และวิเคราะห์โดยใช้โปรแกรม SPSS version 16*

***ผลการศึกษา:*** *ได้รวบรวมผู้ป่วย GBS จำนวน 55 ราย เป็นชาย 26 ราย หญิง 29 ราย อายุเฉลี่ย 43 $\pm$ 17 ปี ประวัติการติดเชื้อที่นำมาก่อนได้แก่: ทางเดินหายใจ 29%, ทางเดินอาหาร 7% ทางช่องหู 2% และการติดเชื้อที่ไม่จำเพาะ 14% อาการแสดงขั้นต้น ได้แก่ แขนขาอ่อนแรง 87% อาการชาแขนขา 78% อาการอ่อนแรงของกล้ามเนื้อควบคุมการพูด และการกลืน 31% อาการอ่อนแรงของกล้ามเนื้อใบหน้า 18% ผลการตรวจทางประสาทสรีรวิทยาพบ demyelination คิดเป็น 54% axonopathy คิดเป็น 46% ผู้ป่วย 29 ราย ได้รับการรักษาโดยการให้สาร immunoglobulin ทางหลอดเลือดดำ ผู้ป่วย 13 ราย ได้รับการรักษาโดยวิธี plasmapheresis ผลของการรักษาทางคลินิกอยู่ในระดับเป็นที่น่าพอใจในผู้ป่วยส่วนใหญ่ และมีผู้ป่วยเพียง 2 ราย ที่เสียชีวิตจากการติดเชื้อรุนแรงและปอดบวม ขณะจำหน่ายผู้ป่วยออกจากโรงพยาบาลมีสภาวะประเมินทางกายภาพของ Hughes ระดับ 1 ถึง 4 คิดเป็นร้อยละ 73, 14, 5 และ 4 ตามลำดับ ปัจจัยการทำนายโรคที่สำคัญที่บ่งว่าจะมีปัญหาเรื่องการหายใจและการหายใจล้มเหลว ได้แก่ อาการนำที่เป็นอาการอ่อนแรงของกล้ามเนื้อในการพูดการกลืน*

***สรุป:*** *กลุ่มอาการ GBS ในการศึกษานี้พบลักษณะทางคลินิกที่สำคัญคือ มีอาการอ่อนแรงของกล้ามเนื้อโดยทั่วไปและมีอาการชาเล็กน้อย ร่วมกับอาการอ่อนแรงของกล้ามเนื้อใบหน้า และกล้ามเนื้อในการพูดการกลืน ซึ่งพบประมาณครึ่งหนึ่งของผู้ป่วย ภาวะหายใจล้มเหลวพบ 9% ของผู้ป่วยที่นำมาศึกษาผลของการรักษาอยู่ในเกณฑ์ที่น่าพอใจทั้งในกลุ่มที่ได้รับการรักษาจำเพาะและกลุ่มที่ได้รับการรักษาไม่จำเพาะ ปัจจัยชี้วัดที่สำคัญต่อการเกิดผลแทรกซ้อนในระหว่างการดำเนินโรคคือ การอ่อนแรงของกล้ามเนื้อควบคุมการพูดการกลืนเป็นอาการแสดงเริ่มแรก ผู้ป่วยที่มีความพิการน้อยในระยะเริ่มแรกจะมีการฟื้นตัวที่ดีกว่า*