

Seasonal Variation of Guillain-Barré Syndrome Admission in a Large Tertiary Referral Center in Southern Iran: A 10 Year Analysis

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Abstract-

Introduction: Guillain-Barré syndrome (GBS) is an acute, acquired, monophasic peripheral neuropathy which has become the most common cause of acute flaccid paralysis. This is an epidemiological report on the seasonal and monthly distribution of GBS and certain patient characteristics in Shiraz, Iran.

Methods: We extracted data from Namazi hospital records retrospectively in a 10 year period (January 2000 to December 2009), the largest tertiary referral center in the south of Iran. In order to compare the frequency of GBS in different months and seasons we used the Chi Square test. In a separate analysis a comparison was made between two subsets of patients regarding sex, duration of admission, month and season of admission.

Results: From 389 cases of GBS, 232 (59.6%) were male and 157 (40.4%) were female. There was seasonal ($P=0.004$) and monthly ($P=0.046$) variation. Spring and winter had the most amount of patients, with admissions from the month of February through June inclusive accounting for 50% of all cases.

Conclusion: Our study shows that there is significant monthly and seasonal variation in the admission rate of patients with GBS in Shiraz.

Key words: Guillain-Barré Syndrom, pandemics, epidemiology, periodicity, seasonal variation, Iran

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INTRODUCTION

Guillain-Barré syndrome (GBS) is an acute, acquired, monophasic peripheral neuropathy which has

become the most common cause of acute flaccid paralysis since the eradication of polio^(1,2). It has an incidence rate of 1 to 2 per 100,000/year in most populations⁽³⁾. While most recover from the disease without adverse

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sequela, 15-20% are left with severe neurological deficits⁽²⁾. The underlying pathogenesis points to cross-reactive immune responses secondary to antibodies produced as a result of molecular mimicry of certain pathogens with components of the peripheral nerve⁽⁴⁾.

We have analyzed the data from hospital records from patients admitted with GBS in Namazi hospital in Shiraz south of Iran. Our aim was to study the epidemiological characteristic of disease occurrence using a large tertiary referral center as reference.

MATERIAL AND METHODS

Shiraz is located in the southern region of Iran (coordinates: 29°37'N 52°32'E). Its climate is moderate with regular seasons⁽⁵⁾. Its total area is 178,891 km² with an elevation of about 1,500 meters above sea level. It has a population of 1,455,073 (2009 est.⁽⁶⁾). We extracted data from the Namazi hospital records retrospectively in a 10 year period (from January 1, 2000 to December 31, 2009), the largest tertiary referral center in the south of Iran. Patient demographics including age, sex, date of admission and discharge were extracted. Information regarding yearly admissions for the entire hospital was also gathered. Diagnosis was coded based on the 9th Revision of the International Classification of Diseases (ICD-9: 357.0). Diagnosis of GBS at our center is based on guidelines provided by the National Institute of Neurological Disorders and Stroke⁽⁷⁾.

Statistical analysis

In order to compare the frequency of GBS in different months and seasons we used the Chi Square test. The analyses were performed on a personal computer using SPSS for Windows (SPSS Inc., Chicago, IL, USA). All tests for statistical significance were two-tailed, with the level of significance at a < 0.05.

RESULTS

From 389 cases of GBS, 232 (59.6%) were male and 157 (40.4%) were female. Mean age and duration of hospitalization of admitted patients did not differ amongst seasons (Table 1). Analyzing the 10 year data cumulatively, there was a significant seasonal and monthly variation in the number of admitted cases (Figures 1 and 2). Spring and winter had the most diagnosed patients of GBS. Admissions from the month of February through June inclusive accounted for 50% of all patients, with February, March and May having over 40 admissions per month. Mean duration of hospital stay for males was 12.3 ± 11.6 and for females 13.7 ± 11.1 (P value=0.239).

Two groups of patients were compared according to age, one <18 years of age (n=164, 42.2%) and one ≥ 18 (n=225, 57.8%). Duration of stay was significantly more in the ≥ 18 age group (15.0 ± 12.5 versus 10.0 ± 9.5 days; P value<0.001). Regarding other characteristics these two groups did not differ with respect to distribution of

Table 1. Mean age at admission in years and duration of admission in days based on season.

	Season	N	Mean	Std. Deviation	95% Confidence Interval for Mean		Minimum	Maximum	P value
					Lower Bound	Upper Bound			
Age	Spring	113	28.18	22.6	24.03	32.34	1.0	76.0	0.891
	Summer	90	30.25	22.6	25.67	34.83	2.0	81.0	
	Autumn	71	29.40	22.9	24.03	34.78	1.0	82.0	
	Winter	115	30.27	23.3	26.04	34.50	1.0	81.0	
	Total	389	29.51	22.8	27.28	31.74	1.0	82.0	
Duration	Spring	113	12.50	12.4	10.20	14.80	1.0	64.0	0.968
	Summer	90	12.80	11.6	10.30	15.20	1.0	63.0	
	Autumn	71	13.20	11.1	10.60	15.80	1.0	55.0	
	Winter	115	13.20	11.2	11.10	15.20	1.0	66.0	
	Total	389	12.90	11.6	11.70	14.00	1.0	66.0	

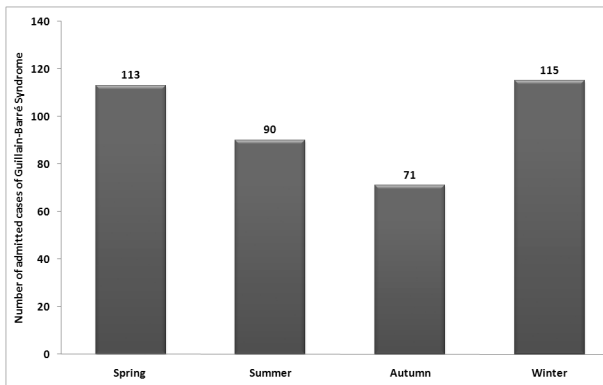


Figure 1. Distribution of GBS admissions according to season during 2000-09 in Namazi hospital (P value =0.004).

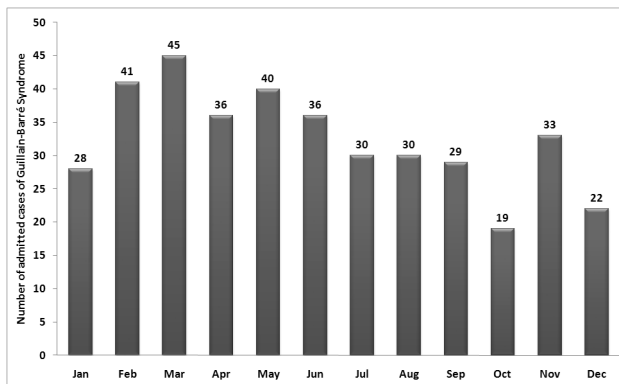


Figure 2. Distribution of GBS admissions according to month during 2000-09 in Namazi hospital (P value =0.046).

sex (P value=0.154), season (P value=0.384) and month (P value=0.510) of acquiring the disease. There was no difference between different sexes acquiring the disease in different seasons (P value=0.654) or months (P value=0.349).

DISCUSSION

We found that the occurrence of GBS varies significantly with respect to month and season. Seasonal variation was not seen in some studies from Brazil, Northwest of Iran, North and South of Italy, and Spain⁽³⁾. In contrast, seasonal variation has been seen in several

other reports (Spring in Northwest Greece⁽⁸⁾ and Taiwan⁽⁹⁾, Spring and Summer in Brazil⁽¹⁰⁾, Summer in China⁽¹¹⁾ and South Korea⁽¹²⁾, Autumn in Sweden⁽¹³⁾, Winter and June in the Netherlands⁽¹⁴⁾). Higher frequency of winter and spring season which was seen in our series was similar to reports from Oxfordshire in the UK⁽¹⁵⁾ and Kuwait⁽¹⁶⁾.

The lack of a certain pattern of seasonal variation may be attributed to heterogeneity of causes of precedent infections. Perhaps the longest known and most established organism to cause this disease is *Campylobacter jejuni*. Forms triggered by this infection tend to be more severe⁽²⁾. There are a number of other well defined microbial and viral infections related to GBS⁽⁴⁾. Of recent interest and currently under investigation is the influenza virus, particularly influenza A H1N1. It appears to involve a different mechanism than that of *C. jejuni* in causing damage to the peripheral nerve. It produces a less debilitating form of disease⁽¹⁾.

Although there have been reports of seasonal variation in GBS occurrence^(2,3), there is no constant seasonal variation in different regions of the world⁽³⁾. This may be because the two proposed causative factors most frequently recognized as triggering events, respiratory and enteric infections, have opposite seasonality⁽¹⁷⁾.

As a study of GBS for temporal patterns a study from Mexico⁽¹⁸⁾ and another from China⁽¹⁹⁾ had found a peak in the acute motor axonal neuropathy subtype during summer, which may have been secondary to gastroenteritis outbreaks. The Axonal neuropathy subtype has also been reported to be more common in those with *C. jejuni* gastroenteritis in northern Iran⁽²⁰⁾.

There are limited studies on the epidemiology of infectious agents proposed to trigger GBS in Iran, so we could not suggest a possible link between an outbreak of any causative organism and our seasonal and monthly variations. We found only one study on gastroenteritis cases leading to diarrhea referred to the same hospital where this study was conducted, which showed *C. jejuni* to be one of the top three causative organisms. But the study was limited to a three month period in 2004 which was just after the peak months of GBS cases according to our study⁽²¹⁾.

As a summary, our study shows that there is significant seasonal variation in the admission rate of patients with GBS in Shiraz.

REFERENCES

1. Lehmann HC, Hartung HP, Kieseier BC, Hughes RA. Guillain-Barré syndrome after exposure to influenza virus. *Lancet Infect Dis* 2010;10:643-651.
2. Nachamkin I, Allos BM, Ho T. *Campylobacter* species and Guillain-Barré syndrome. *Clin Microbiol Rev* 1998;11:555-567.
3. McGrogan A, Madle GC, Seaman HE, de Vries CS. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. *Neuroepidemiology* 2009;32:150-163.
4. Borhani Haghghi A, Sabayan B. Acute axonal polyradiculoneuropathy associated with partially treated brucellosis: a case report. *J Clin Neuromuscul Dis* 2007;9:262-264.
5. Criteria for diagnosis of Guillain-Barré syndrome. *Ann Neurol* 1978;3:565-566.
6. Markoula S, Giannopoulos S, Sarmas I, Tzavidi S, Kyritsis AP, Lagos G. Guillain-Barré syndrome in northwest Greece. *Acta Neurol Scand* 2007;115:167-173.
7. Lyu RK, Tang LM, Cheng SY, Hsu WC, Chen ST. Guillain-Barré syndrome in Taiwan: a clinical study of 167 patients. *J Neurol Neurosurg Psychiatry* 1997;63:494-450.
8. Rocha MS, Brucki SM, Carvalho AA, Lima UW. Epidemiologic features of Guillain-Barré syndrome in Sao Paulo, Brazil. *Arq Neuropsiquiatr* 2004;62:33-37.
9. McKhann GM, Cornblath DR, Griffin JW, Ho TW, Li CY, Jiang Z, Wu HS, Zhaori G, Liu Y, Jou LP. Acute motor axonal neuropathy: a frequent cause of acute flaccid paralysis in China. *Ann Neurol* 1993;33:333-342.
10. Coe, C. J. Guillain-Barré syndrome in Korean children. *Yonsei Med J* 1989;30:81-87.
11. Jiang GX, Cheng Q, Link H, de Pedro-Cuesta J. Epidemiological features of Guillain-Barré syndrome in Sweden, 1978-93. *J Neurol Neurosurg Psychiatry* 1997;62:447-453.
12. Van Koningsveld R, Van Doorn PA, Schmitz PI, Ang CW, Van der Meché FG. Mild forms of Guillain-Barré syndrome in an epidemiologic survey in The Netherlands. *Neurology* 2000;54:620-625.
13. Winner, SJ., Evans, JG. Age-specific incidence of Guillain-Barré syndrome in Oxfordshire. *Q J Med* 1990;77:1297-1304.
14. Ismail EA, Shabani IS, Badawi M, Sanaa H, Madi S, Al-Tawari A, Nadi H, Zaki M, Al-saleh Q. An epidemiologic, clinical, and therapeutic study of childhood Guillain-Barré syndrome in Kuwait: is it related to the oral polio vaccine? *J Child Neurol* 1998;13:488-492.
15. Hughes, RA., Rees, JH. Clinical and epidemiologic features of Guillain-Barré syndrome. *J Infect Dis* 1997;176:S92-S98.
16. Nachamkin I, Arzarte Barbosa P, Ung H, Lobato C, Gonzalez Rivera A, Rodriguez P, Garcia Briseno A, Cordero LM, Garcia Perea L, Perez JC, Ribera M, Aldama PC, Guitérrez GD, Sarnat LF, García MR, Veitch J, Fitzgerald C, Cornblath DR, Rodriguez Pinto M, Griffin JW, Willison HJ, Asbury AK, McKhann GM. Patterns of Guillain-Barré syndrome in children: results from a Mexican population. *Neurology* 2007 23;69:1665-1671.
17. Ho TW, Mishu B, Li CY, Gao CY, Cornblath DR, Griffin JW, Asbury AK, Blaser MJ, McKhann GM. Guillain-Barré syndrome in northern China. Relationship to *Campylobacter jejuni* infection and anti-glycolipid antibodies. *Brain* 1995;118:597-605.
18. Barzegar M, Alizadeh A, Toopchizadeh V, Dastgiri S, Majidi J. Association of *Campylobacter jejuni* infection and Guillain-Barré syndrome: a cohort study in the northwest of Iran. *Turk J Pediatr* 2008;50:443-448.
19. Hassanzadeh, P., Motamedifar, M. Occurrence of *Campylobacter jejuni* in Shiraz, Southwest Iran. *Med Princ Pract* 2007;16:59-62.