Seasonal variations of childhood Guillain-Barre Syndrome in South west Iran

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Abstract:

Background: It was found that the occurrence of Guillain-Barre Syndrome (GBS) varies in respect to the month and season; this variation has not been adequately studied.

Objective: To determine the month and seasonal variation of GBS in children in the Khuzestan province, south west Iran, during a 10-year period (2006-2015).

Patients and methods: We extracted data retrospectively from acute flaccid paralysis committee from healthcare centers in all cities of the province, over a 10-year period (from January 1, 2006 to December 31, 2015). In this study all children under 15 years of age with Guillain-Barre syndrome were surveyed. In order to compare the frequency of GBS in different seasons and months we used the Chi Square test.

Results: From 187 cases of GBS, 101 (54%) were males, 86 (46%) females with sex ratio 1.17:1. The mean age of the children was 5.39 ± 4.02 years. The highest occurrence of GBS was observed in autumn (32.1%) followed by winter (27.3%). The highest number of cases (28; 15%) occurred in December and the lowest (8; 4.3%) in September. There was seasonal (P=0.006) and monthly (P=0.036) variation in occurrence of GBS throughout the year with more prevalence in autumn , September and December.

Conclusion: Our study showed that there is a significant monthly and seasonal variation in children with GBS in Khuzestan province.

Keywords: Guillain-Barre syndrome, seasonal variation, children, South-West Iran

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Introduction:

Guillain-Barre syndrome (GBS) is a nervous system disorder. This syndrome is an autoimmune disease that manifests as an acute and rapidly progressive inflammation of the peripheral nerves which causes loss of sensation and muscle weakness. [1] The underlying mechanism of this disorder is not yet known, but there have been indications that autoimmune processes are involved, as two third of the cases occur after a gastrointestinal or respiratory infection. [2,3] Since poliomyelitis has been eradicated through initiatives of World Health Organization (WHO), GBS has become the most prevalent cause of acute flaccid paralysis in all ages, especially in children.[4] A considerable number of studies have been conducted on GBS in Iran and around the world. Mcgrogan et al (2009) conducted an epidemiologic study on the incidence of GBS around the world and reported the incidence in children under the age of 15 yrs to be 1.1-1.8 per 100,000 people and suggested that GBS incidence varies in different seasons and climates. [5]

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Studies on the incidence of GBS in Asian countries have also indicated that its incidence varies in regions with different climates, and that there is an association with the incidence of seasonal infections. [6] Barzegar et al, have explored epidemiology of GBS in the northwest of Iran and reported its incidents to be 2.27 per 100,000 for children under 15 years of age and suggested that GBS incidents were higher in winter. [7] Higher incidence of GBS in some countries and some particular geographical locations is a topic that has been studied, yet due to some controversies it is still debated. [8, 9, 10, 11, 12] Therefore, it is still necessary to undertake more studies on this topic. Although there are numerous studies on GBS around the world, there has been a lack of studies in Iran on the epidemiology and seasonal variations of GBS for less than 15 year olds old age children, especially in different areas of the country that has different climates. An understanding of epidemiological characteristics of GBS and possible risk factors in its incidents will be helpful in preventing mortality and long term morbidity of this disorder.

Patients and methods:

In this cross-sectional study all children under 15 years of age who were diagnosed with GBS were surveyed. We extracted data from the Acute Flaccid Paralysis Committee (AFPC) records retrospectively over a 10-year period (from January 1, 2006 to December 31, 2015), the largest referral center in Khuzestan province, south west of Iran. During the study period, two hundred fifty four cases were

reported in the AFPC, but only 187 were included in the study, 67 cases that were recorded to have acute flaccid paralysis, paralysis of lower limbs or suspicion of GBS were excluded. They were followed by localy and finally assessed by provincial AFPC for at least 60 days and then the completed data were sent to central AFPC related to ministry of health and medical education of Iran. All children with acute flaccid paralysis from healthcare centers in different cities of the province were seen by trained local pediatricians and finally assessed by provincial pediatric neurologist. The diagnosis of GBS, according to AFP surveillance protocol by WHO was made on history, clinical evaluation, electrophysiological studies, CSF examination and stool sampling for isolation of polio virus.[13, 14] Patient demographics including age, sex, date of onset, admission and discharge were recorded.

Season definition. In Iran spring states from 21 march up to 21 June (In Persian calendar; Farvardin up to Khordâd), summer is from 22 June up to 22 August (In Persian calendar; Tir up to Shahrivar), autumn is from 23 August up to 21 December (In Persian calendar; Mehr up to Âzar) and winter is from 22 December up to 20 March (In Persian calendar; Dey up to Esfand). [15] Data were analyzed with SPSS Software Package version 18.0. In order to compare the frequency of GBS in different month and seasons we used the Chi Square test. All tests for statistical significance were at a < 0.05.

Results:

Out of 187 cases of GBS, there was male predominance with 54% (n=101) while female with 46% (n=86), having male to female ratio of 1:17 to 1 without significant differences between the two sexes. Mean age was 5.39 ± 4.02 years, with 53% being less than 5 years old. The occurrence of GBS in spring, summer, autumn and winter has been showed in table 1. Autumn had the highest incidence 60(32.1%) and summer had the lowest 27(14.4%). Seasonal variation among GBS was observed throughout the year with more prevalence in autumn followed by winter. There was a statistically significant difference in the incidence of GBS in different seasons (p=0.006), as it's seen in table 1

Table1: Seasonal trends in childhood GBS over a 10-year period

Season	Number of cases over 10 years (187)	Percentage%	Significance
Winter	51	(27.3%)	Chi square test of homogeneity (p=0.006)
Spring	49	26.2%	
Summer	27	14.4%	
Autumn	60	32.1%	

The highest numbers of Guillain-Barre Syndrome cases (28; 15%) were seen in December and (19; 10.2%) were in November; and the lowest numbers were seen during September and July with (8; 4.3%) and (9; 4.8%), respectively (Figure 1). There was a statistically significant difference in the incidence of GBS in different months (p=0.036). As it's seen in figure 1.

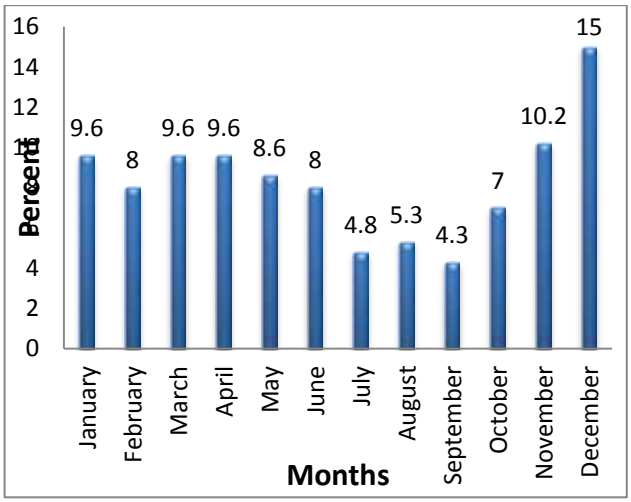

Figure 1: Distribution of GBS according to month during 2006-2015 in Khuzestan, Southwest Iran

Table 2: Comparison of seasonal variation GBS by age and sex

Variables		Seasons	Frequency	%	P-value
Age	Less than 5 year	Spring	24	24.2	0.115
		Summer	17	17.2	
		Autumn	34	34.3	
		Winter	24	24.2	
	Higher than 5 year	Spring	27	30.7	0.032
		Summer	10	11.4	
		Autumn	26	29.5	
		Winter	25	28.4	
sex	Male	Spring	33	32.7	0.054
		Summer	14	13.9	
		Autumn	27	26.7	
		Winter	27	26.7	
	Female	Spring	18	20.9	0.018
		Summer	13	15.1	
		Autumn	33	38.4	
		Winter	22	25.6	

There was a statistical significant difference in the frequency of GBS in different seasons in children by different ages and gender (Table 2). A significantly higher incidence of GBS was found in children higher than 5 years (p = 0.032) when compared with ones; while a higher incidence of GBS was found in female cases (p = 0.018). As it's seen in table 2

Discussion:

Seasonal and monthly trends in the occurrence of Guillain-Barre syndrome was defined more than a century ago but the seasonal variation in children from different studies are not consistent, which might be due to geographical diversity and racial difference. [16] In this study, we found that the GBS occurrence varies significantly with respect to months and seasons. Seasonal variation was not seen in some studies from Spain [5], Northwest of Iran [7], central India [17] and Greece. [18] In contrast,

seasonal variation has been seen in several other studies in different parts of the world. In some studies, higher incidence has been reported in autumn. [19, 20] which is similar to this study, and in other studies in winter. [7, 11] or spring. [21, 22, 23] Others have reported a higher incidence in summer and it has been associated ~~it~~ with the incidence of intestinal infections caused by or campylobacter jejuni. [16, 24] Higher frequency of autumn and winter seasons (colder seasons) which was seen in our study has been similar to the reports in other studies. [7, 11, 19, 20] Frequency of GBS in European countries with similar climates is also reported to be in winter. [25, 26] These results could indicate the role of geography and climate on the seasonal variations of GBS. Akbayram et al, in Turkey [24], Zaheer et al in Pakistan [27], Sharma et al in India [22] and Hughes et al in China [28], have all reported a higher incidence of GBS in summer which is probably due to climate similarities of the locations of these studies. Bae et al, has explored the epidemiology of GBS in Asian countries and have suggested that there is an association between the incidence of GBS and gastrointestinal (GI) infections in summer and respiratory infections in winter. [6] The seasonality of *Campylobacter* has been reported by Singh *et al*. which showed the highest prevalence of *C. jejuni* in the fecal samples during the rainy seasons and in the summer months. [29] In most studies, the highest incidence of GBS was seen in the Colder seasons (autumn and winter); while the lowest incidence was seen in warmer season (summer). This observation can be attributed to the fact that the major preceding infections like gastroenteritis and Influenza tend to occur during these seasons and hence an increasing risk of acquiring GBS. [30] There are a number of other well defined microbial and viral infections related to GBS. Amin et al explored the incidence of GBS in children in a 20-year period in the city of Shiraz in Iran that has a moderate climate, and reported that GBS has a higher incidence in colder months of the year associated with the incidence of particular diseases such as flu or bacterial intestinal infections. [31] In our study because of being retrospective, we cannot recognize the prevalence of upper respiratory infection (URI) and GI infections; it will be better done in prospective studies focusing on recent infections to find any possible relations. Webb et al, have reviewed the literature on the seasonal variations of GBS and have reported that there are differences in seasonal variations of GBS in different parts of the world. [10] The probable reason could be that the gastrointestinal and respiratory infections can occur in various seasons in different regions. Summer in some Asian countries is warm and humid, whereas in European countries it is mild and dry. Therefore, in European countries the climate is not suitable for campylobacter jejuni growth and the resulted gastrointestinal infections, and this may have affected the low incidence of GBS in European countries in summer. In contrast, in some Asian countries in summer have temperatures that can reach up to 40-42 degrees Celsius, with high humidity resulting in growth of campylobacter jejuni and high incidence of gastrointestinal infections and this may have affected the high incidence of GBS in Asian countries in summer. [32, 33] Abdulkarim et al in a similar study in Iraq explored seasonal variation of GBS and reported the lowest incidents of GBS to be in summer [19], which is consistent to the results of our study. The similarity of climates of Khuzestan with a neighbor country of Iraq could justify the similarity of the results of these two studies. Khuzestan province is located in the southwest of Iran with very hot temperature that can exceed higher than 50 degrees Celsius in summer season. This can be associated with decreasing the incidence of some diseases. While there is no evidence to support higher incidents of other infections in those seasons, it is still highly likely that the incidents of infectious diseases in summer with temperatures higher than 50 degrees Celsius will be less prevalent, and infectious diseases especially viral infections could have higher incidence in autumn, where there are more frequent rains and lower temperatures. This will justify the lower incidence in summer and the higher incidence in autumn. 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. Comparison of incidence of GBS between children under or higher than 5 years of age, and between females and males has indicated significant differences. Whilst the incidence of GBS did not differ in children under 5 years old, it was significantly lower in children over 5 years of age in summer. It is probable that similar living conditions and the dependency of children under 5yrs on their parents may be the underlying reason for constant incidence in various seasons. In contrast, the relative independence and freedom of children more than 5 years may justify the seasonal variations of GBS in these age groups. In addition, we identified that the seasonal incidence of GBS varied amongst male and females. GBS had a higher incidence in autumn for females but was considerably lower in spring and winter as compared to males. It is likely that differences in lifestyle and habits of males and females could justify such differences. This study has some limitations; we relied on data from AFPC, which is based on reports collected from health care organization throughout the Khuzestan province; hence due to the retrospective nature of the study and failure to make follows-up on patients. Consequently, validity of our data is dependent upon the accuracy of those reports.

Conclusions:

Our findings showed that there is significant seasonal and monthly variation in the children with GBS. The highest incidence was seen in autumn and

the lowest in summer (p= 0.006). The highest incidence was seen in December and lowest in September (p=0.036).

Authors' Contributions:

A. A. Momen: design, Data collection, study conception, drafting of manuscript and Supervisor
A. Shakurnia: literature research, Interpretation of data, Drafting of manuscript and Critical revision
M. Sarrami: helped in writing and drafting of manuscript
This study has ethics approval from the ethics committee of research department of Ahvaz Jundi Shapur University of Medical Sciences, Ahvaz, Iran (IR.AJUMS.REC.1395.229).

References:

1. *van den Berg B, Walgaard C, Drenthen J, Fokke C, Jacobs BC, van Doorn PA. Guillain-Barre syndrome: pathogenesis, diagnosis, treatment and prognosis. Nat Rev Neurol. 2014; 10:469–82*
2. *Salehiomran MR, Nikkhah A, Mahdavi M. Prognosis of Guillain-Barre syndrome in Children. Iran J Child Neurol. 2016; 10(2):38-41.*
3. *Lamees M. Hussein, Safaa H. Ali, Najeeb H. Mohammed. Electrophysiological evaluation of Guillain–Barre syndrome subtypes in childhood. Fac Med Baghdad. 2017; 59(1):60-4.*
4. *Momen A, Shakurnia A, An epidemiological analysis of Acute Flaccid Paralysis in Khuzestan Province, Southwest of Iran, 2006-2010. Epidemiol Health. 2016; 38:1-6.*
5. *McGrogan A, Madle GC, Seaman HE, de Vries CS. The epidemiology of Guillain-Barré syndrome worldwide. A systematic literature review. Neuroepidemiology. 2009; 32(2):150-63.*
6. *Bae JS, Yuki N, Kuwabara S. Guillain-Barré syndrome in Asia. J Neurol Neurosurg Psychiatry. 2014; 85(8):907-13.*
7. *Barzegar M, Dastgiri S, Karegarmaher MH, Varshochiani A. Epidemiology of childhood Guillan-Barre syndrome in the north west of Iran. BMC Neurology. 2007; 7:22.*
8. *Borhani Haghighi A, Banihashemi MA, Zamiri N, et al. Seasonal variation of Guillain-Barré syndrome admission in a large tertiary referral center in southern Iran: a 10 year analysis. Acta Neurol Taiwan. 2012; 21(2):60-3.*
9. *Mathew T, Srinivas M, Nadig R, Arumugam R, Sarma GR. Seasonal and monthly trends in the occurrence of Guillain-Barre syndrome over a 5-year period: A tertiary care hospital-based study from South India. Ann Indian Acad Neurol. 2014; 17(2):239-41.*
10. *Webb AJ, Brain SA, Wood R, Rinaldi S, Turner MR. Seasonal variation in Guillain-Barré syndrome: a systematic review, meta-analysis and Oxford shire cohort study. J Neurol Neurosurg Psychiatry. 2015; 86(11):1196-201.*
11. *Nebal W. Saadi Al-Dabbas. Guillian Barré Syndrome in a sample of Iraqi Children: Seasonal and sex variation. J Fac Med Baghdad. 2016; 58(1): 8-12.*
12. *Ali Shaila, Zia ur Rehman M, Sultan Tipu. Spectrum of Gillian bare syndrome in children. Pakistan Journal of Neurological Sciences (PJNS). 2017;12(1): 20-4.*
13. *Roodbol J, Marie-Claire Y, Bianca B, Kahlmann V, Drenthen J, Catsman-Berrevoets CE. Diagnosis of Guillain–Barre´ syndrome in children and validation of the Brighton criteria. J Neurol. 2017; 264:856–61.*
14. *Fokke C, van den Berg B, Drenthen J, Walgaard C, van Doorn PA, Jacobs BC. Diagnosis of Guillain-Barre syndrome and validation of Brighton criteria. Brain. 2014; 137: 33–43.*
15. *Heydari-Malayeri M. A concise review of the Iranian calendar. http://aramis.obspm.fr/~heydari/divers/ir-cal-eng.pdf*
16. *Meshram RM, Merchant S, Bokade CM, Bhongade S, Patil S, et al. Seasonal Variation in Childhood Guillain- Barre Syndrome in Central India. J Pediatr Neonatal Care. 2016; 5(6):1-4.*
17. *Shrivastava M, Nehal S, Seema Navaid. Guillain–Barre syndrome: Demographics, clinical profile & seasonal variation in a tertiary care Centre of central India. Indian J Med Res. 2017; 145:203-8.*
18. *Chroni E, Papapetropoulos S, Gioldasis G, Ellul J, Diamadopoulos N, Papapetropoulos T. Guillain-Barre syndrome in Greece: seasonality and other clinico-epidemiological features. Eur J Neurol. 2004; 11(6):383–8.*
19. *Boucquey D, Sindic CJM, Lamy M, Delmée M, Tomasi JP, Laterre EC. Clinical and serological studies in a series of 45 patients with Guillain-Barré syndrome. Journal of the Neurological Sciences. 1991; 104(1): 56-63.*
20. *Farhoudi M, Ayromlou H, Bazzazi AM, et al. Time Frequency of Guillain-Barre Syndrome in Northwest of Iran. Life Sci J. 2013;10(1):223-5.*
21. *Abdul-Kareem AM, Al-Hamdani HA, Al-Rikabi MA, The seasonal variation of Guillain Barre Syndrome in Iraq. Iraqi J Med Sci. 2004; 3(2):167-70.*
22. *Sharma A, Lal V, Modi M, Vaishnavi C, Prabhakar S. Campylobacter jejuni Infection in Guillain-Barré Syndrome: A Prospective Case Control Study in a Tertiary Care Hospital. Neurology India. 2011; 59(5):717-21.*
23. *Huang WC, Lu CL, Chen SC. A 15-Year Nationwide Epidemiological Analysis of Guillain-Barré Syndrome in Taiwan. Neuroepidemiology. 2015; 44(4):249-54.*
24. *Akbayram S, Dogan M, Akgün C, et al. Clinical Features and Prognosis with Guillain-Barré Syndrome. Annals of Indian Academy of Neurology 2011; 14(2): 98-102.*
25. *Sivadon-Tardy V, Orlikowski D, Rozenberg F, et al. Guillain-Barré Syndrome, Greater Paris Area. Emerging Infectious Dis- eases. 2006; 12(6): 990-3.*

26.Van Koningsveld R, Rico R, Gerstenbluth I, et al. Gastroenteritis- Associated Guillain-Barré Syndrome on the Caribbean Is- land Curaçao. Neurology. 2001; 56(11):1467-72.
27.Zaheer M, Naeem M, Nasrullah M. Seasonal Variation and Sex Distribution in Patients with Guillain-Barre Syndrome, Pakistan Journal of Neurological Sciences. 2008; 3(1): 6-8.
28.Hughes RA, Rees JH. Clinical and Epidemiological Features of Guillain Barre Syndrome. The Journal of Infectious Diseases. 1997; 176(2): S92- S98.
29.Singh R, Singh PP, Rathore RS, Dhama K, Malik SV. Studies on effect of seasonal variations on the prevalence of Campylobacter jejuni in poultry faecal samples collected from Western Uttar Pradesh. India J Comp Microbial Immunol Infect Dis. 2008; 29:45–8.
30.Ruiz-Matus C. Guillain-Barre syndrome in children aged <15 years in Latin America and the Caribbean: baseline rates in the context of the influenza A (H1N1) pandemic. J Infect Dis. 2010; 201(5):746–50.
31.Amin R, Al-Yaseen S, Rafie S M. Guillain Barre Syndrome: a 20-year study on pediatrics. KAUMS Journal (FEYZ). 2005; 8 (4):63-8.
32.Barzegar M, Hashemilar M, Bonyadi MR. Campylobacter jejuni infection and childhood Guillain-Barre syndrome. Pak J Med Sci. 2010; 26(2):304-9.
33.Sejvar JJ, Baughman AL, Wise M, Morgan OW. Population Incidence of Guillain-Barré Syndrome: A Systematic Review and Meta-Analysis. Neuroepidemiology. 2011; 36:123–33.