

# Guillain Barré Syndrome in a sample of Iraqi Children: Seasonal and sex variation

Nebal W. Saadi Al-Dabbas\*

MBChB , FICP, CABP, DCH, FIBPN

**Abstract:**

**Background:** Seasonal variation and gender preponderance have not been adequately studied in Guillain-Barre syndrome (GBS).

**Objective:** This study aims to evaluate the seasonal variation and sex preponderance in children with Guillain Barré Syndrome.

**Patients and methods:** A cross sectional study was carried out by reviewing wards' registry of all cases with Guillain Barré Syndrome admitted to Children Welfare Teaching Hospital during a 10-year period (1999 - 2008). Age, sex, seasonal distribution, residence and outcome were analysed.

**Results:** Guillain Barré Syndrome was diagnosed in 217 (126 boys, 91 girls) patients and the annual hospital rate of admission was 22.9 /100000 children. There was increase annual incidence from 1999 till 2008 with a drop in 2006, boys: girls ratio was 1.4:1 and boys were older than girls. Clustering of cases was found during January, March, May and November over the 10-year period, 37% of cases occurred during winter and 52.5% of patients were from Baghdad.

**Conclusion:** Guillain Barré Syndrome is more common in boys. Boys were older than girls. Clustering of cases was found during winter season.

**Key words:** Guillain Barré Syndrome; Iraqi children; seasonal clustering.

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**Introduction:**

Guillain - Barré syndrome (GBS), or Acute Inflammatory Demyelinating polyradiculoneuropathy (AIDP), describes a heterogeneous condition with a number of redundant variants. The classic presentation is characterized by an acute monophasic, non-febrile, post-infectious illness manifesting as ascending weakness and areflexia.. [1] The degree of weakness ranges from minimal weakness in the legs to total paralysis of the muscles of all four extremities and of the trunk. [2] It is thought, in most cases, to result from an aberrant immune response triggered by microbial infections. [3] It is presumed that immune response to specific antigens in infectious organisms attacks similar epitopes in the host peripheral nerves fibers. [4] Most patients have a demyelinating neuropathy, but primarily axonal degeneration is documented in some cases. [5] Since the virtual elimination of poliomyelitis, GBS has become the leading cause of acute flaccid paralysis in western countries. [6] It occurs evenly throughout the Western hemisphere, without geographic clustering and with only minor seasonal variations. [7] Although GBS is a sporadic disease extending throughout the year, seasonal, identifiable outbreaks - such as those in Columbia and Jordan - have occurred where the number of cases exceeded the expected incidence by 20-400 times. Another outbreak occurred in the United States in 1976 after immunization of 45 million people against swine influenza. There have been two outbreaks of GBS in South America after rabies vaccination. [8] In general, the outcome of GBS is more favourable in children than in adults. [1] The aim of this study was to identify any seasonal variation and the

sex predilection in the patients presented to Children Welfare Teaching Hospital.

**Patients and methods**

A cross sectional study was carried out to review the wards and hospital registry of all cases with Guillain Barré Syndrome admitted to Children Welfare Teaching Hospital (CWTH) during the period from January 1999 to January 2008. Ethical approval was obtained from the Research Ethical Committee - Human Resources Development and Training Centre - Ministry of Health, Iraq. Children Welfare Teaching Hospital is the tertiary paediatric referring centre in Baghdad City. Annual total patients' admission is about 9473 children. All registries were reviewed focusing on demographic information, age of hospitalization, sex and discharge status during the period from 1st of January 2009 - 1st of July 2009. Case identification for cases of GBS was based on the hospital registry. All cases of Guillain Barré Syndrome aged from 1 month to younger than 14 years who were admitted to the hospital during the study period were included in the study. Patients included were those registered as to have GBS or post-infectious peripheral neuropathy. Patients admitted to the hospital and were examined by specialist paediatricians. Diagnosis of Guillain Barre Syndrome was based on the presence of symmetrical motor weakness and decrease or disappearance of deep tendon reflexes [Asbury and Cornblath clinical criteria[9]] and that was supported (if applicable or available) by electrophysiological studies and cerebrospinal fluid analysis which showed features consistent of GBS (that required for diagnosis; no more than 50 monocytes or two granulocytes per ml cerebrospinal fluid, and that strongly

\*Dept. of Paediatrics / College of Medicine-University of Baghdad.  
Children Welfare Teaching.  
Email: nebalpedneu2013@gmail.com

supportive of diagnosis; elevation of cerebrospinal fluid protein after one week of symptoms) [7]. During the study period, two hundreds thirty one cases were found in the ward registry, but only 217 were included in the study, 14 cases that were recorded as to have acute flaccid paralysis, paralysis of lower limbs or suspicion of Guillian Barré Syndrome were excluded. To specify the seasonal distribution of months in Iraq, this study depended on a summary that was written and provided by the US Air Force (Air Force Combat Climatology Center) in Asheville, NC [10] which identifies the seasons in Iraq as follow: Winter (December-March), Spring (April-May), Summer (June-September), Autumn (October-November). Statistical analysis: Data were gathered; organized and tabulated using Microsoft Office Word 2003 and percentages and tables were done by Microsoft Office Excel 2003. Discrete variables presented as numbers and percentages and continuous variables

presented as median and mean  $\pm$  SD (standard deviation). Chi square test for independence was used to test the significance of association between discrete variables. Findings with P value less than 0.05 were considered significant.

**Results**

During a 10-year period (1999–2008), 94737 patients were admitted to the Children Welfare Teaching Hospital and the annual distribution of the total number of patients admitted is seen in figure (1).

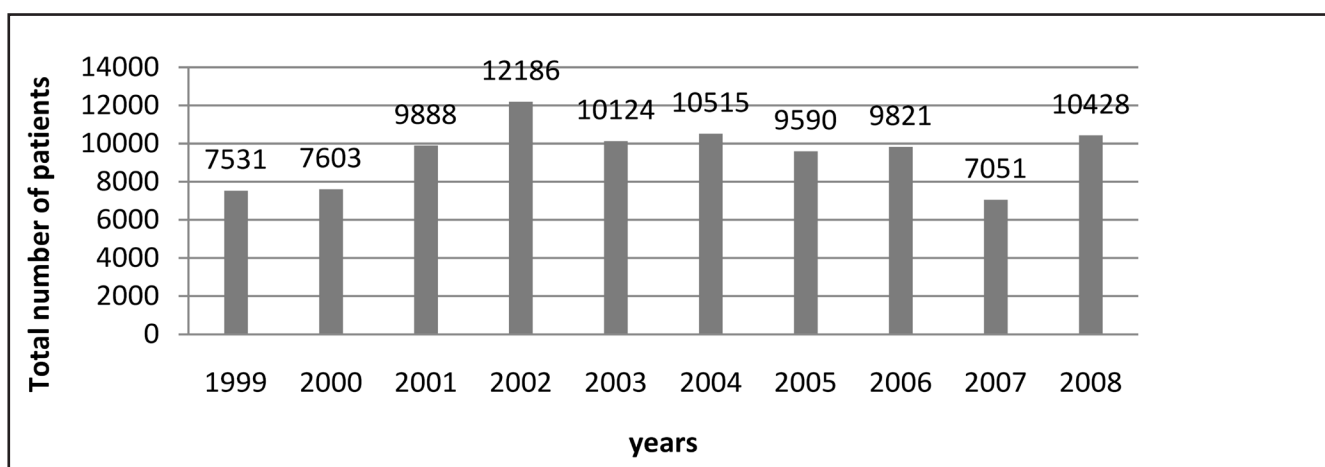


Figure (1): Total number of patients admitted annually to Children Welfare Teaching Hospital

Two hundred seventeen patients were diagnosed as GBS and their annual distribution during the period of study is shown in figure (2), with annual rate of 22.9 cases /100000 admissions.

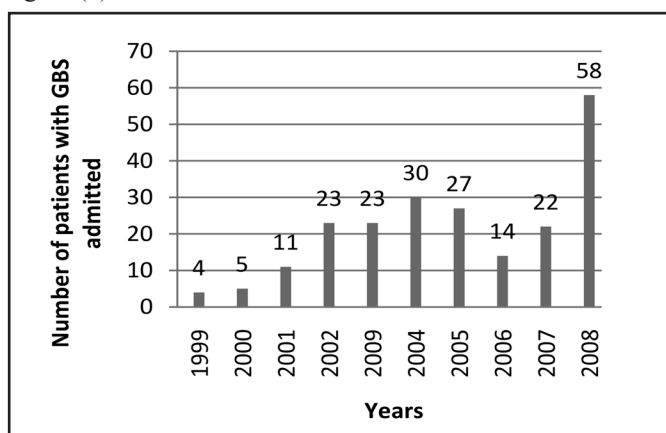


Figure (2): Distribution of Guillian Barré Syndrome cases by year of occurrence

There was increase annual incidence of GBS cases from 1999 till 2005 then followed by drop in that incidence during 2006 and then another increase during 2007 showing the highest peak during 2008 (table (1)).

Table (1): Annual rate of admission of patients with GBS

Year	Annual rate of admission / 100000
1999	53.1
2000	65.8
2001	111.2
2002	188.7
2003	227.2
2004	285.3
2005	281.5
2006	142.6
2007	312
2008	556.2

Regarding gender; boys (126, (58%)) were more than girls (91, (42%)) with boys: girls ratio of 1.4:1. As shown from table (2); boys tend to be older (mean age in year  $4.6 \pm 3.2$  SD) than girls ( $3.9 \pm 2.7$  SD) yet the difference in mean age, between boys and girls, was statistically not significant ( $P > 0.05$ ).

**Table (2): Distribution of the study group by age (in years) and sex**

Age (in year)	Gender		total	P value
	Boys (n=126)	Girls (n=91)		
Range	0.2-13	0.3-12	0.2-13	
Mean ± SD	4.6 ± 3.2	3.9 ± 2.7	4.3 ± 3	0.666*
Median	4	3	3.5	

\*Difference in mean age was statistically not significant (Student's t test)

During the 10-year period, 217 cases proved to have GBS, the cases were distributed monthly in figure (3), with a median of 18 cases per month. It was found that during January, March, May and November the occurrence of cases exceeds the median level, whereas during February, June, July, August, October and December the cases were either equal to the median or just below it, and the lowest numbers were found during April and September.

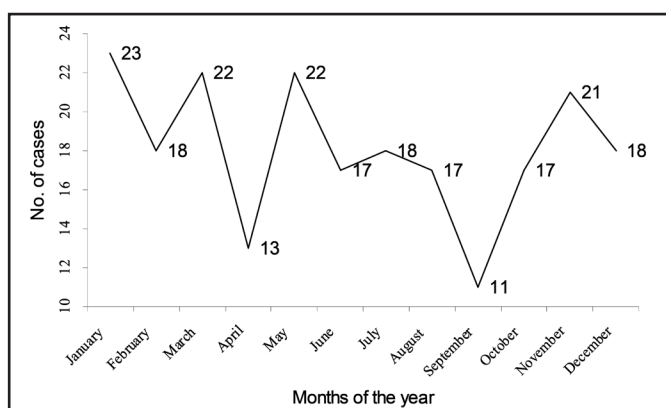
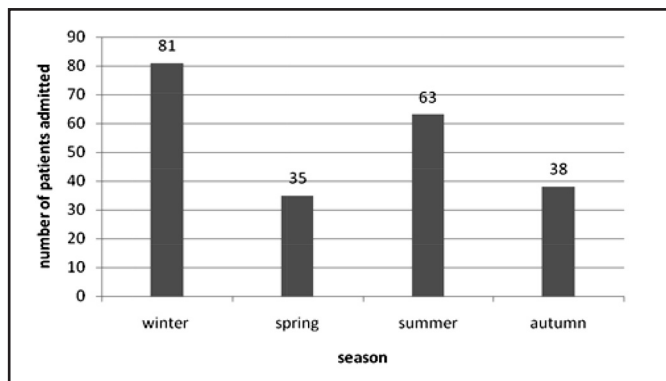
**Figure (3): Trend of GBS cases by months of occurrence**

Figure (4) showed seasonal distribution of cases of GBS and clustering of cases was found in winter months. A statistically significant association was found between the occurrence of cases and seasons of the year. ( $\chi^2$  (Goodness - of - fit for single variable) = 26.299, df= 3, P< 0.000).

**Figure (4): Seasonal distribution of cases of GBS in the last 10 years**

Regarding patients' residency; more than half of the patients (52.5%) were from Baghdad city, the rest were from other governorates except Erbil in Kurdistan region. (Table (3)).

**Table (3): Distribution of the study group by residency**

Province	Number of patients
Baghdad	114
Wasit	18
Diyala	15
Babil	15
Al-Diwanyiah	12
Nasiriyah	12
Anbar	7
Karbala	5
Salahaddin	4
Mosul	3
Najaf	3
Al-Muthana	2
Maysan	2
Al-Sulaymaniyah	2
Basrah	1
Dahuk	1
Kirkuk	1

Regarding patients' outcome, table (4) showed that more than two thirds (155) of the patients had improved while in the hospital and were discharged with a better condition, 14 (6.5%) died, 18 (8.3%) of patients transferred to other hospital, and 17 (7.8%) were admitted in the respiratory intensive care unit in the same hospital. Nineteen patients (8.8%) patients discharged on their parent's responsibility before completing the period of management. 11 (5%) patients were included in other status like being discharged with the same status in term of motor function.

**Table (4): Outcome of patients with Guillian Barré Syndrome**

Patients' Outcome	Numbers	%
Improving and discharged in a better condition	155	71.4
Discharged on parents' responsibility	19	8.8
Died	14	6.5
Transferred to other hospital ( for RCU admission)	18	8.3
Admitted to the RCU in the same hospital	17	7.8
Others	11	5

## Discussion

The annual time trend and sex distribution of Guillain-Barré syndrome in children admitted to the Children Welfare Teaching Hospital were investigated. Up to our knowledge the previous researches about GBS in Iraq didn't focus on the former determinant (seasonal distribution). The mean annual admission was found to be 22.9 cases /100000 admissions, yet this result is not a representative of the Iraqi population, as this was a hospital-based study. Tracing the annual rate of admission from 1999 to 2008 showed that the lowest incidence was in 1999 increasing during the following years, with a drop during 2006, reaching the highest rate during 2008. That may indicate true increase in the incidence or reflects improvement of case ascertainment. The highest incidence in the year 2008 could not be related to any pathogen agent such as campylobacter jejuni as they are not routinely detected in our medical centre. The drop in 2006 may reflect the unstable security circumstances in the country as that was obvious in the reduction in the total patients' admission to the hospital. The increase in the frequency of GBS was reported in a study from Alberta Canada [11] which showed increase in the incidence over period of 11 years [from 1994-2004] from 0.97 to 2.32 per 100000 population. An annual report from Louisiana Office of Public Health-Infectious Disease Epidemiology Section [12] showed an increasing trend in the hospitalization rate of patients with GBS from 1999-2007. Outbreaks of the disease have been reported from different areas in the last few decades. Markoula et al. from Greece; reported an outbreak during 2002. [4] A similar feature was studied / reported in Sweden during 1985 and 1992. [13] An increased incidence of Guillain-Barré syndrome in the USA in 1976 was attributed to 'swine flu' vaccines. [14] Another study from Caribbean island of Curacao by Van Koningsveld et al. showed that incidence rose sharply from 1.62 (per 100 000) between 1987 and 1991 to 3.10 (per 100 000) between 1992 and 1999. [15] Many studies [1, 2, 4, 8, 11, 16, 17, 18, 19, 20] showed that males were more commonly affected by Guillain Barré Syndrome than females. Considering the supposed autoimmune etiology of GBS, the male preponderance is somewhat unexplained. The much higher male preponderance in Lahora's study [8] was justified by the higher exposure to infections among males in that community; alternatively, females (especially those with mild weakness) might not have presented for medical attention due to social limitations in that part of the world. In Iraq, further studies are needed to explain the male preponderance that was found in the current study [male:female ratio of 1.4:1], while a study of GBS in Kuwait showed female:male ratio of 1.4:1. [21] The current study showed male to be older than female, yet that was statistically not significant. Similar result was found in Sao Paulo Brazil study [2] and there was no reasonable explanation for that. Regarding the seasonal distribution of patients with GBS, the occurrence of the syndrome was found to be throughout the year with small peaks in January, March, May & November during the period of the study. The seasonal distribution of months is universally identified to be grouping of 3 months per season. In Iraq climate the temperature means

may show winter distribution (trend) that might extend up to March, or summer trend extend up to September. Looking at the US air force report [10] we can see that mean lows of temperature at winter ranges from 2-7 C all season in mountains, while in the plains, they are 2-7 C in December and January and 7-13 C in February and March. The southern third of Iraq has (7 to 13C) for mean lows all season and the southern Tigris Euphrates valley has (16 to 18C). In February and March, most of Iraq gets subfreezing temperatures 1 day or less per month. Summer is a hot and dry and the mean high temperature ranges from (with the exception of the mountains) 39-43 C all summer including September and extremes high reach 52C. According to the above distribution of temperature, March was included in winter and September in summer and this study depends on that. It was found that (37%) of cases occurred during Winter months, (29%) during Summer months. This couldn't be related to any pathogenic agent as it is not routinely tested for GBS in our hospital. However, as judged from the seasonal predilection in this series, respiratory infectious agents might be an important predisposing factor with onset during winter. Some epidemiological studies showed seasonality pattern, such as those studies identify a higher frequency of the syndrome in winter [16,19] as what was found in the current study, or in summer [8, 17, 18, 20] attributing this to the higher incidence of enteric infections or campylobacter jejuni in that season[2] or in autumn [22] or spring. [2,21, 23]. A study from North West Greece found no consistent seasonal preponderance. [4] This study found that 14 (6.5%) patients died, but couldn't identify the cause of death as these data were obtained from the wards' registry from the statistical department of the hospital and not from patients' records. Those patients who were transported to other hospital were 18 and this is routinely done when there is a need for RCU admission with shortage of this service in the CWTH or the Medical City Campus. So the outcome of those transported patients couldn't be obtained, therefore the death rate was calculated from those cases whose mortality was recorded in the hospital registry and it was found to be nearly 6%. Lower rates were reported in other resources like Louisiana Office Annual Report (3.2%) [12], Newswanger and Warner's study (less than 5%) [9] and others. [7]

## Conclusions

There is an increase incidence of Guillain Barré Syndrome over years. boys are affected more than girls in GBS and the condition occurs throughout the year with small peaks of incidence in different parts of the year, especially winter months.

## Recommendations

Further studies to recognize the seasonal pattern of such syndrome will help the understanding of host-pathogen interactions and will improve the accuracy of public health surveillance & forecasting. Monitoring and surveillance system for Guillain Barré Syndrome is essential to set up in this region.

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