GUILLAIN-BARRE SYNDROME AMONG PALESTINIAN CHILDREN CLINICAL ASPECT AND OUTCOME

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Objective: Evaluation of the incidence and clinical characteristics of GBS in pediatric age. The disease actually represents the major cause of acute flaccid paralysis in healthy people.
Populations and Methods: We reviewed the hospital records of 33 patients who were admitted to Makassed Hospital with the diagnosis of GBS from January 1986 until December 1994. Two patients whose clinical signs and symptoms did not fulfill the criteria were excluded from the study. Mean age was 5 years and 3 months (SD=3years, range 1-14 years), and most of patients (45%) were between 4-6 years. Males were affected slightly more than females 1.4:1. The initial signs of illness started 5 days prior to hospitalization. Seasonal predilection was prominent as more than 77% of patients were seen in winter and spring possibly reflecting seasonal peaks of triggering factors (48% of patients had a viral upper respiratory tract infection two weeks earlier, HBS antigen was positive in (10%), no family history or occupational factors, no history of gastroenteritis or recent vaccination were reported, research for polio virus was negative in all cases).Ten patients(30%) developed severe respiratory distress which required mechanical ventilation. Three patients died (10%).
Discussion: Available data on the epidemiology of GBS rate of 0.6-1.9 cases per 100,000 populations per year, with an average of 0.5 to 1.0, which is considered roughly the same throughout the world, all age group, included. This series is relatively important knowing that the population served by this department was 540.000 in 1986 and around 800.000 by the end of the study in 1994. Children under 15 years represent 50% of the designed population (Ramallah, East Jerusalem, Jericho, Bethlehem and Hebron districts). During the study period 3 other cases were not hospitalized as diagnosed late and remained stable and about 15 other cases without respiratory distress were kept in other facilities. The annual incidence rate is estimated for the studied period at least to be 1 in 100,000 for the age group of under 15 years which can be considered high for the pediatric age group in this community. Further studies are indicated to confirm these data.

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INTRODUCTION

Guillain-Barre syndrome GBS is an acute demyelinating disorder of the peripheral nervous system. The characteristic clinical features are the development of progressive, usually symmetric, ascending flaccid paralysis and areflexia. It is not a rare disorder in childhood and its incidence increase with age; it is rarely seen in infants less than one year of age.

POPULATIONS AND METHODS

The diagnosis of GBS was based on clinical criteria (1,2) progressive motor weakness of more than one limb ranging from minimal weakness of the legs to total paralysis of all four extremities in addition to areflexia. The diagnosis was supported by the presence of high CSF protein and electrodiagnostic studies.
We reviewed the hospital records of 33 patients who were admitted to Makassed Hospital with the diagnosis of GBS from January 1986 until December 1994. Patients whose clinical signs and symptoms did not fulfill the criteria were excluded from the study (two cases).

RESULTS

From the 33 patients reviewed 31 patients met the criteria for the diagnosis of GBS and two patients were excluded.
One was a six years old male who presented with paraplegia of acute onset; CSF analysis showed: WBC 100, 60% lymphocytes and 40% neutrophils, protein 20 mg/dl, with normal EMG and nerve conduction studies.
The second was a 3 year old, he presented with ataxic gait and tremors, power was 5/5 all over, CSF protein was 41mg/dl; he improved spontaneously within 3 days.

Mean age was 5 years and 3 months (SD=3years, range 1-14 years),and most of patients(45%) were between 4-6 years. Males were affected slightly more than females 1.4:1 (Table I).

TABLE I: AGE DISTRIBUTION

AGE GROUP	MALE	FEMALE	TOTAL (%)
<24 MONTHS	2	1	3 (9.7)
25-48 MONTHS	6	3	9 (29)
49-72 MONTHS	6	6	12(38.7)
73-96 MONTHS	2	1	3 (9.7)
> 96 MONTHS	2	2	4 (12.9)
TOTAL	18	13	31 (100)

The initial signs of illness started 5 days prior to hospitalization (SD=4 days, range 1-14 days).

Seasonal predilection was prominent as more than 77% of patients were seen in winter and spring possibly reflecting seasonal peaks of triggering factors (Table II).

TABLE II: SEASONAL DISTRIBUTION

MONTHS	N	%
DECEMBER-FEBRUARY	12	38.7
MARCH-MAY	12	38.7
JUNE-AUGUST	4	12.9
SEPTEMBER-DECEMBER	3	9.7
TOTAL	31	100

48% were found to have a viral infection mainly upper respiratory tract within two weeks of presentation, 3 patients had positive HBS antigen (10%), one patient had positive monospot test (3%), one patient had history of mumps within one month of presentation (3%), one patient had positive throat culture for *group A streptococcus* (3%), no family history or occupational factors, no history of gastroenteritis or recent vaccination were reported. Research for poliovirus was negative in all cases.

TABLE III: ASSOCIATED TRIGGERING FACTORS

TRIGGERING FACTOR	N (%)
URTI	15 (48.4)
HEPATITIS B	3 (9.7)
INFECTIOUS MONONUCLEOSIS	1 (3.2)
MUMPS	1 (3.2)
GROUP A STREPTOCOCCUS	1 (3.2)
UNKNOWN	10 (32.3)

All patients presented with progressive symmetrical muscle weakness that started in the lower limbs with diminished deep tendon reflexes. Cranial nerves were involved in 8 patients (26%), 6 had dysphagia-dysphonia. One developed ophthalmoplegia initially and one had nystagmus. Most of the patients had bilateral facial weakness with only 2 having asymmetrical facial involvement. Five patients (16%) developed hypertension that required antihypertensive treatment, four of them had severe respiratory symptoms and required mechanical ventilation. Three patients (10%) had disturbances in the heart rhythm (tachycardia or bradycardia), and one patient had micturition problem in the form of urine retention. Fifteen patients (48%) had history of pain mainly in the low back and calves. Ten patients (32%) developed severe respiratory symptoms that required mechanical ventilation (Table IV).

Cerebrospinal fluid analysis revealed high protein in 28 patients (90%), and normal levels in 3 patients but the other criteria for diagnosis of GBS were present. EMG and NCV studies were done on 14 cases; results were consistent with GBS in all.

TABLE IV: SIGNS IN GBS CASES

CLINICAL SIGNS	PATIENTS (%)
PROGRESSIVE WEAKNESS	31 (100)
DIMINISHED DTR	31 (100)
HIGH CSF PROTEIN	28 (90)
MUSCULAR PAIN	15 (48)
RDS	10 (32)
SEVERE HYPERTENSION	5 (16)
ARRHYTHMIA	5 (16)
URINE RETENTION	2 (6)
OPHTHALMOPLEGIA	1 (3)
NYSTAGMUS	1 (3)

RESPIRATORY DISTRESS (Table V)

Ten patients developed severe respiratory distress, which required mechanical ventilation. All but one had high CSF protein. Seven had dysautonomic signs and 5 had cranial nerve involvement. Patients who had dysautonomic manifestations were more prone to develop respiratory distress (Fischer exact test 0.0003); the association with cranial nerve involvement and respiratory distress was less significant (Fischer exact test 0.04).

TABLE V: PATIENTS WITH RDS

cn	AGE/ SEX	I	DA	CNI	IMV CPAP	HS	COMMENTS
4	5/F	4	HT	DGP	4	20	Walked 3ms
7	5/F	4	0	9,10	7	39	walked 2ms dysphagia 6ms
8	13/M	4	0	0	7-10	31	IG,walked 6ms
13	4/M	3	HT,A,S	0	10	42	IG,walked 3ms
15	4/F	2	0	NYS	20	31	D*
16	2/M	2	HT,A	0	11	23	IG, walked 2ms
19	12/M	1	HT,A,S	DGP	80	13 0	plasmapheresis IG
21	14/F	1 4	A	DGP	30	30	D*
28	2/F	2	A	0	14	36	D*
33	7/M	6	HT	0	7	17	IG, walked 2ms

I:interval between the initiation of the disease and hospitalization, DA:Dysautonomic signs, CNI:cranial nerve involvement, IMV:intermittent mandatory ventilation, HS:duration of hospitalization, HT:hypertension, DGP:dysphagia-dysphonia, A:arrhythmia, S:sweating, , IG:gammaglobulin IV, NYS:nystagmus, D*:death.

Age and respiratory distress as an indicator for the severity of the disease showed no significant relation in this series (Table VI). All patients had initially received short courses of prednisone therapy of 1-2 mg/kg for 5 to 10 days. Naso-tracheal tubes were used for all and 1 underwent tracheostomy at 4 weeks of IMV (case 19).

Impending respiratory failure was the indication for the use of IV immunoglobulin in our unit (0.4 g/kg for 4 days). It was indicated in 9 cases (case 21 excluded for severe brain damage). It was made available for 4 immediately and for one only one week after plasmapheresis. The other four did not receive the drug due to lack of family consent (2 cases) or for its unavailability in the local market. All patients who received IV Ig survived and in 4 cases we got the impression that the duration of respiratory failure was shortened. Case 19 did not respond to plasmapheresis and the use of IV Ig did not alter the course of the disease. The same patient remained ventilator dependent for 4 months, developed neurogenic paraosteopathy and recovered independent walking after 20 months. Two of the patients who did not receive IV Ig died.

TABLE VI: ASSOCIATION OF MAJOR SIGNS WITH PATIENTS' SEX AND AGE

	RDS	CNI	DA	>5 yrs	<5 yrs	M	F
RDS	**10**	5	5	4	6	5	5
CNI	5	**8**	2	2	6	3	5
DA	7	2	**8**	4	4	4	4
>5 yrs	4	2	4	**9**	0	5	4
<5 yrs	6	6	4	0	**22**	13	9
M	5	3	4	5	13	**18**	0
F	5	5	4	4	9	0	**13**

RDS:respiratory distress, CNI:cranial nerves involvement , DA:dysautonomic signs (arrythmia,hypertension,urine retention)

DEATHS

Three patients died (9%): the first one (case 15) was a four year old female who presented with progressive weakness and severe respiratory symptoms that required mechanical ventilation, she died after one month due to septicemia and DIC (in an other hospital where she was referred at the family's request). The second (case 28) was a two-year-old female who presented with rapid progressive weakness and respiratory failure;

she developed cardiac arrhythmia while on ventilator after 2 weeks of admission with consequent severe brain damage and remained ventilator dependent till death. The third (case 21) was 14-year-old female, with congenital hypothyroidism who developed arrhythmia and cardiac arrest on admission to the emergency room, after resuscitation she showed signs of severe brain damage. She died 4 weeks later.

PATIENT FOLLOW UP

Patients were seen at 2, 4, and 6 weeks after discharge then after 3, 6, and 12 months. In few cases they are still followed by the pediatric outpatient clinic. Among the 28 patients discharged one had a short relapse that responded well to prednisone, he initially received IV Ig and no other relapse occurred after 8 years of follow up (case 8). One of the patients who had short respiratory assistance had severe dysphagia, which persisted for 6 months and was fed by a gastrostomy tube (case 7). Most of the patients recovered independent walking within six months of the beginning of their illness except 2. One of them had severe respiratory distress and a tracheostomy was performed (case 19) and the other had severe weakness that lasted 14 months, this same patient developed focal epilepsy 5 years later.

DISCUSSION

Available data on the Epidemiology of Guillain-Barre indicate an occurrence rate of 0.6-1.9 cases per 100,000 populations per year, with an average of 0.5 to 1.0, which is considered roughly the same throughout the world (3). The disease actually represents the major cause of acute flaccid paralysis in healthy people.

This series is relatively important knowing that the population served by this department was 540.000 in 1986 and around 800.000 by the end of the study in 1994. Children under 15 years represent 50% of the designed population (Ramallah, East Jerusalem, Jericho, Bethlehem and Hebron districts).

During the study period 3 other cases were not hospitalized as diagnosed late and remained stable and about 15 other cases without respiratory distress were kept in other facilities.

The annual incidence rate is estimated for the studied period at least to be 1 in 100,000 for the age group of less than 15 years of age.

The disease is uncommon under 2 years but few cases were described in the first year of life (4, 5). The youngest case in this series was 12 months and 77% of cases occurred between 2 and 7 years. Males were more affected than females in this series as reported in other studies (4,6). Seasonal preponderance of GBS has been reported in some series. It was more common during autumn and winter in USA (7) and in summer in Japan (6). In this series more than two-thirds of the cases were seen during winter and spring. Muscular pain is commonly reported in GBS (8), nearly 50% of patient present moderate to severe muscular pain mainly in the lower limbs and at time diagnosis was delayed because of this mode of initiation of the disease (9). Episodes of diarrheal disease or gastroenteritis were not reported in this series as a preceding symptom during the last 4 weeks prior to the illness. A firm association of GBS with *Campylobacter jejuni* was reported in recent years (10, 11, and 12). The serological evidence of *Campylobacter jejuni* infection or CMV infection was not investigated in any of our patients. Patients were systematically tested for HBS Ag and 3 (10 %) were positive, the area served is considered as moderately endemic for hepatitis B (13). Patients with severe respiratory distress who required artificial ventilation were 10 (30 %). Respiratory failure occurred usually before 2 weeks of the beginning of the disease. Our policy is to send home stable children maximum at 15 days of the beginning of their illness. No patients were readmitted for respiratory failure after discharge. Dysautonomic manifestations and cranial nerves involvement were more commonly found in patients who developed respiratory failure in this series as stated by others (6). No significant association was found between respiratory distress and age.

Treatment of GBS is supportive in the majority of cases (14). Steroids used for a long time revealed actually ineffective in the acute form (15).

Plasmapheresis was used in severe forms but the use of IV Ig is easier and at least equally efficient (16). No real guidelines exist yet for the use of IV Ig in less severe forms or in the beginning of the disease (17). IV Ig was only used in this series in patient with respiratory failure. No deaths were registered in the 5 patients where it was used and in two out of four

cases where it was indicated and could not be used.
No further conclusion could be drawn from this limited experience but we have the impression that the use of IV Ig reduced the duration of respiratory assistance.
GBS was found to be relatively common in the pediatric age in this community. Further studies to determine the possible other triggering factors and the natural history of this disease are to be undertaken.

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