www.jmscr.igmpublication.org
Index Copernicus Value: 79.54
ISSN (e)-2347-176x ISSN (p) 2455-0450
crossref DOI: https://dx.doi.org/10.18535/jmscr/v7i5.120

IGM Publication
Journal Of Medical Science And Clinical Research
An Official Publication Of IGM Publication

Guillain Barre Syndrome - A Case Series

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Abstract

Objective: *To assess retrospectively the clinical profile, nerve conduction velocity studies and outcome of Guillian Barre Syndrome (GBS) in children.*

Materials and Methods: *The clinical and electrophysiological data of 184 children, who attended Kalawati Saran Children Hospital from Jan 2001 to Sept 2005 and were diagnosed as GBS based on Asbury-Cornblath criteria, were analyzed in the study. Severity of weakness was graded according to Hughes staging. Outcome was determined according to the functional recovery and independent ambulation. It was assessed in follow up at 1 month, 3 months and 6 months after the onset.*

Results: *A total of 184 patients were diagnosed as GBS during the study period, with an age range from 1-to15 yrs. (Mean-4.99_+ 2.95). Of this 37.4 % of cases were less than 3 years of age. There was a male preponderance with 71.7% of them being males. Seasonal preponderance was evident in more than 50% cases, developing the disease in summer season (May to Aug). Acute respiratory infections in 39/101 (38.61%) were the most common antecedent event followed by diarrhoea in 16/101(15.84%) and others (1-Tuberculosis, 1-measles, 2-skin infection). The most common symptom at the time of presentation was limb weakness, which was seen in all patients, followed by pain/paraesthesia in 31% and respiratory symptoms in 10% of the patients. Bulbar weakness was the most common type of cranial nerve involvement seen in 13%of them. Majority of the patients 140/184(76.08%) presented in stage IV {a-57 (40.71%), b-83 (59.28%)} followed by 29/184(15.76%) in stage III. Respiratory system involvement in the form of respiratory distress with potential respiratory failure was present in 33/184(18.08%), of which 19 (10.32%) patients required ventilator support. Cerebrospinal fluid (CSF) studies could be conducted in 31% of the patients who were admitted in the hospital and 70% of them showed some elevation of protein and cells in the CSF. Nerve conduction study (NCV) could be done only in 94/184(51.09%) patients and demyelination was the commonest finding in 51/94(54.26%). There were total 14(18.42%) deaths among the 76 patients who were admitted in the hospital and the commonest cause for death was respiratory failure. Seventy- nine cases were examined at 1 month out of which 51.89% were ambulatory with/ without support, 65% patients were seen at 3 month of which 50.42% recovered completely and 26.05% were ambulatory with minimum deficit. At 6 months follow-up, only 26 patients reported back, of which 15 (57.70%) had full recovery and rest of them were in the favorable group (100%) i.e. in stage III or less.*

Conclusion: *The most common symptom at the time of presentation was limb weakness. Respiratory system involvement was seen in only 18 % of the patients and only 10% of them required ventilator support. Seventy percent of the patients in whom CSF study was done showed elevation of proteins. Demylination was the commonest finding in nerve conduction study. Outcome is good with general supportive care.*

Introduction

The ongoing program for eradication of polio has resulted in a sharp decline in the incidence of paralytic poliomyelitis in our country. This has led to the emergence of Guillain Barré Syndrome (GBS) as the most common cause of acute flaccid paralysis.[1]

GBS is usually a rapidly progressive, predominantly motor neuropathy, which often results in bulbar and respiratory compromise. Residual motor-sensory deficits can persist, and death, when occurs, is usually early in the disease course, and as a result of respiratory compromise or autonomic failure or intensive care unit complications.

While the exact etiology of GBS still remains elusive, many investigators have thus far concluded that it has an autoimmune pathophysiology. These events are most likely triggered by common infections. Environmental and seasonal factors also play a role through incompletely understood mechanisms. Both components of immunity- humoral as well as cellular- are involved, leading to inflammatory cell infiltration and demyelination of the peripheral nerves. This is not the only pathology, as the current definition of GBS encompasses other variants such as acute motor axonal neuropathy (AMAN), acute motor-sensory axonal neuropathy (AMSAN), and Miller Fisher Syndrome (MFS) etc.[2, 3, 4, 5]

Guillain Barré Syndrome affects all age groups, from infancy to old age, with age-specific features. In general, functional recovery is reported to be better in the pediatric age group.

GBS is a global disease. Though reportable in the national acute flaccid paralysis surveillance program, there have been only few systematic studies of this syndrome, especially so in the north India, with very few reports available. The purpose of our study is to review the key presenting features and outcome of patients of Guillain Barré Syndrome (GBS) presenting as outpatients and inpatients to the Kalawati Saran Children's Hospital, New Delhi, India, over a period of five years.

Materials and Methods

We retrospectively studied the medical records of all the patients diagnosed with acute Guillain Barre Syndrome from January 2001 to September 2005 in the Kalawati Saran Children's Hospital, New Delhi. This tertiary level medical facility, the largest of its kind in north India, is a 350 bedded hospital attached to the Lady Hardinge Medical College, New Delhi. This hospital caters to the children from Delhi as well as the adjoining northern states of Haryana, Rajasthan, Uttar Pradesh, and Uttaranchal etc.

Between January 2001 and September 2005, a total of approximately 15 lacs patients attended the outpatient department of the hospital and about 1.1 lacs were admitted as inpatients. Records of 207 patients diagnosed with acute GBS were subjected to scrutiny, and out of these, 184 cases were confirmed as GBS; 23 cases were excluded from analysis because an alternate diagnosis could not be ruled out with confidence. Asbury's criteria were applied to all the patients for diagnosis and categorization into severity grades.[6] We recorded data on age, sex, preceding events, clinical features including symptoms, results of CSF study, results of electrophysio-logical studies, and specific treatments including steroids and intravenous immunoglobulin (IV Ig). Disability assessment was done for all the cases at the time of admission, during hospital stay (if applicable), and during follow-up visits, using Hughes criteria with some modification.[7] Grade 0- Normal functional state without neurological deficit, grade I- Minor signs or symptoms, grade II- Able to walk 5 meters across an open space without assistance, grade III- Able to walk 5m across an open space with the help of walking frame, stick or sticks, grade IV- a) wheelchair bound; able to sit with support and b) Bedridden- not able to sit even with the support. Grade V- requiring assisted ventilation. Grade VI- death. Patients were also studied in groups, one group of

patients less than three years of age and the other of more than or equal to three years.

Outcome was determined according to the functional recovery and independent ambulation. It was assessed in follow up at 1 month, 3 months and 6 months after the onset. Some of the follow-up data was collected from the WHO AFP surveillance cell. Favorable outcome was taken as one grade improvement at 1 month and Grade 3 or less at 6 months. Poor outcome was defined by death in acute stage or persistent disability after 6 months.

All the data were recorded in Microsoft Excel software program. Seasonal preponderance was tested by goodness of fit test assuming a null hypothesis of no seasonal variation. Main baseline and clinical course characteristics are expressed as mean ± SD. Student's *t* test, two-sided Fisher's exact test and two-sided Chi square test were used for comparative analysis. Follow-up data of the two groups were compared by Kolmogorov Smirnoff test.

Results

A total of 184 patients were diagnosed as GBS during the study period, with an age range from 1-to15 yrs. (Mean-4.99_+ 2.95) {Table 1}. There was a male predominance with 132/184 (71.74%) males. Majority of the patients108/184 (58.69%) were managed on outdoors basis and rest 76/184 (41.30%) were admitted in the hospital either because they presented in the early stage of the disease or had some complications.

Seasonal preponderance was evident as majority of the patients 99/184(53.80%) develop the disease in summer i.e. from May to August.

Various preceding events within the 4 weeks before the onset of the illness were found in 101/184(54.89%) of the patients. Acute respiratory infections in 39/101(38.61%) were the most common antecedent event followed by diarrhea in 16/101(15.84%) and others (1-T.B., 1-measles, 2-skin infection).

The most common symptom at the time of presentation was limb weakness which was seen in all patients, followed by pain/parasthesia in 58/184 (31.52%) and respiratory symptoms in 19/184(10.32%). Of the various physical signs, quadriparasis was seen in 140/184(76.08%) of the patients, however deep tendon reflexes were present in upper limbs in 77/184(41.85%) and in 2/184(1.08%) patients in lower limbs. Bulbar weakness was the most common type of cranial nerve involvement seen in 24/184(13.04%), followed by facial nerve palsy in only 2/184 (1.08%).

There was variable motor weakness in patients at the time of the presentation. They were classified according to the Hughes's staging I to VI. Majority of the patients 140/184(76.08%) presented in stage IV {a-57 (40.71%), b-83 (59.28%)} followed by 29/184(15.76%) in stage III, 9/184(4.89%) in stage II and only 6/184 (3.26%) in stage V.

Respiratory system involvement in the form of respiratory distress with potential respiratory failure was present in 33/184(18.08%), of which 19 (10.32%) patients required respiratory support. The mean duration of ventilation required was 7.37+-3.88 days. Severe dys-autonomia with hypotension was seen in 14/184(7.65%) of the patients, and 2/184 had severe hypertension with papillidema. The mean days to reach peak illness were 4.75+- 2.92 days.

Cerebrospinal fluid studies could be conducted in 24/76(31.57%) of the patients who were admitted in the hospital. Normal study was obtained in 07/24(29.16%), and 17/24(70.83%) showed some elevation of protein and cells in the CSF.

Nerve conduction study could be done only in 94/184(51.09%) patients. Demyelination was the commonest finding in 51/94(54.26%), followed by nerve not excitable in 32/94(34.04%) and axonopathy in 11/94(11.70%).

All the patients were given supportive care. Of the 136 (73.91%) patients who were in stage IV at the time of presentation, 18 (13.23%) patients were given intravenous immunoglobulin (IVIG) within the first week of the onset of illness. Other

patients could not be given IVIG due to non-avaibility of the same.

The hospitalized patients were discharged when the disease progression stopped, vital signs stabilized and treatment of the complication, if any, was complete. The mean duration of hospital stay was 10.18 +_ 5.99 days.

There were total 14(18.42%) deaths among the 76 patients who were admitted in the hospital. However details were available only for nine deaths of which four died due to respiratory failure alone, three with associated autonomic dysfunction and shock, and 2 with associated massive aspiration. Only one patient died in the immunoglobulin group secondary to massive aspiration. The rest 5 died after going LAMA (leave against medical advice) from the hospital. Details about these deaths could not be procured.

Therapeutic outcome was measured at 1, 3, and 6 months after the onset of illness. About seventy-two patient (42.60%) came for follow up after one month of illness, of which 27(37.50%) were in grade IV, 44(62.50%) were in the favorable group i.e. in stage III or less and one had complete recovery. At 3 months, 122 (72.20%) patients turned up for the follow-up, of which 61(50.00%) patients completely recovered, 114 (93.40%) were in favorable group (stage III or less) and only 8 (06.55%) patients were in stage IV. At 6 months follow-up, only 26 patients reported back, of which 15 (57.70%) had full recovery and rest of them were in the favorable group (100%) i.e. in stage III or less.

Table 1: Demographic and clinical features

Variable	Total (n = 184)	≤3 yrs (n = 40)	≥3yr (n =144)	p value
Age (mean ± SD)	4.99 ± 2.95	1.97 ± 0.46	5.83 ± 2.79	
Sex				
Male (%)	132 (71.74)	27(67.50)	105(72.92)	0.72
Female (%)	52 (28.30)	13 (32.50)	39(27.08)	0.56
Sex Ratio (M: F)	2.54:1	2.08:1	2.69:1	
Preceding illness				
Not reported (%)	83 (45.11)	15 (37.50)	68(47.22)	0.41
URI (%)	39 (38.61)	9 (36.00)	30(39.47)	0.83
Diarrhea (%)	16 (15.84)	7 (28.00)	9(11.84)	0.03
Others (%)	46 (45.54)	9 (36.00)	37(48.68)	0.72
Presenting complaints				
Muscle weakness	184 (100.00)	40 (100.00)	144 (100.00)	
Pain/ paresthesia	58 (31.52)	07 (17.50)	51 (35.42)	
Respiratory Problems	19 (10.33)	5 (12.50)	14(9.72)	
Signs				
Quadriparesis	140 (76.08)	29 (72.50)	111 (77.08)	
DTR+ UL	77 (41.85)	16 (40.00)	61 (42.36)	
LL	2 (1.08)	0 (00)	2 (1.38)	
Hughes's Staging				
II	9 (4.89)	1 (11.11)	8 (88.88)	
III	29 (15.76)	5 (17.24)	24 (82.75)	
IV	140 (76.08)	33 (23.57)	107 (76.42)	
IV a	57 (40.71)	11 (19.39)	46 (66.33)	
IV b	83 (59.28)	22 (26.50)	61 (73.69)	
V	6 (3.26)	1 (16.66)	5 (83.33)	

Respiratory System involvement	33 (18.08)	7 (17.50)	26 (18.05)
Cranial Nerve involvement	26 (14.13)	7 (17.50)	19 (13.19)
Duration of hospital stay in days (mean ± SD) n=76	10.18 ± 5.98	9.85 ± 6.57	10.25 ± 5.85

Percentages are in parenthesis.
URI = Upper Respiratory Infection;
DTR=Deep Tendon Reflexes
UL=Upper limb
LL=Lower limb
SD=Standard Deviation
N=Total Number

Table 2: Laboratory investigations

Cerebrospinal Fluid Examination
(Done in indoor patients (24/76 (31.57%) only)

Normal	7/ 24 (29.16%)
Albumino-Cytological dissociation	17/ 24 (70.83%)

Nerve Conduction Velocity	Total (n = 184)	≤ 3 yrs (n = 40)	>3yrs (n =144)
Done in	94/184(51.09%)	19/40 (47.50)	75/144 (52.08)
Demyelination	51/ 94 (54.26)	8/ 19 (42.10)	43/ 75 (29.86)
Non excitable nerve	32/ 94 (34.04)	11/ 19 (57.89)	21/ 75 (14.58)
Axonopathy	11/ 94 (11.70)	0/ 19 (00.00)	11/ 75 (7.64)

Percentages are in parenthesis
N=total number

Chart 1

Age group affected

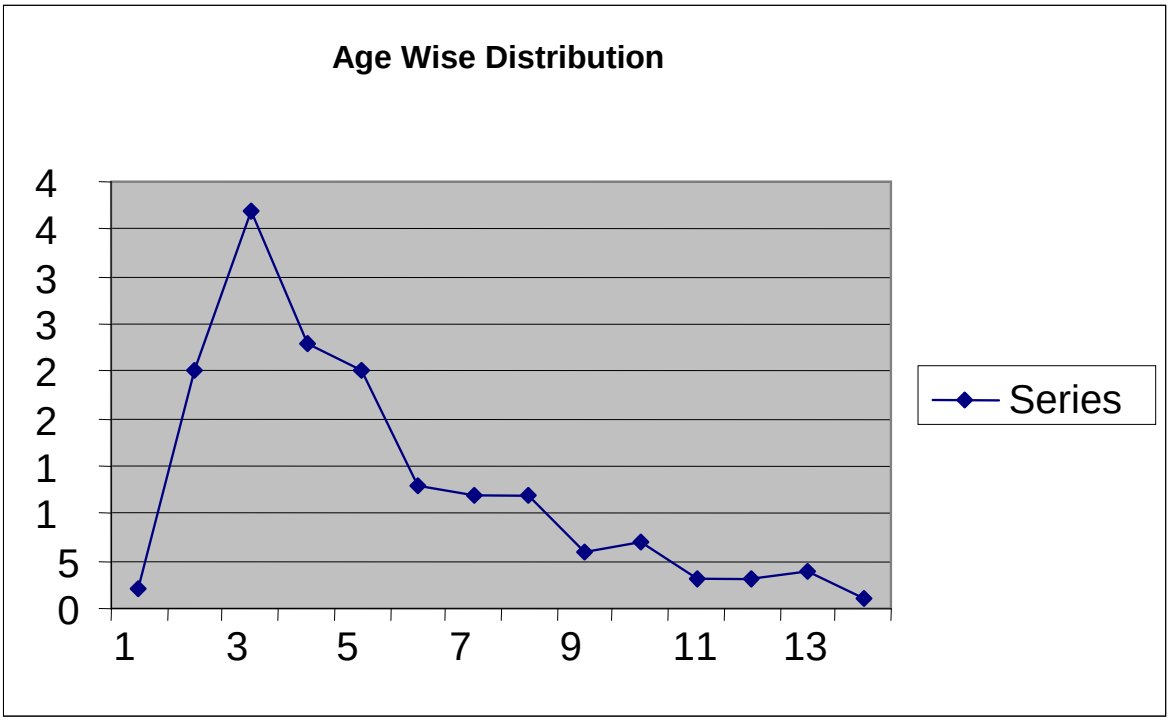
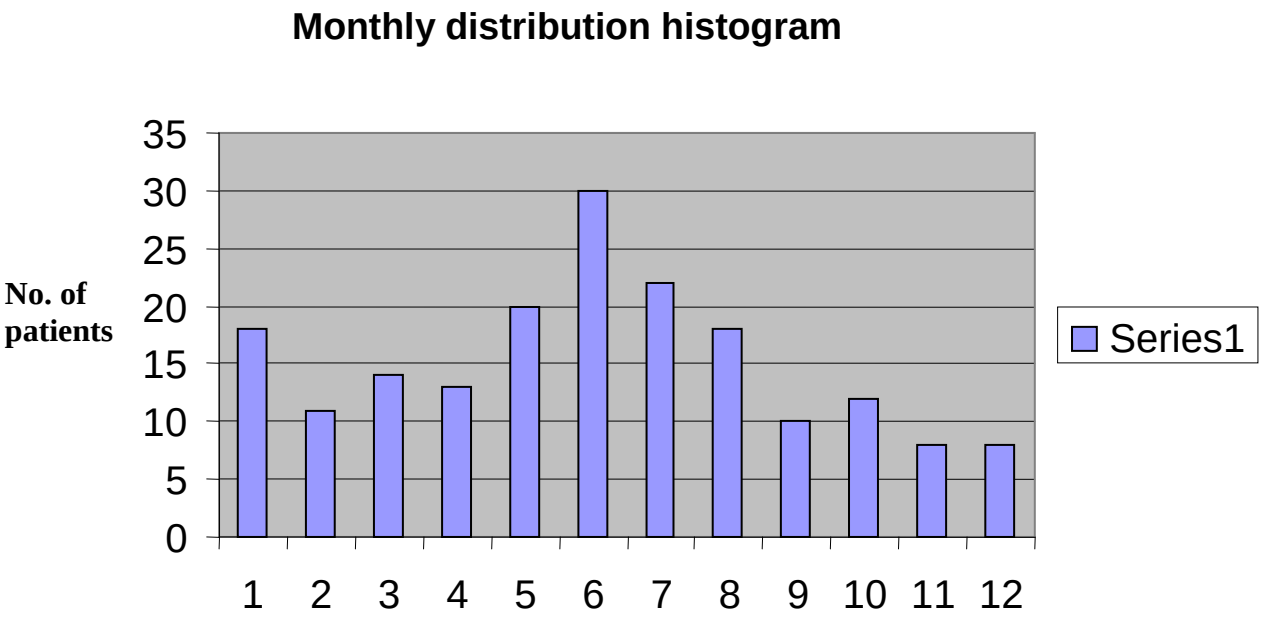


Chart 2:



Discussion

After the near total eradication of poliomyelitis, GBS has emerged as the most common cause of acute flaccid paralysis in children less than 15 years old.[1]

This study was based on the data collected over a period from Jan 2001 to Sept 2005 at Kalawati Saran Children hospital, New Delhi. Being a nodal center for AFP cases, a large number of GBS cases were managed in the said hospital.

It was found that GBS occurs at all the ages in children (up to 18 years of age), however, the peak incidence in our study was between 2-4 years of age. There were 40/184 (21.73%) cases below 3 years of age. The youngest reported case in our study was a 13-month-old male child. Similar were the finding in a comparative study done at Aga Khan University College in Karachi, Pakistan.[8] In one study on GBS from Brazil, the authors reported 2 peaks one at 2-4 years of age and another in the adult population.[9]

In accordance with most of the western and Asian studies, GBS was more common in males in our study, with 71.74% being males and male female ratio was 2.54:1. No precise cause for that was found.

There was a definite pattern of seasonal variation with maximum number of children presenting during the summer and early rainy season. We observed two peaks, one in the summer and early rainy season and the second in winter. (Fig 1) It can be attributed to the sudden increase in waterborne diseases during summer season. The second peak coincides with the increased number of acute respiratory infection (ARI) in the winter season. Similar were the findings of a study from northern China where seasonal predominance was evident in the summer months and was correlated with infection with Campylobacter jejuni and poor personal hygiene.[10,11] In contrast, a Taiwanese study reported a seasonal predominance in the winter time due to increase in ARI in those months and ARI being the most frequent antecedent infection in their patients.[10] In the present study children with diarrhea as an antecedent event were associated with more severe disease in 76.47% of patients.

In comparison to GBS in the adults, childhood GBS takes shorter time to reach the peak weakness and also has a shorter recovery period. In our study we found that the mean duration to reach peak weakness was 4.75±2.92 days whereas

Hung el al reported it as 9.7±7.0 and 10.7±11.1 days for children and adults respectively.[10]

The most common clinical manifestation in our children was muscle weakness (100%) followed by pain/paresthesia in 31.52% of them, which was consistent with other studies. Cranial nerve involvement was found in less number of patients (bulbar palsy in 13.11% and 7th nerve palsy in 1.07%) in comparison to other studies where the cranial nerves were involved in more than 30-42% of the cases. [10] No case of Miller-Fisher variant was found.

Nineteen patients (10.32%) were put on mechanical ventilation during the hospital stay, of which 5 patients died due to respiratory complications and associated severe autonomic dysfunction. Patients with respiratory failure associated with bulbar palsy and autonomic dysfunction had poorer outcome as compared to the patients with respiratory failure alone.

Regarding the NCV, our findings of demyelinating polyneuropathy, as the most common presentation is consistent with most of the studies done on both children and adults. But quite a large number of children (34.04%) remained unclassified (non excitable nerve) in our series. The possible explanation for this could be that the NCV study was done in the 2nd week of the onset of illness whereas the mean duration of peak illness was 4.75+-2.92 days in our study, and as the disease progress rapidly in children as compared to adults and with diffuse changes after complete progression, nerves become not excitable and we could not classify these cases. Also, no standardization of electrophysiological criteria for children <5 years of age are available.[12, 13]

The mean duration of hospitalization is less as compared to the studies done in adults. The possible explanation could be that the children take shorter time to reach nadir, have shorter recovery time and in our case the patients were discharged from the hospital as soon as they cross the nadir stage, instead of judging by improvement in clinical grades.

Eighteen (13.23%) patients received intravenous immunoglobulin (IVIG) within the first week of the onset of illness. Other patients received supportive treatment only. The mortality was only 5.55% in the IV IG group as compared to 17.11% in the non IV IG group. Therapeutic outcome at 3 months indicated walking independently with/without support in 93.44% of cases and 50% had fully recovered till that time. All cases (n=26) seen after 6 months were in favorable group. Eighty five percent cases in immunoglobulin group were walking independently or with support at 3 months. Singhi el al reported 72.70% patients in favorable group at 3 months follow up in patients with IV IG therapy.[14]

Conclusion

Nine patients presented in stage II; 7 of these (77.77%) recovered completely within 3 months of the onset of illness, one of the patient after worsening to two stage higher is now walking independently with minimal disability at 6 month follow-up, while one case was lost to follow-up.

Of the 29 patients who presented in stage III, 17 (58.62%) improved completely, while 5 were ambulating independently with minimal neurological deficit within 3 months from the time of presentation and the rest 7 patients were lost to follow-up.

19 (33.33%) of 57 patients who came in stage IV a recovered completely, 23 (40.35%) had a favorable outcome, and 13 showed partial recovery but still were not able to walk without support at 3 months. When followed up at 6 months, 5 were walking independently with mild neurological deficit. 1 was lost to follow-up while one died due to respiratory failure during hospital stay.

Of 83 patients presenting in stage IV b, 18 (21.68%) recovered completely within 3 months, 24 (28.91%) were in favorable staging (stage III or less) at the end of 3 months, 9 showed partial recovery but still were not able to walk without support even at 6 months, 10 died due to various

causes related to GBS and there was no follow-up data for 22 patients.

6 patients who were in stage V at the time of presentation, 3 died during the acute stage of illness, 2 recovered and were walking independently with minimal deficit within 6 months while the remaining one patient was lost to follow-up.

As there was no long-term sequealae found in our patients, this reaffirms that if pediatric patients are managed optimally in the acute stage, complete recovery can be ensured.

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