Original Research Article

Predictors of mortality in acute encephalitis syndrome in children

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ABSTRACT

Background: Encephalitis is an important cause of morbidity, mortality and neurological sequelae in children globally. Causes are diverse and include viral and non-viral etiology as well as autoimmune processes. In the west autoimmune encephalitis are now most common than any single infectious cause, but in India infectious causes are still most common. It is critical to evaluate the immediately to reduce mortality and sequalae in Acute Encephalitis Syndrome (AES) patients. This study has been done to find out different predictors of mortality in outcome of AES at the end of hospital stay.
Objectives: To find out the predictors of mortality in children with acute encephalitis syndrome between age group of 1 month to 14 years.
Materials and Methods: This was a cross sectional analytical study conducted over a period of two years. A total of 310 subjects were included in the study. Different clinical and laboratory parameters were taken to know the different significant predictors of mortality.
Results: A total of 310 cases were taken for the study from the age group of 1 month to 14 years. Out of these AES cases 22.5% cases died and 77.5% patients were discharged. Higher mortality was seen in 11-14 years of age group and females had higher mortality as compared to males. Only 5 variables that is refractory seizure, GCS<8, features of raised ICT, shock and requirement of ventilatory support were found to be significant (p<0.05) in predictors of mortality. Other variables like age, sex, socioeconomic status, fever altered sensorium, seizure, meningeal sign, laboratory investigations like serum sodium, total leucocyte count, serum creatinine, duration of hospitalisation were not found to be significant(p>0.05).
Conclusion: AES is a disorder of multiple and varying etiology with significant mortality and morbidity. Early diagnosis, appropriate investigation, prompt management go a long way in reducing mortality and sequalae in AES. Refractory seizure, Glasgow Coma Score<8, features of raised Intracranial Tension, Shock and requirement of ventilatory support prognosticate the outcome of Acute Encephalitis Syndrome.

1. Introduction

Intense encephalitis disorder is an arising general medical condition asserting a huge number of lives and the infection most normally influences kids and youthful grown-ups and can prompt impressive mortality and morbidityand undermining close to half of the world's population.[1] The expression "encephalitis" in a real sense implies irritation of part or all of the "encephalon" or cerebrum parenchyma. Internationally, intrusion by a microorganism causing direct neuronal injury is the most well-known reason for encephalitis.[2] In created nations, 50-60% of overcomers of viral encephalitis with clear etiologies had an unfortunate visualization after long haul follow-up.[2,3] The reason for AES might be irregular like herpes simplex encephalitis (HSE), or pestilence like Japanese B encephalitis (JE).[4]

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At present, microbe location for viral encephalitis isn't generally utilized for clinical determination and treatment in India; the finding is to a great extent founded on clinical information and helper assessment of patients[5,6].In expansion, research shows that something like 30-40 % of encephalitis cases can be pathogenically analyzed, of which Japanese encephalitis (JE) is the most well-known cause in India.[7,8] The greater part of pathogenically analyzed viral encephalitis had a poor prognosis. On the other hand, 10-30% of patients with clinically analyzed viral encephalitis likewise have a poor prognosis.[9]

In India aside from Jammu and Kashmir, Himachal Pradesh, and Uttaranchal, virtually all states have detailed Japanese encephalitis. The Northeast piece of India has been encountering intermittent episodes of Japanese Encephalitis as the primary driver of AES with various extent from July to October each year.

The etiological specialists are shifted, and doctors treating such kids frequently feel restricted by the absence of accessibility of demonstrative testing for the greater part of these specialists. There are various lacunae in our insight, issues in epidemiological examinations, absence of analytic offices, as well as troubles in dealing with these basically sick kids in more modest focuses in our country. Therefore, this study was directed to decide the various indicators of mortality of AES in hospitalized youngsters for better comprehension of the illness movement and the result.

2. Aim & Objective

2.1. Research question

What are the predictors of mortality in acute encephalitis syndrome in children?

3. Aim

To study the predictors mortality in children with acute encephalitis syndrome.

4. Objective

To find out the predictors of mortality in children with acute encephalitis syndrome between age group of 1 month to 14 years.

5. Materials and Methods

After getting clearance from institutional ethical & research committee, the study was conducted in Pediatric ICU (PICU) & indoor of department of paediatrics, VIMSAR, Burla from November 2019 to October 2021. This was a cross sectional analytical study.

5.1. Study subjects

Patients admitted in PICU & indoor between age group of 1 month to 14 years were taken as study subjects.

5.2. Inciusion criteria of cases

Patient admitted with fever of <15 days duration with altered sensorium such as confusion, disorientation, coma or inability to talk and/or seizure, headache, vomiting, paralysis in varying combinations.

5.3. Exclusion criteria of cases

Patients having following manifestations were excluded from the study like head injury, simple febrile seizure, seizure disorders heat stroke, metabolic disorders, dys-electrolytemia, syndromic baby, toxic encephalopathy, endocrinal encephalopathy, Children with Central Nervous System (CNS) malformations & other major congenital anomalies predisposing to CNS infections, e.g spinal bifida, pilonidal sinus, CSF Rhinorrhoea, meningocele etc., Mental retardation, Space occupying lesion, Granuloma.

5.4. Study tools and techniques

Every patient was concentrated on in a calculated way in predesigned primary proforma subsequent to getting composed assent from guardians or gatekeepers with respect to their readiness to take part in the review.

After affirmation, point by point history was taken from the guardians or watchmen in regards to span and example of fever, whether modified sensorium began alongside fever or after how long of fever, whether the above episode was related with seizure, cerebral pain, retching or shortcoming of any appendages. Any previous history of comparable episodes was asked. History of immunization was additionally asked. At first tolerant's vitals were settled and afterward clinical assessments were finished. Pressing strong administration, and blood tests were sent for various standard biochemical tests. Blood and pee tests were sent for culture and responsiveness in all cases by keeping up with legitimate aseptic strategy. Neuroimaging and CSF examination were acted in all instances of fever with changed sensorium.

The clinical factors recorded were pulse, respiratory rate and examples, blood pressure(average of three accounts, utilizing mercury sphygmomanometer, by auscultatory technique), temperature, sensorium (utilizing adjusted Glasgow Coma Scale), higher capability and cranial nerve shortfall, pupillary size and reaction to light, additional visual development, pose, engine design (recorded emotionally by surveying the uninvolved tone), profound ligament reflexes, plantar sign, tangible, seizure if any, kind of seizure, compulsory development and fundus picture, autonomic framework inclusion, spine and skull

irregularities. Other framework anomalies were likewise searched for.

5.5. Data collection methods

Every one of the important information were gathered in a predesigned case report design (CRF). Information the board: Data approval and information cleaning was done physically by two separate people not associated with the review.

5.6. Data analysis

Persistent information were communicated in mean ± SD; clear cut information were communicated in extents. Information business as usual testing of persistent information was finished by Shapiro Wilk's test and Greenhouse Geisser rectification was finished by SPSS v 25 (IBM, New York). For all measurable reason p esteem <0.05 was viewed as huge.

5.7. Observation

The total study population comprises of 310 cases out of which 188 (60.6%) cases were male and 122(39.3%) cases were female.Table 1

Maximum percentage patients (36.7%) were from age group 1 month to 5yr followed by 6-10 years (32.9%) followed by 11 to 14 year (30.4%).Table 2

Majority of patients were from low socioeconomic groups that is 41.3% cases from lower socioeconomic status according to Modified Kuppuswamy Socioeconomic Scale (2021) and least patients are from upper middle socioeconomic status group.

The most common presentation in AES cases is fever and altered sensorium, ubiquitously present in almost all cases100%. Other clinical features found are seizure (79%). Some patients also had refractory seizure 36(11.4%).Table 3

Examination of AES cases on admission GCS score was ≤8 in 52 16.7% of patients. Other important findings present during admission were signs of meningeal irritation in 110 (35.5%) of patients features of raised ICT in 92 (29.6%) of patients. Shock was present in 26 (8.3%) of patients and inotropes were required in those patients.Table 4

The course of hospitalisation reveals hyponatremia in 66 (21.3%) cases, hypernatremia in 28 (9%) cases and in rest 216 (69.7%) serum sodium was within normal level. Total leucocyte count is normal in 211(68%) of cases, leukocytopenia in 37 (11.9%) of cases and leucocytosis in 62 (20%) of cases. Serum creatinine was within normal level in 259 (83.5%) of cases and elevated in 51 (16.5%) of cases.Table 5

During the course of treatment out if 310 patients ventilator support was required in 83 (26.7%) of cases. Out of 310 AES cases hospitalised duration ≤7 days in 54(17.4%) of cases and more than 7 days in 256(82.6%) of cases.Table 6

Out of 310 cases maximum mortality is seen in age group of 11-14 years (27.6%) but the age criteria as a predictor of mortality was not significant as p value is 1.140 (>0.05). Males are more commonly affected (60.6%), mortality rate was more in females (26.2%) as compare to males (20.2). But the gender criteria as a predictor of mortality in AES cases was insignificant [P value 0.266(>0.05)]. Proportion of mortality in AES cases was more in absence of seizure (24.6%), than in the presence of seizure (22%). Presence or absence of seizure as a predictor of mortality in AES cases was insignificant [P value 0.739(>0.05)]. Mortality in AES cases was significantly higher in presence of refractory seizure (43.7%) than in absence of seizure (18.7%). %). Presence or absence of refractory seizure as a predictor of mortality in AES cases was significant statistically [P value 0.001(<0.05)]. Presence of GCS <8 in AES cases was significantly associated with mortality (80.7%) than those had GCS ≥8 (10.8%). GCS as a predictor of mortality in AES cases was significant statistically [Pearson chi square 144.210; P value 0.000(<0.05)]. Presence of meningeal sign was associated with lower proportion of mortality (21.8%) than those not having meningeal sign (23%). Signs of meningeal irritation as a predictor of mortality in AES cases was not significant statistically [P value 0.887(>0.05)]. Presence of features of raised ICT in AES cases was significantly associated with mortality (54.3%) than those not having features of raised ICT (9.2%). Presence of features of raised ICT as a predictor of mortality in AES cases was significant statistically [P value 0.000(<0.05)]. AES cases presenting with shock or developing shock during hospitalisation and requiring inotropes were significantly associated with mortality (46,2%) than not had shock. Presence of shock and need of inotropes as a predictor of mortality in AES cases was significant statistically [P value 0.006(<0.05)]. Leucocytosis was associated with higher mortality (64.5%), but TLC as a predictor of mortality in AES cases was not significant p value 1.00(>0.05). Hypernatremia was associated with higher mortality (64.5%), but serum sodium as a predictor of mortality in AES cases was not significant p value 0.959(>0.05). Increased level of creatinine was also associated with higher mortality (43.1%), but serum creatinine as a predictor of mortality in AES cases was not significant p value 1.00(>0.05). AES patients hospitalised ≤7 days had higher mortality (46.3%), but duration of hospitalisation as a predictor of mortality in AES cases was not significant p value 0.231(>0.05). AES patient requiring ventilator support had higher mortality (77.1%) than those did not required it (2.6%). Requirement of ventilator support as a predictor of mortality in AES cases was significant statistically [P value 0.000(<0.05)].Table 7

In the study out of 16 independently significant variables only 5 variables that is refractory seizure, GCS<8, features

Table 1: Demographic Profile of Acute Encephalitis Syndrome Patients

Age	Male	Female	Total	Percentage
1 mth-5yr	66	48	114	36.7%
6-10yr	62	40	102	32.9%
11-14yr	60	34	94	30.4%
Total	188(60.6%)	122(39.3%)	310	100

Table 2: Distribution of AES cases in different socioeconomic status groups according to Modified Kuppuswamy Socioeconomic Scale (2021).

Socio economic status	No of AES cases (310)	Percentage
Upper	15	4.8%
Upper middle	10	3.2%
Lower middle	81	26.2%
Upper lower	76	24.5%
Lower	128	41.3%

Table 3: Clinical profile of AES patients

Clinical profile		No. of patients (310)	Percentage (%)
Fever	Present	310	100%
Altered sensorium	Present	310	100%
seizure	Present	245	79%
	Absent	65	21%
Refractory seizure	Present	36	11.6%
	Absent	274	88.4%

Table 4: Examination findings of AES cases

Parameter		No. of patients (310)	Percentage (%)
GCS	<8	52	16.7%
	≥8	258	83.3%
Meningeal signs	Present	110	35.5%
	Absent	200	64.5%
Features of raised ICT	Present	92	29.6%
	Absent	218	70.4%
Shock and need of inotropes	Present	26	8.3%
	Absent	284	91.7%

Table 5: Laboratory findings of AES cases

Parameter	Reference value	No cases	Percentage
Serum Na	<135 (meq/l)	66	21.3%
	135-145 (meq/l)	216	69.7%
	>145 (meq/l)	28	9%
TLC	<4000 (cells/cumm)	37	11.9%
	4000-11000 (cells/cumm)	211	68.1%
	>11000 (cells/cumm)	62	20%
Serum creatinine	≤1.5 mg/dl	259	83.5%
	>1.5mg/dl	51	16.5%

Table 6: Interventions done in hospital in AES patients

Parameter		No of cases (310)	Percentage
Requirement of ventilator support	Yes	83	26.7%
	No	227	73.3%
Duration of hospitalisation	≤7 days	54	17.4%
	> days	256	82.6%

Table 7: Outcome of AES in different age groups.

Variables		No (%)	Survival	Death%	P value
Age	1 month-5yr	114(36.7%)	79%	21%	
	6-10yr	102(32.9%)	80.4%	19.6%	1.140
	11-14yr	94(30.4%)	72.3%	27.6%	
Gender	Male	188(60.6%)	79.8%	20.2%	0.266
	Female	122(39.4%)	73.8%	26.2%	
seizure	Absent	65 (21%)	75.4%	24.6%	0.739
	Present	245 (79%)	78%	22%	
Refractory seizure	Absent	274(88.4%)	81.3%	18.7%	0.001
	Present	36(11.6%)	56.3%	43.7%	
GCS	<8	52(16.7%)	19.3%	80.7%	0.0001
	≥8	258(83.3%)	89.2%	10.8%	
Meningeal sign	Absent	200(64.5%)	77%	23%	0.887
	Present	110(35.5%)	78.2%	21.8%	
Features of raised ICT	Absent	218(70.4%)	90.8%	9.2%	0.0001
	Present	92(29.6%)	45.7%	54.3%	
Shock and need of inotropes	Absent	284(91.7)	79.6%	20.4%	0.006
	Present	26(8.3)	53.8%	46.2%	
TLC(cells/cumm)	<4000	37(11.9%)	94.6%	5.4%	
	4000-11000	211(68.1%)	69.9%	30.1%	1.00
	>11000	62(20%)	35.5%	64.5%	
Serum sodium(meq/l)	<135	66(21.3%)	72.8%	27.2%	
	135-145	216(61.8%)	52.2%	47.8%	0.959
	>145	28(9%)	75%	25%	
Serum creatinine	≤1.5	259(83.5%)	81.9%	18.1%	1.000
	>1.5	51(16.5%)	56.8%	43.1%	
Duration of hospitalisation	≤7 days	54(17.4%)	53.7%	46.3%	0.231
	>7days	256(82.6%)	82.5%	17.5%	
Requirement of ventilator support	No	227(73.3%)	97.4%	2.6%	0.0001
	yes	83(26.7%)	22.9%	77.1%	

of raised ICT, shock and requirement of ventilatory support were found to be significant (p<0.05).

6. Discussion

AES is a disorder of varied etiology and is now one of the leading causes of morbidity and mortality in children in India also in Odisha. AES is a disease of major public health importance due to its high epidemic potential, high case fatality rate (CFR). In Odisha there was also epidemics of AES in the past. Hence studies about AES is essential to achieve better cure rate and early diagnosis. In the past many studies were done in different hospitals in AES cases but studies regarding predictors of mortality in AES cases was very few. So, on seeing the disease burden and public health importance we conducted the study on different predictors of mortality in AES cases in western Odisha. In the current review, we have attempted to dissect the elements deciding the indicators of mortality in intense encephalitis disorder patients. A superior comprehension of introducing elements, causes and result is crucial for help to work on the methodology towards determination and to design levelheaded administration of AES.

In the current concentrate a large portion of the patients were between age gathering of multi month-5 years (36.7%) however greatest mortality happened in the age gathering of 11-14 years. Studies done by Rajarshi Basu, MD Kalamuddin[10] which shows that 43.66% of patients have a place age gathering of 1-5 years and furthermore greatest mortality happened under 5 years of age[10] Similar discoveries were found by Kamble et al[11] where most cases have a place with 1-5 years old with mean period of 4.1years and SD:39.2.133 But review done by Dr.Umesh Kumar, Dr.Bankey Bihari Singh et al[12] observed that larger part of patients were in the age gathering of over 10 years131 (32.6%) however greatest mortality happened in 1-5 years old.

In the present study most cases were males (60.6%) and 39.4% were female. Studies done by RajarshiBasu, MD Kalamuddin[10] found Similar results where (57.7%) males were affected as compare to females (42.26%) .also found in studies done by Kamble et al[11] where the proportion of AES was high in males (64.7%) than females (35.9%). And similar findings found by Sudhir et al.[13] But studies done by Kakoti et al[14] found that most affected cases were females (52.24%) and males (47.8%)

In this present study most of the cases were from lower socioeconomic status that is lower middle (26.2%) and lower (41.3%) according to Modified Kuppuswamy Socioeconomic Scale (2021). This is because of overcrowding in lower SES, poor hygiene that leeds to more transmission of viral and vector borne diseases in these group of populations. Similar results were found in Kamble et al.[11] Beig et al[15] in U.P. that is 73.6% were from lower SES.

In this study out of 310 cases, all had fever and altered sensorium, similar findings found by RajarshiBasu, MD Kalamuddin[10] where all cases had fever and altered sensorium. Studies done by Dongol S, Shrestha S[16] found that fever was present in all cases but altered sensorium was present in 18.7% oc cases.

In the present study convulsion was present in 79% of patients. Study done by Khinchi Y R et al[17] found that seizure occurred in 90.1% of patients. Similar findings were found in studies done by Kakoti et al.[13] where 82% patients had seizure and Anuradha et al,[18] Khinchi et al[17] which showed that all patients had fever and altered sensorium, 90% had seizures. Out of patients having seizure death occurred in 22% of patients but patients not having seizure 24.6% had died. In the study done by RajarshiBasu, MD Kalamuddin[10] 77.4% of patients had seizure and out of patients having seizure 22.7% died.130

In our study refractory seizure occurred in 11.6% of cases showed significant mortality (p value: 0.001). similar findings were found in study done by CM Bokade et al.[19] Where refractory seizure occurred in 35.2% of patients and it showed significant mortality with p value 0.001.149

In our study features of raised ICT was present in 29.6% of cases and out of patients having features of raised ICT death occurred in 54.3% of patients showing significant mortality p value 0.000. Study done by Rajarshi Basu, MD Kalamuddin[10] found that features of raised ICT present in 9.1% of patients and death occurred in 23.07% of cases having it and found to be not significant predictors of mortality. Another study done by Kumar umesh, Singh BB[12] Found that features of raised ICT found in 32% of cases. Study done by CM Bokade, RR Gulhane[19] found that features of raised present in 56.8% of patients and death occurred in 24% of cases with p value 0.071 without any significant mortality.

Meningeal signs at the time of admission was present in 35.5% of patients. Among those patients having meningeal sign at the time of admission death occurred in 21.8% of patients and 78.2% got discharged but those patients not having meningeal sign at the time of admission 23% died. In the study done by Rajarshi Basu, MD Kalamuddin[10] found that meningeal sign was present in 34.5% of patients out of which 34.69% of cases died having meningeal sign. This showed significant mortality with p value 0.001.signs of meningeal irritation was present in 55.2% of cases in studies

done by Kakoti et al[14] out of which mortality occurred in 18.18% which was not significant.

In the present study shock was present in 8.3% of cases, out of all those patients having shock and required iontrope support during hospitalization significant mortality occurred in 46.2% of patients (p value0.006) but those patients not having shock death occurred in 20.4% of patients. In the study done by RajarshiBasu, MD Kalamuddin[10] shock was present in 6.33% of cases and significant mortality occurred in 55.55%of patients having shock (p value0.012). Studies done by Kumar Umesh, Singh BB.,[12] CM Bokade, RR Gulhane.,[19] Sudhir SK, Prasad MS,[13] found similar findings that presence of shock causes significant mortality with p value 0.017, 0.025, 0.012 respectively. Similar finding were also found by Khinchi Y R et al,[17] Bandyopadhyay Bhaswati et al,[20] Avabratha et al[21] and Dongol S et al.[15]

In the present study GCS was above 8 in most of the patients (83.3%) and patients having GCS <8 had significant mortality with p value 0.000. Similar findings were found in studies done by RajarshiBasu, MD Kalamuddin.[10] 130 where 33.09% of patients had GCS<8 with significant mortality of 44.68% with p value 0.001. Study done by CM Bokade, RR Gulhane.[19] found similar finding that GCS<8 causes significant mortality with p value 0.001. Other studies also done by Kumar umesh, Singh BB.,[12] Kakoti et al,[14] DongolS et al[16] also found similar findings that AES cases having GCS<8 causes significant mortality with p value <0.05.

In our study requirement of ventilator support was found in 26.7% of cases and out of these patients significant mortality occurs (77.1%). Similar findings found by Rajarshi Basu, MD Kalamuddin.[10] Where 62.06% death occurs in patient requiring ventilator support causing significant mortality. This result was in accordance with the previous studies done by Sudhir SK, Prasad MS,[13] who found significant mortality in patients requiring ventilatory support with p value <0.001.

In our study 17.4% of cases had duration of hospitalisation ≤7 days but it found to be a non significant predictor of mortality in AES. This observation was similar to study done by Sudhir SK, Prasad MS.[13]

On laboratory investigation in most of the cases total leucocyte count, serum sodium and serum creatinine were in the normal range in the present study. Similar findings were found in studies done by Kamble S, Raghvendra B.[11] This result was also in accordance with the previous studies done by Sudhir SK, Prasad MS,[13] who found TLC, serum sodium and creatinine were not the significant predictors of mortality in AES cases with p value 0.072, 0.344, 0.125.

In present review, out of 310 offspring of AES conceded in pediatric Intensive Care Unit (PICU) 240(77.5%) were released and demise happened in 70 (22.5%) of patients. The current outcomes are in concordance with past

perception in an emergency clinic put together review with respect to AES by DuBray et al.[22] where 67.4% of cases released with full recuperation. Study done by Khinchi et al.[17] in Nepal observed that 40.6% encephalitis patients were released and 34.3% were lapsed. Kakoti et al[14] study in Assam showed 63.9% patients were totally recuperated on release and 14.7% terminated.

In the current review, we have attempted to break down the elements deciding the result of patients confessed to PICU with AES highlights. In the concentrate out of 16 autonomously huge factors just 5 factors that is hard-headed seizure, GCS<8, highlights of raised ICT, shock and prerequisite of ventilatory help were viewed as critical (p<0.05) in indicators of mortality in AES patients. Different factors like age, sex, financial status, fever changed sensorium, seizure, meningeal sign, lab examinations like serum sodium, all out leucocyte count, serum creatinine, length of hospitalization were not viewed as significant(p>0.05). These discoveries were almost like investigations of Bokade et al,[19] Idro et al.[23] Nayana Prabha et al.[24]

7. Limits of the Review

The review included just couple of boundaries of clinical elements, examinations. A lot more examinations ought to be completed to figure out the etiology of sickness, the reason and the indicators of the sequelae of the patients who are getting released.

8. Conclusion

AES is a major illness affecting children of Western Odisha as well as other parts of state and country with significant morbidity and mortality. Its control is very important from public health aspect as it has significant impact on resources of state, nation and public exchequer.

Since AES is a disorder of multiple and varied etiology, better understanding of clinical features, causes and outcome will definitely help in diagnosis and better approach towards treatment of the patients as well as the health infrastructure of state and country.

Refractory seizure, Glasgow Coma Score<8, highlights of raised Intracranial Tension, Shock and prerequisite of ventilatory help visualize the result of Acute Encephalitis Syndrome.

All in all one might say that counteraction by immunization, early determination, suitable examinations, severe observing of the gamble elements of mortality and brief administration go quite far in diminishing mortality and sequalae in AES.

9. Authors' Contribution

Subas Chandra Majhi - Study concept, Research design, Gyana Ranjan Sahoo - Literature, Data collection, Sameer Kiro - Data compilation, Method, Himanshu Nayak- Data analysis, Method, Sitanshu Kumar Meher - Method, design, Mangal Charan Murmu - Manuscript preparation & Editing, Coordination

10. Conflict of Interest

11. Source of Funding

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