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Incidence and risk factor profile of adult patients with acute kidney injury admitted to a tertiary care centre of North India

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Abstract
Background and Objectives: Epidemiological data on risk factors and causes of Acute Kidney Injury (AKI) in adult hospitalised patients in Indian subcontinent are lacking. This study aims at finding incidence, risk factor profiles and causes of AKI among hospitalised adults in one of the tertiary care centre of North India and to assess the predictors of mortality in AKI.
Methods: This was a single centre retrospective cohort study in hospitalised adult (≥12yrs) patients of AKI. Patients with pre-existing chronic kidney disease (Stages 3-5) and renal transplant recipients were excluded. Patients' demographic data, risk factor profiles, causes and in-hospital outcomes of AKI such as mortality, recovery, and haemodialysis requirement were examined.
Results: AKI incidence was 5 per 1000 hospitalised adults. The mean age was 50.0±18.7. Males constituted 58.2%. DM, CLD, COPD and pre-existing CKD were the major risk factors in them. The causes of AKI were Sepsis (64.6%), Hypovolemia (5.0%), acute pancreatitis (1.9%), Poisoning (1.1%), Toxins / Nephrotoxic drugs (0.8%). In 54.1% of cases, the exact source of sepsis could not be ascertained but LRTI (12.6%) remained the most common known source of sepsis. 12.4% cases needed haemodialysis and 30.8% died in hospital. Aging (≥60yrs) and cancer were the two risk factors significantly associated with higher mortality.
Conclusion: The incidence of AKI in hospitalised adults though is not as high as found in other counties, but in-hospital mortality is very high particularly in elderly and advanced cancer patients.

Keywords: acute kidney injury, incidence, North India, predictors, risk factors

Introduction

Acute kidney injury (AKI) is a common disorder, characterized by an abrupt or rapid decline in renal filtration function. The epidemiology, risk factor profile, causes and outcome of AKI vary from one country to another and also from one region to another within the same country. In one of the largest study from China, the incidence of AKI was as high as 11.6% in hospitalised adults [1]. In few other studies from USA and Canada, AKI is estimated to occur in up to 15% of hospitalized patients and up to 60% of critically ill patients [2, 4]. One another study from china shows the incidence of hospital acquired AKI (HA-AKI) is 3.1% [5] and another from UK is 2.1% [6]. The incidence of AKI in acute medical care units in almost every part of the world is increasing with time due to rise in aging population and increased number of critically ill patients with multiple chronic co-morbidities [7, 8]. Though, ample studies exist on AKI in hospitalized patients worldwide, but only few studies [9-11] are available from Indian subcontinent despite India being the world's 2nd largest populous country [12]. Only one study from a tertiary care centre of North India showed an incidence of community acquired (CA-AKI) to be 2.5% [13].

In patients of AKI, early diagnosis and identification of risk factors and its causes is the key to prevent short and long term complications and poor outcomes including mortality. Various studies have identified risk factors of AKI in hospital and community settings. Sepsis, hypovolemia, advanced age, hypotension, poisoning and nephrotoxic drugs are the well-established causes very often associated with AKI [14]. Perioperative complications, contrast induced nephropathy and other iatrogenic complications are also found to be commonly associated with HA-AKI [15, 16]. In another study, pre-existing CKD, cardiac failure, ischemic heart disease, hypertension, diabetes, dementia, and cancer were the predominant risk factors of AKI [6]. But in hospitalised adult patients, relevant data on AKI and its risk factors vary from one region to another even within the Indian subcontinent, which are geographically distant. The etiologic spectrum has been demonstrated to change over passage of time. For example, in the study by Prakash *et al*. from the eastern part of India comparing AKI between 1983–1995 and 1996–2008, it was found that the incidences of obstetrical, surgical, and

diarrhoeal AKI decreased significantly, whereas AKI associated with malaria, sepsis, nephrotoxic drugs, and liver disease increased [17]. In one of North Indian study from Chandigarh involving 1862 patients over a period of 21 years (1965–1986), the bulk of AKI cases were medical causes 60%, whereas obstetric and surgical constituted 15% and 25% causes of AKI, respectively [18]. One south Indian study from Chennai reported diarrhoea as the most common cause of AKI, followed by drugs, glomerulonephritis, sepsis, snakebite, leptospirosis, malaria, and copper sulphate as other common causes [19].

Haemodialysis (HD) is one of the effective lifesaving modes of treatment in AKI, though most of the patients of AKI do recover with conservative treatment only. The rate of HD requirement varies among hospital settings and countries. Few studies only highlight on this issue. The Chinese study showed around 3.5% to 4.7% of AKI patients required HD [1], whereas 27.8% of paediatric patients required HD in one of the Indian studies [20]. Haemodialysis though is very effective, but an expensive mode of treatment, which is not available at all health care set up in this country. There is definitely a paucity of data on adult patients of AKI requiring HD. Considering the huge patient load on the resource crunch tertiary care hospitals, the knowledge on incriminating risk factors associated with AKI patients requiring haemodialysis is imperative for Government's planning and policy making for health care.

Health care and health care settings in India are different from that of Western and South Asian countries. Hence, finding the prevalence of AKI and its contributing factors in hospital settings will be crucial in preventing the adverse outcomes, limiting the hospital stay and hospitalisation cost. Therefore, this study aimed to determine the incidence, risk factors and outcome of AKI in adult patients hospitalised to a tertiary care hospital of north India and to find out the significant risk factors associated with the mortality. A clear understanding of which patients are at greatest risk of AKI is a prerequisite for prompt recognition and effective management in order to prevent complications and prolong survival.

Material and Methods

Study Designs, setting & populations

This study is a retrospective cohort study conducted in Hindu Rao Hospital, Delhi, which is a tertiary care teaching hospital of North India. The study cohort included hospitalised patients aged 12–99 years, diagnosed as AKI between January 1, 2017 and June 30, 2018, and referred to Nephrology unit for review. AKI patients with CKD (stages 3–5) and those receiving maintenance dialysis or renal transplantation were excluded from the study.

Data Source

Data were collected from case sheets of all those admitted patients of AKI coming under the defined population and period with prior permission from Medical Record Department (MRD) of the hospital. Medical ethics committee of the hospital approved our study protocol. Basic demographic and clinical data such as age, gender, comorbidities (Risk factors) and causes of AKI were obtained. The outcome data on Recovery, HD (Haemodialysis) requirement and Mortality were also collected for analysis.

Identification of AKI

Identification of case with AKI was done based on KDIGO criteria [21]. Patients who met at least one of the following criteria were identified as having AKI:*(1)* Serum creatinine (SCr) change on the first day of admission met the KDIGO definition; and *(2)* SCr during admission was ≥1.4 mg/dl in men or ≥1.1 mg/dl in women (corresponding to 1.5-fold of the SCr level in a 60-year-old man or woman with an eGFR of 90 ml/min per 1.73 m^2) and ≥1.5 fold of minimal SCr level during hospitalization. In those cases where baseline creatinine was not available, the lowest SCr during hospitalization was used as the baseline.

Patients with CKD were diagnosed and excluded from AKI with the following criteria; A baseline eGFR, 60 ml/min per 1.73 m^2 in patients with AKI, or the highest eGFR, 60 ml/min per 1.73 m^2 in patients without AKI.

Determination of Risk factors & Causes

The presence of comorbidities was identified as mentioned in the patients' medical record at admission and discharge summary. The documented comorbid conditions in our cohorts were diabetes mellitus (DM),hypertension (HT), chronic obstructive pulmonary disease (COPD), coronary artery disease (CAD), congestive heart failure (CHF), tuberculosis (TB), chronic kidney disease(CKD), benign prostatic hypertrophy (BPH) /obstructive uropathy, chronic liver disease (CLD), cancer, cerebrovascular accident (CVA), thyroid and haematological disorders. These are considered as risk factors of AKI for our study purposes.

Immediate incriminating causes leading to acute kidney injury were also noted from medical record of each case. Sepsis, Hypovolemia, Acute pancreatitis, Poisoning, complicated Malaria, Toxins & Drugs were important causes of AKI in these cases.

Definition of outcomes

The primary outcomes in this study were in-hospital deaths and renal recovery. Other outcome included AKI with HD requirement. Renal recovery of AKI was defined as a decreasing SCr to within 25% of the non-AKI range and at least 0.3 mg/dl below the peak level without RRT.

Statistical analysis

Categorical data related to clinical characteristics (DM, HT, COPD, CAD, CLD, CHF, TB, Hypothyroidism, and CVA), causes of AKI (Sepsis, Hypovolemia, Toxins & Drugs, complicated Malaria, Acute pancreatitis, and Poisoning), sources of sepsis (LRTI, Urosepsis, Abscess, Post-operative, Peripartum, Cholecystitis, Cellulitis, and Peritonitis) and outcome were presented as frequencies/percentages. Continuous variables such as age were presented as mean ± SD. The comparison of survivors or non-survivors was carried out by independent Student's t-test/Mann–Whitney U-test, whichever was appropriate. Logistic regression was used to identify the individual factors associated with outcome. All statistical analysis was carried out with 5% significance, and P

value < 0.05 was considered significant.

Results

Total number of adults patients (≥12yrs) hospitalised during the study period was 64,288. The incidence of AKI is about 5 per 1000 hospitalised adults. 364 patients were identified to have AKI for our study purposes based on our inclusion and exclusion criteria. Of 364 AKI, males were 212(58.2%) and females were 152(41.7%). Commonly associated co-morbid conditions (Risk factors) in patients of AKI were DM (14.3%), CLD (11.0%), COPD (9.9%), Pre-existing CKD (5.2%), HT (4.9%), CAD (4.4%), TB (4.4%) and CHF (4.1%). Common causes of AKI in this study population were Sepsis (64.5%) followed by Hypovolemia (4.9%), Acute Pancreatitis (1.9%), Poisoning (1.1%), Toxins & Drugs (0.8%) and complicated malaria (0.3%). The exact cause of AKI could not be determined in 96 (26.3%) of cases. Table-I: shows the baseline characteristics, prevalence of associated risk factors and causes of AKI.

Sepsis, being the most common cause of AKI was further analysed for source of sepsis. In 197 (54.1%) cases, exact source of sepsis could not be ascertained from the available medical records. Other sources of sepsis were; Lower respiratory tract infections (LRTI) in 46 (12.6%), Abscess (Internal & external) in 25 (6.9%), Urosepsis in 22 (6.0%), Peripartum sepsis in (3.6%), Postoperative sepsis in 20 (5.5%), Cellulitis in 15 (4.1%), Peritonitis in 13 (3.6%) Cholangitis & biliary sepsis in 8 (2.2%), disseminated Koch's in 2 (0.5%), Infected implants in 2 (0.5%), Meningitis/Encephalitis in 1 (0.3%). Figure-1: depicts the sources of sepsis in frequency & percentage. All these AKI patients were treated either by conservative medical management or haemodialysis (HD) support. 12.4% of patients needed HD and the rest 87.6% patients were on conservative treatment. During the hospitalisation period, 112(30.8%) died, recovery to pre AKI stage (Clinically & biochemically) was noted in 250(68.6%) and whereas status of 2 patients is not known.

Further univariate analysis is done to find out the association of risk factors & causes of AKI with the mortality outcome, which showed that Age ≥60yrs and cancer are the independent risk factors associated with the mortality at the 'P' value of 0.002 and 0.034 respectively, as shown in Table-II & Table-III

Discussion

This study is the first from this institution to give an insight into the incidence of AKI in hospitalised adults. Our health care facility is a teaching hospital well-equipped with 1000 beds for hospitalisation and acute care. Many of the patients were having community acquired AKI and some other developed AKI during their hospital stay (Hospital acquired). The incidence of AKI in adults is about 5 per 1000 hospitalisations. The incidence of AKI in our study is much less compared to the previous studies, which had raw incidence of around 10.7% [1], 6.4% [21] and 2.5% [13]. Ours is probably not the true reflection of AKI incidence, as we included only those AKI patients, who were referred to nephrology unit for opinion and hence many cases might had been treated and discharged from different departments without nephrology consultation. More than one third (39%) of total AKI patients were older adults (≥60 yrs), the reason being this critical group of population is often hospitalised with multiple co-morbidities and in a state of already compromised renal reserve to withstand acute illness, shock and hypovolemia. Males out number females in our cohorts (58.2% Vs 41.7%) as also found in different studies from other centres. Assessment of associated risk factors with AKI in our series shows that DM is the most commonly prevalent risk factor in AKI, followed by CLD, COPD, CKD and HT. These risk factor profile of our AKI group are almost comparable to most of the studies done in other countries [1, 6, 14] except higher percentage of patients with DM,COPD and HT were found in our study.

Sepsis is the most common cause of AKI (64.6%) in this study, which is much higher than that of other Indian and International studies. In a recent prospective study from south India, sepsis was present in 12.9% patients [22] ; in the study on CAAKI by Kaul *et al*. from Lucknow, 13.9% had sepsis[13]; in the study from Himachal Pradesh (both CAAKI and HAAKI) 32% had sepsis [23]. In a study from Yemen on CAAKI, only 6.9% had sepsis [24]. In contrast, in a study from Spain (both CAAKI and HAAKI) sepsis constituted almost 50% of AKI cases [25]. However, more recent data from Chennai show that sepsis is emerging as the most common medical cause of AKI [26], which was around 24.0%. The reason of higher incidence of sepsis in our hospitalised patients is because of our hospital setup being a tertiary acute care centre receiving a lot of complicated referred cases from peripheral polyclinics and dispensaries.

In an attempt to find out the possible source of sepsis, we found that, in majority (54.1%) of sepsis induced AKI, the obvious source of infection could not be ascertained. LRTI remained the most common known source of sepsis. Pneumonia and bronchitis were the two common form of LRTI found in this group. Abscess and Urosepsis were found to be important source of sepsis in 6.9% and 6.0% of cases respectively. Abscesses were either subcutaneous or deep organ abscess (liver, spleen &lung).

In India, AKI due to acute diarrheal disease ranged from 20.6% to 30.5% [23, 25, 27]. In our study, Hypovolemia was found in 5.0% of AKI, mainly due to two reasons, either by excessive external/internal bleeding (1.4%) or sudden body fluid loss (3.6%) secondary to acute diarrhoea, vomiting or excessive diuretic use. AKI due to acute gastroenteritis in our study is found in almost same number of patients as reported in another south Indian study conducted in an acute care hospital, which was 4.8% [22]. This low incidence of post-diarrheal AKI in recent studies is probably because, acute diarrheal disease has been decreasing over the past few years due to better hygiene, better facilities, and effective management in primary and secondary level hospital. Acute pancreatitis (1.9%) and herbicidal poisoning (1.1%), though less common were found to be important causes of AKI.

All the patients of AKI were treated either by conservative medical management or haemodialysis support, wherever indicated. 12.4% of patients required HD support and the rest were treated conservatively. Haemodialysis was considered only those patients, who strictly fit into the criteria of its requirement because the procedure is very expensive and there

is an institutional infrastructure limitation for dialysis. RRT requirement in previous studies have been found to be variable, ranging from 7.8% (UK) to 36% (Spain) to 53% (Himachal Pradesh) to 83% (Lucknow) to 22% (Pudducherry) [13, 23, 28, 22]. The different RRT requirement rates are also probably due to the different inclusion criteria used. Studies done in nephrology units have always shown higher percentages of RRT requirement. Of 364 AKI patients, 250(68.6%) recovered well, 112(30.8%) succumbed to death. More number of deaths 57(50.9%) were in older age (≥60yrs), which is similar to other studies showing the higher mortality in older people with AKI [26, 29]. The outcome status of the 2 patients was not known, because they had either absconded or left the hospital against medical advice. The predictors of mortality in AKI as shown in other study were presence of hypotension, mechanical ventilation, thrombocytopenia, and anuria [3, 6, 11, 23]. In this retrospective cohorts, we found old age (≥60yrs) and Cancer independently associated with an increased mortality. This explains the vulnerability of older people to deteriorate faster in view of their multiple co-morbidities at the background of age related structural and functional renal decline leading to increased mortality.

Table 1: Basic characteristics, Risk Factors & Causes of AKI patients (n=364).

Characteristics	Frequency	Percentage (%)
Age		
12-59yrs	222	61.0
>=60yrs	142	39.0
Gender		
Female	152	41.7
Male	212	58.2
Risk Factors(Comorbidities)		
DM	52	14.0
HT	18	4.9
COPD	36	9.9
CAD	16	4.4
TB	15	4.1
CHF	14	3.8
CKD	19	5.2
BPH	7	1.9
CLD	40	11.0
Cancer	2	0.5
Haematological dis.	4	1.1
Thyroid	3	0.8
CVA	11	3.0
Causes of AKI		
† Indeterminate	96	26.3
Sepsis	235	64.6
Haemorrhage	5	1.4
Fluid Loss	13	3.6
Complicated malaria	1	0.3
Toxins & Drugs	3	0.8
Poisoning	4	1.1
Acute Pancreatitis	7	1.9
Treatment of AKI		
Conservative	319	87.6
Haemodialysis	45	12.4
Outcome		
Status- Not known	2	0.5
Recovered	250	68.6
Death	112	30.8

† Cause of AKI could not be ascertained

Table 2: Association of Risk Factors with Mortality

Characteristic	AKI patients (Recovered) (n=250)		AKI patients (Died) (n=112)		P value*	Total sample (n=362) ‡ (n=2)	
	Number	Percentage (%)	Number	Percentage (%)		Number	Percentage (%)
Age							
12-59yrs	165	66.0	55	49.1	0.002*	220	60.8
>=60yrs	85	34.0	57	50.9		142	39.2
Gender							
Female	104	41.6	46	41.0	0.624	150	41.4
Male	146	58.4	66	58.9		212	58.6
Diabetes Mellitus							

No	213	85.2	97	86.6	0.724	310	85.6
Yes	37	14.8	15	13.4		52	14.4
Hypertension							
No	239	95.6	105	93.8	0.454	344	95.0
Yes	11	4.4	7	6.2		18	5.0
Chronic Obstructive Pulmonary Disease							
No	230	92.0	97	86.6	0.109	327	90.3
Yes	20	8.0	15	13.4		35	9.7
Coronary Artery disease							
No	238	95.2	108	96.4	0.599	346	95.6
Yes	12	4.8	4	3.6		16	4.4
Tuberculosis							
No	242	96.8	105	93.8	0.178	347	95.9
Yes	8	3.2	7	6.2		15	4.1
Congestive Heart Failure							
No	240	96.0	107	95.5	0.838	347	95.9
Yes	10	4.0	5	4.5		15	4.1
Chronic Kidney disease							
No	235	94.0	108	96.4	0.338	343	94.8
Yes	15	6.0	4	3.6		19	5.2
BPH / Obstructive Uropathy							
No	246	98.4	109	97.3	0.483	355	98.1
Yes	4	1.6	3	2.7		7	1.9
Chronic Liver Disease							
No	227	90.8	95	84.8	0.094	322	89.0
Yes	23	9.2	17	15.2		40	11.0
Cancer							
No	250	100	110	98.2	0.034*	360	99.4
Yes	0	0	2	1.8		2	0.6
Haematological Disorders							
No	246	98.4	112	100	0.178	358	98.9
Yes	4	1.6	0	0		4	1.1
Thyroid disorders							
No	249	99.6	111	99.1	0.559	360	99.4
Yes	1	0.4	1	0.9		2	0.6
CVA							
No	246	98.4	105	93.8	0.054	351	97.0
Yes	4	1.6	7	6.2		11	3.0

*P value is statistically significant <0.05, ‡ Outcome status: not known

Table 3: Association of Causes of AKI with Mortality

Characteristic	AKI patients (Recovered) (n=250)		AKI patients (Died) (n=112)		P value*	Total sample (n=362) ‡ n=2	
	Number	Percentage (%)	Number	Percentage (%)		Number	Percentage (%)
Sepsis							
No	91	36.4	38	33.9%	0.684	129	35.6
Yes	159	63.6	74	66.1%		233	64.4
Haemorrhage							
No	245	98.0	112	100	0.132	357	98.6
Yes	5	2.0	0	0		5	1.4
Fluid Loss							
No	239	95.6	110	98.2	0.217	349	96.4
Yes	11	4.4	2	1.8		13	3.6
Malaria							
No	249	99.6	112	100	0.503	361	99.7
Yes	1	0.4	0	0		1	0.3
Toxins/Drugs							
No	249	99.6	110	98.2	0.179	359	99.2
Yes	1	0.4	2	1.8		3	0.8
Poisoning							
No	249	99.6	109	97.3	0.055	358	98.9
Yes	1	0.4	3	2.7		4	1.1
Pancreatitis							
No	247	98.8	108	96.4	0.130	355	98.1
Yes	3	1.2	4	3.6		7	1.9

*P value is statistically significant <0.05, ‡ Outcome status: not known

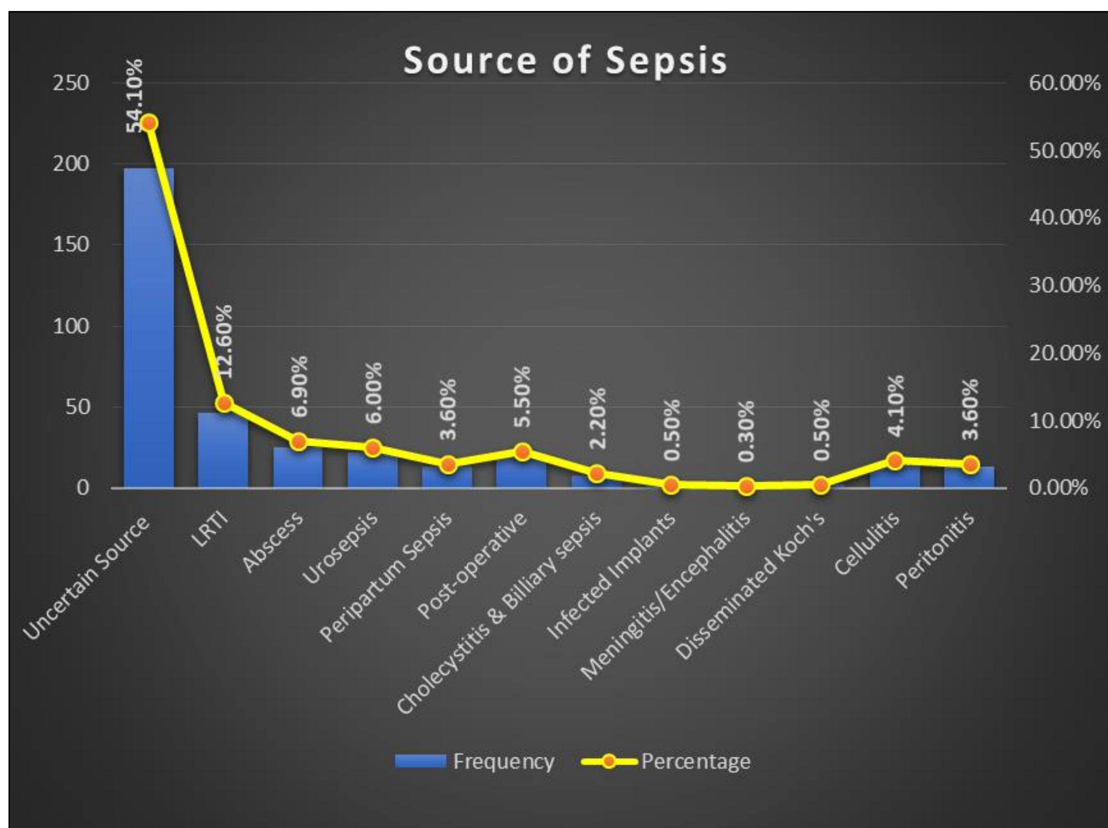

Fig 1: Sources of Sepsis

Conclusion

In this retrospective cohort of hospitalised patients, the incidence of AKI is 5 per 1000 adult hospitalisation. More than one third of AKI patients are aged ≥60yrs. Aging and cancer are the predictors of increased mortality in AKI. Early detection of associated risk factors or comorbidities in elderly is the key to prevent incident AKI, HD requirement and mortality. This will certainly provide inputs for planning and framing of health policy for elderly population with increasing life expectancy.

Limitation of study

1. The incidence of AKI in our study may not reflect the true incidence, as we included only adult patients' ≥12yrs of age. Further we included only those patients referred for nephrology consultation, so some patients with AKI might have been treated and discharged from other department or units.
2. Being retrospective nature it could not ascertained as to how many patients in recovered arm progressed to CKD in follow up. A prospective study with an aim in that direction would help to establish long term consequences of acute kidney injury in future.

Conflicts of Interest

Authors declare that there are no conflicts of interest regarding publishing the article and there are no financial grants or funding involved in this study.

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