



Acute Post Streptococcal Glomerulonephritis among Children from Sokoto, North-Western Nigeria

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Authors' contributions

This work was carried out in collaboration among all authors. Author FBJ conceptualization, study design, statistical analysis, and writing the original draft. Authors PKI and NMJ reviewing, editing. Author MHA data collection and literature search. All authors read and approved the final manuscript.

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ABSTRACT

Aims: To determine the clinical and laboratory profile of children with acute post streptococcal glomerulonephritis (APSGN) admitted into Usmanu Danfodiyo University Teaching Hospital (UDUTH) Sokoto, the outcome, and factors associated with in-hospital mortality.

Study Design: A 5- year retrospective study.

Place of Study: Emergency Paediatric Unit (EPU) and Paediatric Medical Ward (PMW) of the Department of Paediatrics, UDUTH Sokoto.

Methodology: The records of children aged 4 to 14 years with the diagnosis of APSGN were reviewed. Relevant history, physical examination findings, laboratory and radiologic investigation findings were extracted from their case folders and recorded into a proforma sheet. Data was analyzed using SPSS version 23. (IBM SPSS Inc., USA). The level of statistical significance was set at 5%, which is p-value < 0.05.

Results: Fifty-four (0.9%) of the 6128 children were managed for APSGN giving a prevalence of 10.8 APSGN cases per 1000 children. Forty-one folders were utilized for the study. There were 21(51.2%) females and 20(48.8%) males, with F:M ratio of 1.1:1. Mean age at presentation was 9.1± 3.1 years. Majority (92.6%) were ≥5 years and mainly 22(53.7%) of low socio-economic

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status. The main features were body swelling 40(97.6%), fever 25(61.0%), oliguria 24(58.5%), systemic hypertension 37(90.2%), proteinuria 41(100.0%), and haematuria 41(100.0%). Acute kidney injury was the commonest 25(61.0%) complication. Thirty (73.2%) cases were discharged, 5 (12.2%) died, 6(14.6%) left against medical advice. Low social status (0.03), requirement for dialysis ($p=0.003$), congestive cardiac failure ($p=0.01$), and pulmonary oedema ($p=0.04$) were significantly associated with in-hospital mortality. Requirement for dialysis ($p=0.005$) was the independent predictor of in-hospital mortality. At three months post discharge, 20(48.8%) of the 31 cases had achieved complete resolution of APSGN.

Conclusion: APSGN is common in Sokoto and similar in pattern to other reports from Nigeria. The presence of complications at presentation increases the risk of in-hospital mortality.

Keywords: Acute post streptococcal glomerulonephritis; children; pattern; outcome; Sokoto.

1. INTRODUCTION

Acute glomerulonephritis (AGN) is a complex of findings which is marked histologically by generalized glomerular inflammation and can usually be recognized by the clinical picture of hematuria, fluid overload (edema and hypertension), and some evidence of renal insufficiency (elevation of BUN and creatinine) [1]. Acute post-streptococcal glomerulonephritis (APSGN) is the prototype of AGN and it usually follows a streptococcal sore throat or skin infection by various types or strains of streptococcus [2]. In most resource constraint settings including Nigeria, AGN following throat or skin infection has been linked closely to low socio-economic status and poor environmental hygiene [3]. Acute post-streptococcal glomerulonephritis remains the leading renal cause of childhood morbidity in the developing countries in contrast to the observed marked decline in its incidence in the well-resourced countries [4-12]. However, even in some well-resourced countries, post-streptococcal glomerulonephritis is still common in children living in remote communities where scabies is common and group A streptococcal pyoderma is endemic [13-16].

The true incidence of APSGN is difficult to determine because of the under-recognition of the milder cases of APSGN and the transient nature of the illness, with the subclinical cases thought to be 4–19 times more common than symptomatic disease [17]. Varying epidemiology and clinical features of APSGN has been reported in Nigeria, notably in terms of incidence, place and time of the year [2,5,6,8,18]. Although a good number of children with the diagnosis of APSGN are said to recover from the disease, long term complications in the form of chronic kidney disease (CKD) and hypertension has been reported in well-resourced countries and

APSGN is said to be associated with a 5- to 6-fold increased risk of CKD [14,19]. Predicting those likely to develop CKD from APSGN in our setting might be difficult as there is a dearth of studies on long term follow-up of children with APSGN in Nigeria, with no reports on features likely to predict the development of CKD in the affected children to the best of the authors knowledge.

There are no documented reports on the clinical profile and outcome of childhood APSGN from Sokoto, North- Western Nigeria, despite its recognition as a cause of acute kidney injury in a study conducted among children in this location [20]. Sokoto being from a disadvantaged region of Nigeria in the context of socio-economic development [21] with a significant number of its people living below poverty level could be said to be a high risk location for the development of infectious diseases such as those caused by group A beta haemolytic streptococcus among its inhabitants, with subsequent development of non-suppurative complications like APSGN. We sought to determine the pattern and outcome of childhood APSGN in Sokoto, to compare findings from this study to those of other regions of Nigeria and beyond, to determine the factors associated with in-hospital mortality, and to provide baseline information for stakeholders to refer to, in the development of preventive strategies to curb the development of APSGN among children in the study location.

2. MATERIALS AND METHODS

2.1 Study Area

The study was conducted at the paediatric wards (emergency paediatric unit and paediatric medical ward) of Usmanu Danfodiyo University Teaching Hospital (UDUTH), Sokoto, a tertiary

institution located in Sokoto the capital of Sokoto State, Nigeria, over a five-year period from January 2016 to December 2020. Sokoto State is located in the dry Sahel region and is surrounded by sandy Savannah with an annual average temperature of 28.3°C, the highest temperatures reach up to 45°C during the hot dry months of March/ April. The rainy season begins in May and lasts till September with an average annual rainfall of about 640mm while the dry season comprises the hot dry season before the rains from March to April and the cold dry season from November to February [22].

2.2 Study Design

This was a retrospective study of children aged 4 to 15 years, who were admitted into the paediatric wards of UDUTH, Sokoto with the diagnosis of APSGN. Acute glomerulonephritis was defined as abrupt onset of variable degrees of haematuria, proteinuria, hypertension, oedema, oliguria and impaired kidney function with the unusual presentation being a combination of some of these features in addition to either encephalopathy, cardiac failure, or pulmonary oedema [23]. Hypertension was defined as systolic or diastolic blood pressure above the 95th percentile for the age, gender, and height of the child [24]. Urinary tract infection (UTI) was defined as the pure growth of 100,000 or more colony forming units (CFU) of a bacteria per microliter of a midstream or clean catch urine sample or any growth on culture of suprapubic specimen of urine [25]. For the purpose of this study, antecedent history of sore throat, pyoderma, or both, positive culture of streptococcus species, or positive ASO titer result was considered as recent evidence of streptococcal infection [26]. Incomplete records and readmissions were excluded from the study.

2.3 Data Collection

We reviewed the records of all patients with a diagnosis of APSGN. Information about age, gender, address, ethnicity, educational status and occupation of parents, history, physical examination findings, dipstick urinalysis, urine microscopy, throat swab microscopy, culture, and sensitivity, antistreptolysin O (ASO) titre, serum electrolytes, urea and creatinine (E/U/Cr), and renal ultrasonography were extracted from their case folders and carefully recorded into a proforma sheet. Further investigations that were carried out on the patients depending on the provisional diagnosis included complete blood

count, urine microscopy, culture, and sensitivity, spot urine-protein creatinine ratio, serum proteins, serum lipid profile, and hepatitis B and C serology. Facilities for C3 AND C4 components of the complement system, anti-DNase B titre and kidney biopsy were not readily available in the study location. The socio-economic status was determined using Oyedemi classification with social class assigned to the child using the average scores of the parental educational and occupational status into upper, middle, and low socio-economic classes [27]. The duration between the occurrence of first symptom and hospital presentation, intervention sought before presentation, number of days from first symptom to clinical recovery (before discharge), duration of admission, complications, outcome, and follow-up at intervals were also recorded.

2.4 Data Analysis

Data was analyzed using SPSS version 23. (IBM SPSS Inc., USA). The prevalence of APSGN was presented as percentage while the age distribution of the subjects was analyzed and expressed as mean and standard deviation. Frequency distribution tables were used to illustrate results. Chi square test was used to determine the association between categorical variables and in-hospital mortality and Fischer's exact test was used as applicable. Logistic regression analysis was used to determine the variable that was independently associated with in-hospital mortality. The level of statistical significance was set at 5%, which is p-value < 0.05.

3. RESULTS

3.1 Demographics

A total of 6,128 children were admitted during the 5-year study period. Fifty-four (0.9%) of the children were managed for APSGN giving a prevalence of 10.8 cases of APSGN per 1000 children. However, only 41 folders were utilized for the study as some had incomplete data, while others were missing. There were 21(51.2%) females and 20(48.8%) males, giving a female:male ratio of 1.1:1. The mean (standard deviation (SD)) age was 9.1 (3.1) years, with a range of 4 - 14 years. Majority (92.6%) of the cases belonged to the age group category 5-15 years. They were mainly 22(53.7%) of low socio-economic status. (Table 1).

3.2 Clinical Manifestations of Cases of APSGN

The mean duration from onset of first symptom to presentation was 15 days, with 12(29.3%) and 11(26.8%) having sought for intervention from a patent medicine store or ingested herbal concoctions respectively before presentation to UDUTH Sokoto. The presentation of the illness was most common 20(48.8%) cases, between November and February. Preceding history of sore throat was obtained from 18(43.9%) of the cases, skin infection in 15(36.6%), and history of sore throat or skin infection was not ascertained

in 8(19.5%) of the cases. The clinical features of the cases were mainly body swelling 40(97.6%), fever 25(61.0%), oliguria 24(58.5%), passage of coke- coloured urine 22(53.7%), cough 21(51.2%), and difficulty in breathing 20(48.8%). Most 37(90.2%) of the cases had systemic hypertension at presentation (Table 2). The mean duration between onset of symptoms and clinical recovery was 14 days with a range of 5-31 days, and average duration of hospital admission was 9 days with a range of 4-21 days. There was significant association between late presentation (p=0.001) and poor blood pressure control (p=0.04) with prolonged hospital stay.

Table 1. Socio-demographic characteristics of the APSGN cases (N=41)

Variables	Frequency (n)	Percentage (%)
Age group (Years)		
< 05	003	07.4
5-10	019	46.3
>10-15	019	46.3
Mean (SD)	9.1± 3.1	
Gender		
Male	020	48.8
Female	021	51.2
Social class		
Upper	002	04.8
Middle	017	41.5
Lower	022	53.7

Table 2. Clinical manifestation of the APSGN cases

Characteristics*	Frequency (%)
Body swelling	40(97.6)
Fever	25(61.0)
Oliguria	24(58.5)
Anuria	02(4.9)
Normal urine output	15(36.6)
Coke-coloured urine	22(53.7)
Gross haematuria	04(9.8)
Dysuria	04(9.8)
Cough	21(51.2)
Difficulty in breathing	20(48.8)
Headache	18(43.9)
Convulsion	07(17.1)
Coma	04(9.8)
Vomiting	07(17.1)
Abdominal pain	04(9.8)
Dizziness	01(2.4)
Easy fatigability	01(2.4)
Systemic hypertension	37(90.2)

* Multiple clinical features were present in some cases

3.3 Laboratory Profile of Cases of APSGN

The main laboratory parameters were proteinuria and haematuria in 41(100.0%) cases with 9(22.0%) having nephrotic range proteinuria. Massive proteinuria was commoner among females 7(77.8%) but was not statistically significant (p=0.07). Other common laboratory features were red blood cell casts in 32(78.0%), granular casts in 21(51.2%), raised antistreptolysin O titre in 29(70.7%), and various grades of renal parenchymal inflammatory changes in 32(78.0%) cases. Eleven (26.8%) of the cases had positive urine culture result with *Escherichia coli* being the commonest 7(63.6%) isolated organism. (Table 3). There was no significant difference in the occurrence of APSGN- UTI co-morbidity between males and females (p=0.65).

3.4 Complications Encountered among Cases

The commonest complication that was observed at presentation among the patients was acute kidney injury in 25(61.0%) of cases with 8(19.5%) of them having indications for dialysis due to severe metabolic acidosis 5(62.5%), hyperkalaemia 2(25%), and uraemic encephalopathy 1(12.5%). Other complications were congestive cardiac failure in 19 (46.3%), hypertensive encephalopathy in 9(22.0%), and pulmonary oedema in 5(12.2%) of the cases.

3.5 Outcome of Cases of AGN and Follow Up Post-discharge

Thirty (73.2%) of the 41 patients were discharged following medical and supportive treatment, 6(14.6%) of the patients left against medical advice (three out of the six cases required dialysis), and 5 (12.2%) mortalities were recorded. (Fig. 1). Low social status (0.03), requirement for dialysis (p=0.003), congestive cardiac failure (p=0.01), and pulmonary oedema (p=0.04) were significantly associated with in-hospital mortality. There was no association between age group category (p=0.26), gender (p=0.18), and the use of herbal medications (p=0.07), with in-hospital mortality. (Table 4). The only independent predictor of in-hospital mortality on logistic regression analysis was requirement for dialysis (p=0.005). At three months post discharge, 20(48.8%) of the 31 cases that were discharged, had complete resolution of acute glomerulonephritis, 7(17.1%) were lost to follow up visits, 2(4.9%) had features suggestive of chronic kidney disease (deranged creatinine), and systemic hypertension persisted in 1(2.4%) of the cases. Clearance of haematuria on dipstick urinalysis occurred in 20(48.8%) of the cases over a range of 10-120 days post detection on urinalysis. Isolated microscopic haematuria persisted in 3(7.3%) cases as at 3 months of routine follow up visit.

Table 3. Laboratory profile of the APSGN cases

Variable*	Frequency (%)
Proteinuria	41(100.0%)
Haematuria	41(100.0%)
Nitrituria	04(9.8)
Leucocyturia	01(2.4)
Red blood cell cast	32(78.0)
Granular cast	21(51.2)
Hyperkalaemia (serum potassium >5.2mmol/l)	02(4.9)
Severe acidosis (bicarbonate <12mmol/l)	05(12.2)
Anaemia (PCV < 30%)	18(43.9)
Leukocytosis (WBC > 11,000 X10 ³ µl)	24(58.5)
Azotemia (elevated serum urea and creatinine)	25(61.0)
Positive ASO titre (>200 Todds units)	29(70.7)
Positive throat culture	24(58.5)
Positive urine culture	11(26.8)
Renal inflammatory changes (ultrasound scan)	32(78.0)

Key: *More than one laboratory finding was documented among cases; PCV= Packed cell volume; WBC= White blood cell count

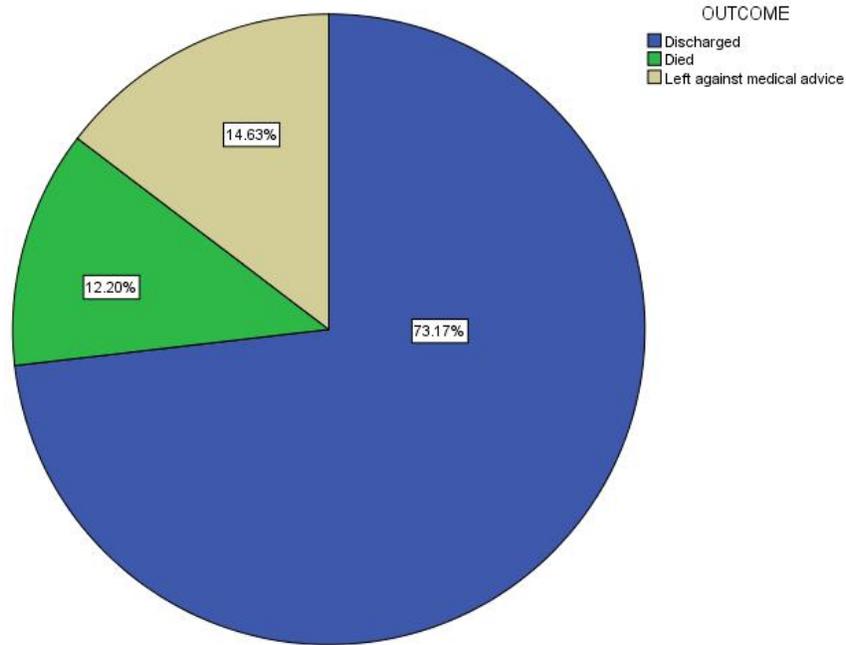


Fig. 1. Outcome of APSGN cases (in percent)

Table 4. Factors associated with in-hospital mortality

Characteristics	Chi square (χ^2) test or fisher's exact test	p-value
Age group category	2.66	0.26
Gender	1.88	0.18
Social status	4.92	0.03
Use of herbal medications	3.19	0.07
Congestive cardiac failure	6.59	0.01
Pulmonary oedema	4.11	0.04
Requirement for dialysis	13.26	0.003
Hypertensive encephalopathy	0.01	0.70
APSGN-UTI co-morbidity	0.13	0.59

4. DISCUSSION

The prevalence of APSGN in our study was comparable to reports from other parts of Nigeria, further suggesting the relatively common occurrence of APSGN in these settings [18,28,29]. This is despite the fact that sub-clinical forms are said to be much more common than the clinically apparent forms, [17] with the severe forms being under-reported, [9] indicating that the true prevalence is likely to be higher if community screenings for APSGN were to be carried out among children of high risk. The incidence in this study as observed in other studies still remain higher than in the high income countries, [11,30] reflecting the persistently poor hygienic conditions and low

socio-economic development over the years in these regions, with inadequate preventive strategies or intervention in the treatment of infectious diseases such as acute pharyngitis and pyoderma caused by group A haemolytic streptococcus. Notably, majority of the cases in this study were from low socio-economic status that resorted to alternative treatment modalities, before subsequently presenting late to the health facility with various degrees of complications.

A single yearly peak incidence of APSGN that was noticed in this study is comparable to reports from Delta state and Benin City in Nigeria, [2,29] but contrasts with reports from those studies conducted in other parts of Nigeria and elsewhere [6,8,15,18]. The peak incidence of

APSGN in this study coincides with the cold dry dusty harmattan season from November to February, a season in which infection by streptococcus is said to be at its peak with about 20% of school aged children being asymptomatic pharyngeal carriers [31]. Although not significant, preceding history of sore throat as the probable focus was higher than skin infection in this study. The absence of the history of likely focus of infection was reported in 19.5% of cases. This finding is not unusual as ascertaining the history of antecedent infection is said to be frequently unavailable but does not exclude the possibility of APSGN [1]. Previous studies have reported variable histories suggestive of antecedents of streptococcus infection among the APSGN cases with the variability linked to differences in hygiene practices and ability of the patients to recall [2,18,28].

The gender prevalence of APSGN in this study was almost equal with slight female preponderance. Female preponderance was reported by Ibadin *et al*²⁹ in their study on childhood acute glomerulonephritis in Benin. This study also contrasts with various other reports in which there was male predominance [3,5,8,10,18,28,32,33]. The reason for the male preponderance in the previous studies was said not to be clear and was thought to be probably linked to higher rates of group A streptococcal infection among males [28]. The finding from this study however, suggests that the gender of individuals may have no or little role to play in the development of APSGN. Rather, genetic susceptibility or variability might explain why certain individuals with recent infection by group A haemolytic streptococcus eventually develop APSGN while others do not. In contrast to reports from previous studies, [2, 28, 29, 32] the incidence of APSGN among age group categories 5-10 years and >10 –15 years in this study is similar, suggesting that these age group categories could have similar risk factors for the development of APSGN.

The clinical manifestations of APSGN in this study are consistent with reports from other studies with the typical features of oedema and hypertension being among the commonest findings [2,10,18,28,29,34,35]. Haematuria and proteinuria as constant features of APSGN in this study is also in consonance to reports from other studies [2,18,28,29]. The finding of UTI as a co-morbid condition in this study is similar to reports from other studies, [29,32] but lower in prevalence compared to report by Ibeneme *et al*

in their study of childhood acute glomerulonephritis in Umuahia where they documented UTI-AGN co-morbidity of 47.4% [28]. The incidence of UTI-AGN co-morbidity in this study is however, higher than the 9% reported by Adedoyin *et al* from Ilorin, Nigeria [36]. Comparing our finding with reports from other studies, it could be assumed that there are no known plausible reasons for the variability in the occurrence of UTI-AGN co-morbidity but it is clear that for some reasons yet to be elucidated, the tendency for increased susceptibility to the development of UTI in patients with APSGN exists and needs to be further explored. Quite a number of cases in this study presenting with complications as at the point of admission signifies delay in presentation or rapidity in the progression of the disease, which has been documented to occur in some cases of APSGN [9].

The most striking complications at presentation among cases in this study were acute kidney injury and congestive cardiac failure which occurred among 61.0% and 46.3% of the cases, respectively. The occurrence of AKI in this study was higher than as reported by other studies [2,28,32] with associated electrolyte derangements (severe metabolic acidosis, uraemia, and hyperkalaemia) requiring dialysis. Therefore, there was association of in-hospital mortality with the requirement for dialysis but most of the cases needing dialysis could not benefit from it because of financial constraint or lack of some required materials for dialysis. Dialysis as a modality of treatment of AKI in cases with indication for it has been reported to improve the outcome of cases of APSGN [2]. The frequency of hypertensive encephalopathy in this study was similar in occurrence to reports from other studies [3,32,34] Pulmonary oedema as a complication in 12.2% of cases in this study was comparable to 10.5% reported in the study from South- East Nigeria, [28] but in contrast to reports from Benin City and Port Harcourt where higher prevalences were reported [29,32]. The occurrence of complications at the point of hospital admission is further confirmed by this study. In addition to the typical features of APSGN, efforts should be made by healthcare providers to identify these features and manage accordingly, to avert unfavorable outcome of cases of APSGN.

Although majority (73.2%) of the cases in this study were discharged, the recorded mortality rate of 12.2% is higher than reported by other

studies [2,18,28,32]. It is also likely that some of the patients that left against medical advice could have succumbed to illness in the absence of intervention. Three of the cases that left against medical advice required dialysis, which could increase the risk of mortality if not offered where available. Complications at presentation increased the mortality rate in this study, in addition to the low socio-economic status of the cases with resultant inability to afford available treatment options. The lack of some materials for dialysis was an additional factor that increased mortality in this study. For example, unlike two cases that had peritoneal dialysis using improvised Ringer's lactate preparation, standard dialysate could not be improvised using Ringer's lactate for the two AKI patients who had hyperkalaemia and there was no haemodialysis facility for children in the study location. Resolution of features in most of the successfully managed cases of APSGN at discharge with no residual kidney disease at 3 months follow-up visit is in keeping with the expected outcome of APSGN, as prognosis has been reported to be good among children without underlying additional risks, than in the adult or elderly population with persistent nephrotic range proteinuria [14,19].

5. CONCLUSION

This study has shown that APSGN is common in the study location and the pattern of presentation is similar to those of studies conducted in other parts of Nigeria. The presence of complications at presentation increases the risk of in-hospital mortality, especially in the phase of low socio-economic status and unavailability of the needed facilities for intervention. Emphasis should be on multiple prevention and control measures against the risk factors for the development of infection by group A streptococcus organism by all stakeholders in the study location, as well as making available the needed facilities for the management of cases of APSGN. The short term prognosis is good among successfully managed cases with resolution of features of APSGN in most of them. However, default from follow up visits remains high, making it impossible to determine the outcome of cases of APSGN on long term basis in our environment.

6. STUDY LIMITATIONS

This study's limitation is in its retrospective design. This is because of the absence of records or missing information, making it not

possible to study some of the records of cases of APSGN that were managed during the study period. By implication, the true prevalence of APSGN is likely not to have been reported in this study. Causal relationships could also not be determined in this study because of the nature of the study design. The lack of facilities to assay the C3 and C4 components of the complement system, anti-DNase titer, kidney biopsy, and renal replacement therapy are other limitations of this study.

CONSENT

As per international standard, parental written consent has been collected and preserved by the author(s).

ETHICAL APPROVAL

Ethical approval for the study was sought and obtained from the Health Research and Ethics Committee of Usmanu Danfodiyo University Teaching Hospital Sokoto. The data obtained were treated with utmost confidentiality.

DISCLAIMER

The company name used for this research is commonly and predominantly selected in our area of research and country. There is absolutely no conflict of interest between the authors and company because we do not intend to use this company as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the company rather it was funded by personal efforts of the authors.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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