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Common Clinical Presentation and Outcome of Severe Malaria in Pediatric Age Group (1-12 years) at Allama Iqbal Teaching Hospital, Dera Ghazi Khan, Pakistan

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ABSTRACT

Malaria remains a significant public health challenge worldwide, particularly in tropical and subtropical regions. **Objectives:** To determine the clinical presentation and outcomes of severe malaria in children aged 1-12 years. **Methods:** This prospective observational study was conducted in the Pediatrics Department, Allama Iqbal Teaching Hospital, DG Khan, from May 2024 to January 2025, including children aged 1–12 years with severe malaria, selected via non-probability consecutive sampling. Demographic and clinical data were recorded at admission, and all patients received IV artesunate. Successful discharge was defined by full clinical recovery and stable vitals. Data analysis was done using SPSS version 26.0, employed chi-square/Fisher's exact tests for categorical and t-tests for continuous variables, with $p<0.050$ considered significant. **Results:** In a total of 120 children, 80 (66.7%) were male. The median age was 7.0 (4.0-10.0) years. Malnutrition was identified in 59 (49.2%) children. *Plasmodium vivax* was the predominant malarial parasite identified in 84 (70.0%) children. The most common clinical presentations were severe anemia, impaired consciousness, seizures, and respiratory distress, observed in 82 (68.3%), 50 (41.7%), 30 (25.0%), and 22 (18.3%), respectively. Mortality was reported, and all children were successfully discharged. Significantly longer hospital stay was noted among children with seizures (8.0 [5.0-11.0] vs. 6.0 [4.0-8.0], p=0.024). **Conclusions:** Severe malaria in children most commonly presents with severe anemia, impaired consciousness, and seizures, with Plasmodium vivax as the predominant causative organism. All enrolled children recovered and were discharged without mortality, indicating favorable short-term outcomes under the current management protocol.

INTRODUCTION

Malaria remains a significant public health challenge worldwide, particularly in tropical and subtropical regions where the disease is endemic [1]. According to the WHO, malaria is responsible for an estimated 241 million cases and 627,000 deaths annually, with children under five years being the most vulnerable group [1]. However, older children also bear a substantial burden, particularly in endemic regions like Pakistan [2]. Pakistan is among the countries with a high burden of malaria, primarily caused by *Plasmodium vivax (P. vivax)* and *Plasmodium falciparum (P. falciparum)* [3, 4]. The disease is prevalent in rural and low-resource settings, where access to prompt diagnosis and treatment remains a challenge [5]. Severe malaria can result in life-threatening complications such as cerebral malaria, severe anemia, respiratory distress, acute kidney injury, and multi-organ failure [6]. According to WHO estimates, children account for nearly 76% of global malaria-related deaths, with most fatalities due to P. falciparum infection [7, 8]. In Pakistan, malaria accounts for 2-3 million cases annually, with a rising incidence in endemic areas such as South Punjab [9, 10]. *P. falciparum* contributes to 30-40% of malaria cases in Pakistan, with an increasing proportion of severe malaria cases [11]. Although pediatric malaria remains a significant

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contributor to childhood morbidity and mortality in South Punjab, most available literature is either outdated or originates from tertiary care centers in major urban settings, which may not reflect the unique epidemiological, socioeconomic, and healthcare challenges faced by resource-limited districts such as DG Khan [12]. There is a paucity of recent, systematically collected data describing the clinical spectrum, management, and short-term outcomes of severe malaria in children presenting to secondary-level hospitals in this region. This study directly addresses this gap by providing prospective, hospital-based evidence from a representative cohort in South Punjab, focusing on both the clinical characteristics and real-world outcomes following standardized treatment protocols. By delineating the prevailing clinical presentations, complications, and discharge outcomes among children with severe malaria, our findings offer actionable insights for frontline clinicians, local policymakers, and public health authorities to tailor intervention strategies, allocate resources more effectively, and refine region-specific clinical guidelines. This targeted approach is especially important in the context of persistent poverty, malnutrition, and healthcare barriers that can influence disease progression and response to treatment in this population.

Although malaria remains a major contributor to pediatric morbidity in Pakistan, region-specific data on the clinical spectrum and short-term outcomes of severe malaria in South Punjab are limited. Most existing studies originate from large urban tertiary centers or are outdated, potentially overlooking evolving epidemiological trends such as the increasing role of *Plasmodium vivax* in severe disease. Furthermore, systematic prospective evaluations linking clinical manifestations with hospitalization outcomes in secondary-level hospitals are scarce. Therefore, updated local evidence is needed to guide region-specific clinical management and resource allocation. This study aims to determine the clinical presentation and outcomes of severe malaria in children aged 1-12 years.

METHODS

This prospective observational study was conducted at the Department of Pediatrics, Allama Iqbal Teaching Hospital, DG Khan, Pakistan, from May 2024 to January 2025, after obtaining approval from the Institutional Ethical Review Board (PM. U-I/008/1027/A.I. T Hosp, DGK). Sample selection was done using a non-probability consecutive sampling technique. A sample size of 120 was calculated using the online OpenEPI sample size calculator, considering the proportion of anemia in children with malaria as 87.1% [13], with a 95% confidence level and a 6% margin of error. The inclusion criteria were children of any gender, aged 1-12 years, who were diagnosed with severe malaria based on clinical and laboratory criteria outlined by the WHO 2022 guidelines. The exclusion criteria were known hematological disorders, like sickle cell disease or hemolytic anemia. Children diagnosed with meningitis or encephalitis, or with concurrent infections (e.g., dengue or typhoid fever), were also excluded. Severe malaria was labeled based on the presence of *P. falciparum*, or P. vivax parasitemia on peripheral blood smear or rapid diagnostic test (RDT), along with one or more severe manifestations such as impaired consciousness (Glasgow Coma Scale <11 or Blantyre Coma Scale <3 in younger children), seizures, severe anemia (Hb <7 g/dL), respiratory distress, metabolic acidosis, circulatory collapse (shock), jaundice, renal impairment, or hypoglycemia (<40 mg/dL). Informed consent was obtained from all participants or legal guardians after explanation of study objectives and procedures. Upon admission, demographic information like age, gender, residential status, and vaccination status was obtained. Relevant laboratory investigations were evaluated. All children were treated with IV artesunate at a weight-based dosage according to WHO 2022 guidelines, as 3.0 mg/kg for children weighing <20 kg, and 2.4 mg/kg for those >20 kg. Artesunate was administered at 0, 12, and 24 hours, followed by once-daily dosing thereafter. Treatment continued with IV artesunate until the patient was clinically stable and able to tolerate oral therapy, typically within 48 to 72 hours. After that, a full 3-day course of oral artemisinin-based combination therapy was initiated to complete the antimalarial regimen. Supportive treatment, including IV fluids, blood transfusions, anticonvulsants, oxygen therapy, or mechanical ventilation (for respiratory failure), was provided as per clinical requirements. Outcomes were recorded in terms of in-hospital mortality or discharge, and duration of hospital stay. Once children were able to tolerate oral therapy, they were transitioned to a full course of oral artemisinin-based combination therapy to complete the antimalarial treatment as per WHO guidelines. Successful discharge was defined as clinical resolution of severe malaria features, including restoration of consciousness, cessation of seizures, correction of anemia and metabolic disturbances, and stabilization of vital parameters, allowing the child to be safely discharged home. Data were collected using a structured proforma. Statistical analysis was performed using IBM-SPSS Statistics, version 26.0. Normal distribution of the data was checked using the Shapiro-Wilk test. Odds ratio with 95 confidence interval (CI) was calculated to measure the effect size. The chi-square test or Fisher's exact test, and the independent t-test or Mann-Whitney U test were used, taking $p<0.050$ as significant.

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RESULTS

In a total of 120 children, 80 (66.7%) were male. The median age was 7.0 (4.0-10.0) years, while the mean weight was 18.8 (15.5-23.5) kg. The residential status of 74 (61.7%) children was rural. Malnutrition was identified in 59 (49.2%) children. *P.vivax* was the predominant malaria parasite identified in 84 (70.0%) children. The most common clinical presentations were severe anemia, impaired consciousness, seizures, and respiratory distress, observed in 82 (68.3%), 50 (41.7%), 30 (25.0%), and 22 (18.3%), respectively (Figure 1).

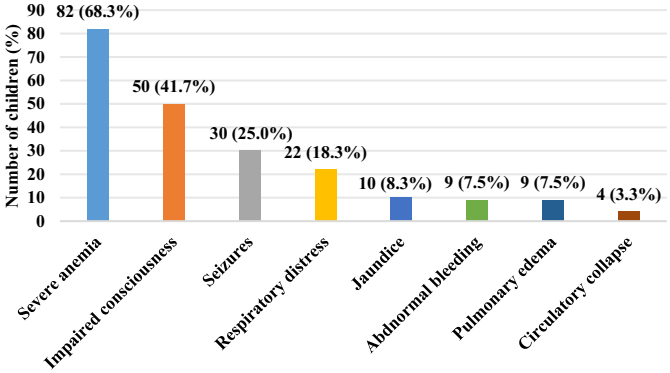

Figure 1: Most Common Clinical Manifestations of Severe Malaria (N=120)

No mortality was reported in this study, and all children were successfully discharged. Overall, the median duration of hospital stay was 7.0 (4.0-9.0) days. Evaluation of seizures to demographic, clinical, and laboratory parameters (Table 1) showed no significant associations except for malarial agent (p=0.033), lower haemoglobin (p=0.006), and a significantly longer hospital stay (p=0.024), table 1.

Table 1: Association of Seizures with Various Demographic, Clinical, and Laboratory Parameters (N=120)

Characteristics		Seizures		Chi-square Value	p-value
		Yes (n=30)	No (n=90)		
Gender	Male	21 (70.0%)	59 (65.6%)	1.22 (0.50-2.95)	0.655
	Female	9 (30.0%)	31 (34.4%)	Reference	
Age (Years)	1-5	11 (36.7%)	34 (37.8%)	Reference	0.913
	6-12	19 (63.3%)	56 (62.2%)	1.05 (0.46-2.41)	
Residence	Rural	17 (56.7%)	57 (63.3%)	0.76 (0.33-1.78)	0.515
	Urban	13 (43.3%)	33 (36.7%)	Reference	
Malnutrition		18 (60.0%)	41 (45.6%)	1.79 (0.79-4.06)	0.171
Malarial Agent	*P. vivax*	19 (63.3%)	65 (72.2%)	Reference	0.033
	P. falciparum	11 (36.7%)	16 (17.8%)	2.35 (0.98-5.61)	
	P. falciparum + P. vivax	-	9 (10.0%)	0.15 (0.01-2.66)	
Hemoglobin (g/dl)		6.4 (5.8-6.9)	6.8 (6.3-9.0)	-	0.006
Hematocrit (%)		32.3±6.5	34.1±6.3	-	0.176
Platelets (109/L)		115.5 (66.0-170.5)	118.5 (70.3-169.3)	-	0.966
Blood Glucose (mg/dl)		87.8±13.7	84.0±14.3	-	0.202
Blood Urea (mg/dl)		32.0±9.7	34.8±10.6	-	0.201
Serum Creatinine (mg/dl)		0.88±0.27	0.8±0.3	-	0.104
Alanine Aminotransferase (U/L)		37.8 (29.7-55.0)	36.3 (27.4-48.3)	-	0.532
Aspartate Transaminase (U/L)		44.3 (29.5-61.8)	48.3 (30.8-59.7)	-	0.689
Serum Bilirubin (mg/dl)		1.6 (1.3-2.1)	1.6 (0.9-2.2)	-	0.759
Hospital Stays (days)		8.0 (5.0-11.0)	6.0 (4.0-8.0)	-	0.024

No demographic or laboratory parameters demonstrated a significant association between children with and without respiratory distress, table 2.

Table 2: Association of Respiratory Distress with Various Demographic, Clinical, and Laboratory Parameters (N=120)

Characteristics		Respiratory Distress		OR (95% CI)	p-value
		Yes (n=22)	No (n=98)		
Gender	Male	11 (50.0%)	69 (70.4%)	0.42 (0.16-1.08)	0.067
	Female	11 (50.0%)	69 (70.4%)	Reference	
Age (Years)	1-5	6 (27.3%)	39 (39.8%)	Reference	0.273
	6-12	16 (72.7%)	59 (60.2%)	1.76 (0.63-4.90)	
Residence	Rural	12 (54.5%)	62 (63.3%)	0.70 (0.27-1.77)	0.447
	Urban	10 (45.5%)	36 (36.7%)	Reference	
Malnutrition		9 (40.9%)	50 (51.0%)	0.66 (0.26-1.70)	0.391
Malarial Agent	*P. vivax*	15 (68.2%)	69 (70.4%)	Reference	0.215
	P. falciparum	7 (31.8%)	20 (20.4%)	1.61 (0.58-4.49)	
	P. falciparum + P. vivax	-	9 (9.2%)	0.24 (0.01-4.27)	
Hemoglobin (g/dl)		6.8 (6.4-9.5)	6.5 (6.2-8.2)	-	0.229
Hematocrit (%)		32.7±6.7	33.9±6.3	-	0.433
Platelets (109/L)		120.5 (63.0-170.5)	118.5 (70.3-169.3)	-	0.962
Blood Glucose (mg/dl)		83.7±11.4	85.2±14.8	-	0.658
Blood Urea (mg/dl)		38.1±10.8	34.2±10.2	-	0.066
Serum Creatinine (mg/dl)		0.9±0.2	0.8±0.3	-	0.352
Alanine Aminotransferase (U/L)		40.9 (32.8-57.5)	36.3 (27.8-47.1)	-	0.160
Aspartate Transaminase (U/L)		45.7 (33.3-60.6)	46.5 (29.9-59.9)	-	0.908
Serum Bilirubin (mg/dl)		1.6 (0.9-2.2)	1.6 (1.1-2.1)	-	0.984
Hospital Stays (days)		8.0 (5.0-10.0)	6.5 (4.0-9.0)	-	0.521

Details about the association between anemia and demographic, clinical, and laboratory parameters, table 3.

Table 3: Association of Severe Anemia with Various Demographic, Clinical, and Laboratory Parameters (N=120)

Characteristics		Severe Anemia		OR (95% CI)	p-value
		Yes (n=82)	No (n=38)		
Gender	Male	55 (67.1%)	25 (65.8%)	1.06 (0.48-2.34)	0.890
	Female	27 (32.9%)	13 (34.2%)	Reference	

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Age (Years)	1-5	29 (35.4%)	16 (42.1%)	Reference	0.478
	6-12	53 (64.6%)	22 (57.9%)	1.31 (0.60-2.85)	
Residence	Rural	49 (59.8%)	25 (65.8%)	0.78 (0.35-1.72)	0.527
	Urban	33 (40.2%)	13 (34.2%)	Reference	
Malnutrition		36 (43.9%)	23 (60.5%)	0.51 (0.24-1.09)	0.090
Malarial Agent	*P. vivax*	55 (67.1%)	29 (76.3%)	Reference	0.207
	P. falciparum	22 (26.8%)	5 (13.2%)	2.32 (0.81-6.68)	
	P. falciparum + P. vivax	5 (6.1%)	4 (10.5%)	0.66 (0.17-2.60)	
Hemoglobin (g/dl)		6.4 (6.1-6.8)	9.5 (8.6-10.0)	-	<0.001
Hematocrit (%)		34.0±6.0	32.9±7.2	-	0.390
Platelets (109/L)		119.5 (68.0-170.8)	112.5 (70.6-162.3)	-	0.716
Blood Glucose (mg/dl)		86.3±14.0	82.0±14.3	-	0.120
Blood Urea (mg/dl)		33.1±9.9	36.2±11.3	-	0.130
Serum Creatinine (mg/dl)		0.8±0.3	0.8±0.2	-	0.940
Alanine Aminotransferase (U/L)		37.7 (28.8-48.3)	36.5 (25.0-50.5)	-	0.771
Aspartate Transaminase (U/L)		44.4 (29.1-61.8)	49.4 (34.9-56.6)	-	0.531
Serum Bilirubin (mg/dl)		1.5 (0.9-2.1)	1.9 (1.5-2.7)	-	0.009
Hospital Stays (days)		7.0 (4.0-9.0)	7.0 (4.8-8.3)	-	0.880

Details about the evaluation of impaired consciousness about demographic, clinical, and laboratory parameters, and no significant associations were found, table 4.

Table 4: Association of Impaired Consciousness with Study Variables in Children with Severe Malaria (N=120)

Characteristics		Impaired Consciousness		OR (95% CI)	p-value
		Yes (n=50)	No (n=70)		
Gender	Male	33 (66.0%)	47 (67.1%)	0.95 (0.45-2.03)	0.897
	Female	17 (34.0%)	23 (32.9%)	Reference	
Age (Years)	1-5	18 (36.0%)	27 (38.6%)	Reference	0.774
	6-12	32 (64.0%)	43 (61.4%)	1.12 (0.54-2.32)	
Residence	Rural	32 (64.0%)	42 (60.0%)	1.18 (0.57-2.46)	0.657
	Urban	18 (36.0%)	28 (40.0%)	Reference	
Malnutrition		30 (60.0%)	29 (41.4%)	2.07 (1.02-4.22)	0.045
Malarial Agent	*P. vivax*	32 (64.0%)	52 (74.3%)	Reference	0.071
	P. falciparum	16 (32.0%)	11 (15.7%)	2.37 (0.99-5.67)	
	P. falciparum + P. vivax	2 (4.0%)	7 (10.0%)	0.46 (0.09-2.27)	
Hemoglobin (g/dl)		6.4 (6.1-8.2)	6.8 (6.3-8.4)	-	0.025
Hematocrit (%)		33.0±6.5	34.1±6.3	-	0.313
Platelets (109/L)		132.0 (71.0-169.3)	111.0 (68.0-166.3)	-	0.270
Blood Glucose (mg/dl)		82.6±15.3	86.6±13.2	-	0.130
Blood Urea (mg/dl)		33.7±9.4	34.3±11.1	-	0.767
Serum Creatinine (mg/dl)		0.8±0.3	0.8±0.3	-	0.921
Alanine Aminotransferase (U/L)		33.9 (26.2-45.8)	39.9 (30.5-61.0)	-	0.070
Aspartate Transaminase (U/L)		46.2 (27.6-61.0)	48.0 (31.2-59.7)	-	0.960
Serum Bilirubin (mg/dl)		1.5 (1.1-2.1)	1.6 (1.0-2.1)	-	0.616
Hospital Stays (days)		7.0 (4.0-8.0)	7.0 (4.8-9.0)	-	0.365

DISCUSSION

It was found that 66.7% children with severe malaria were male, while the mean age was 6.99±3.51 years. These findings align closely with those reported by Murmu *et al.*, who similarly found a male predominance and a high incidence among younger children (1–5 years, 40.29%) [14]. This demographic similarity highlights the vulnerability of relatively younger children, particularly males, possibly reflecting gender-based disparities in exposure or healthcare-seeking behaviors in South Asian contexts [15]. Malnutrition was identified in nearly half of the children (49.2%) in the current study. Nutritional status is crucial in influencing susceptibility and severity of infections, particularly malaria [16]. The high rate of malnutrition observed is reflective of the socioeconomic status and healthcare infrastructure prevalent in rural South Punjab, similar to Chiabi *et al.*, who documented malnutrition as a significant risk factor affecting clinical outcomes in severe malaria cases in Cameroon [17]. Data from Northeast Ethiopia is also consistent with the present findings, where Debash et al. reported both malaria and undernutrition as a common entity among children [18]. *P. vivax* infection accounted for 70.0% of cases. Global literature exhibits *P. falciparum* to be the dominant species associated with severe malaria. Murmu *et al.* reported 80.5% *P. falciparum* involvement, reinforcing the pathogenic severity of this species [14]. Contemporary regional data by Babar *et al.* and Gehlawat *et al.* have shown increasingly recognized *P. vivax* as a significant contributor to severe malaria [19, 20]. The most common clinical presentations were severe anemia, impaired consciousness, seizures, and respiratory distress, observed in 68.3%, 41.7%, 25.0%, and 18.3%, respectively. Murmu *et al.* documented altered sensorium, seizures, and jaundice as common presentations [14]. In this study, 41.7% exhibited impaired consciousness compared to studies from Murmu *et al.* (50%) and Voloc *et al.* (75.4% cerebral malaria) [14, 21]. The variation in clinical manifestations of severe malaria in the pediatric population could be attributed to regional differences in parasite virulence, host genetic factors, or timing of healthcare-seeking behavior, which might influence the early diagnosis and thus mitigate severe neurological complications. Seizures and respiratory distress are significantly associated with prolonged hospital stays to Kalinga *et al.*, where respiratory distress and neurological manifestations were predictors of prolonged hospitalization [22]. Namayanja *et al.* reported acidosis as the

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major determinant of hospital stay, highlighting that variability in clinical presentations influences hospital resource utilization and management strategies [23]. Clinically significant hypoglycemia (<40 mg/dL) was not found in this study, with the mean blood glucose levels maintained above the critical range (84.93±14.17 mg/dL). This contrasts with Manning *et al.*, who documented higher prevalence rates of hypoglycemia in African children [24]. Variations in nutritional status, early glucose monitoring, or protocol-driven clinical management differences may explain these discrepancies. Previous study highlighted that prompt diagnosis and immediate artesunate administration are crucial in preventing metabolic complications, a practice possibly adhered to rigorously in the present study context [25]. Regarding laboratory parameters, not much significant association was found between platelet count, serum creatinine, alanine aminotransferase, or aspartate transaminase and severe clinical manifestations. This contrasts with Murmu *et al.* and Voloc *et al.*, where thrombocytopenia and hepatic dysfunction correlated significantly with severe outcomes [14, 21]. The relatively mild derangement in laboratory parameters herein might reflect early presentation and prompt management, reducing severe organ dysfunction. Genetic variability in host responses or differences in parasite strains could contribute to these variations [26]. Although global trends identify *P. falciparum* as the main cause of severe malaria, this study indicated a substantial burden of severe disease due to *P. vivax* [27]. While rigorous diagnostic protocols were followed, the possibility of species misidentification cannot be entirely excluded due to morphological overlaps, especially in mixed or low-density infections. The absence of mortality in the current study contrasts markedly with global reports. Namayanja *et al*. observed a mortality rate of 6.3%, Chiabi *et al.*, 3.8%, and Voloc et al. reported a considerably higher rate of 18.6% [17, 23]. The zero-mortality observed herein could reflect early hospital presentation, prompt and appropriate treatment protocols involving intravenous artesunate, and effective supportive care, including intensive monitoring and management practices. Conversely, higher mortality rates in other studies might reflect late healthcare-seeking behavior, delayed initiation of antimalarial treatment, or limited availability of critical care facilities. The clinical implications of the findings of this study are substantial. The recognition of *P. vivax* as a significant cause of severe malaria emphasizes the need for revised public health guidelines and awareness campaigns in South Punjab. High malnutrition rates underline the necessity of addressing underlying nutritional deficiencies through integrated pediatric care and community interventions. The study's single-center design limits generalizability to broader populations. Long-term outcomes post-discharge were not evaluated, precluding insights into chronic sequelae such as neurological deficits or recurrent infections. Genetic factors influencing host susceptibility were not assessed, which could provide valuable insights into disease severity variation.

This study was limited by its single-center design and non-probability sampling technique, which may restrict the generalizability of findings to other endemic regions. The absence of long-term follow-up prevented assessment of post-discharge complications or neurological sequelae. Additionally, molecular confirmation of parasite species was not performed, which may limit precise species differentiation. Future multicenter, longitudinal studies incorporating molecular diagnostics and long-term outcome assessment are recommended to better understand disease patterns and optimize pediatric malaria management strategies.

CONCLUSIONS

Severe malaria in children most commonly presents with severe anemia, impaired consciousness, and seizures, with Plasmodium vivax as the predominant causative organism. All enrolled children recovered and were discharged without mortality, indicating favorable short-term outcomes under the current management protocol.

Authors' Contribution

Conceptualization: SI,
Methodology: SI, SAL, AA, IJ, AU
Formal analysis: SI, AA, IJ, AU
Writing and Drafting: SI, MSA
Review and Editing: SI, MSA, SAL, AA, IJ, AU

All authors approved the final manuscript and take responsibility for the integrity of the work

Conflicts of Interest

All the authors declare no conflict of interest.

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