Ro J Pediatr. 2026;75(1)
DOI: 10.37897/RJP.2026.1.1

Exploring the clinical and microbiological landscape of pediatric infective endocarditis: a 3-year single-center review

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ABSTRACT

Background. Infective endocarditis is an infection of the heart's endothelial surfaces. Despite being more prevalent in adults, its incidence is increasing in the pediatric population. Congenital heart disease remains the most important predisposing factor to the infection. In our locality, the characteristics, management, and outcomes of infective endocarditis are not well documented and therefore we aimed to provide a descriptive local overview regarding different aspects of the condition.

Methods. A retrospective single-center observational study was conducted using tertiary referral hospital records from January 2022 to December 2024. The data of patients under 18 years diagnosed with infective endocarditis were reviewed. Variables such as demographics, geographic location, clinical presentation, and microbiological data were evaluated. Two separate sets of blood cultures were obtained from each patient. Antimicrobial susceptibility testing was performed using disk diffusion, and results were interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines. Treatment plans and outcomes were also described.

Results. A total of 15 patients younger than 18 years were diagnosed with infective endocarditis during the study period. Of these, 66.7% were female, and the mean age at diagnosis was 7.6 years. Congenital heart disease was present in 80% of patients, with ventricular septal defect as the most common type (40%). Blood cultures were positive in 10 out of 15 patients (66.7%), while 5 of 15 patients (33.3%) had culture-negative results. The most commonly encountered pathogen was *Staphylococcus aureus* (33.3%). Echocardiography demonstrated vegetations in 73.3% of patients, most commonly on the ventricular septal defect. Most patients received ceftriaxone plus vancomycin as empiric therapy. The mortality rate was estimated to be around 6.7%.

Conclusion. Infective endocarditis is a rare condition that predominantly affects children with congenital heart disease. Despite the study's limitations, our findings are broadly consistent with published reports. Our findings revealed that two-thirds of patients had positive culture, and *Staphylococcus aureus* was the most frequently isolated organism. At our center, careful antibiotic use is recommended to limit the emergence of resistant strains, and highlight the needs of larger population studies.

Keywords: infective endocarditis, congenital heart disease, pediatrics, cardiology

Abbreviations

CHD	– congenital heart disease	PA	– pulmonary atresia	R-L shunt	– right-to-left shunt
ECHO	– echocardiography	PABs	– pulmonary artery branches	TOF	– tetralogy of Fallot
IE	– infective endocarditis	PDA	– patent ductus arteriosus	VSD	– ventricular septal defect
MAPCAs	– major aortopulmonary collateral arteries				

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Article History:
Received: 30 November 2025
Accepted: 16 March 2025

INTRODUCTION

Infective endocarditis (IE) is a rare microbial infection with inflammatory involvement of the endocardium, the valves (native or prosthetic), and other intracardiac structures. IE is far more prevalent in older individuals than in children [1]. However, the number of pediatric cases has increased in recent years [2]. Globally, the incidence of pediatric IE has been reported to be approximately 0.43-0.69 per 100,000 children per year [3].

More than 350 years ago, IE was first described by the Italian physician Giovanni Battista Morgagni. Subsequent contributions to the understanding of IE were made by physicians such as William Osler and Emanuel Libman [4]. Historically, rheumatic heart disease was the most common etiologic factor associated with pediatric IE. In recent years, advances in diagnostic and therapeutic procedures have improved survival among children with congenital heart disease (CHD), which is now recognized as the most common predisposing factor for IE [1,2]. In some studies, up to 50%–70% of IE cases have been reported in patients with CHD [3,5]. Causative pathogens vary according to underlying conditions and age group. Viridans group streptococci have been reported as the most common organisms, followed by Staphylococcus aureus [6]. Diagnosis is generally based on the modified Duke criteria [7], although diagnosis can be more challenging in children because manifestations are often nonspecific and may be confused with more common conditions [1,3]. Empiric antibiotic therapy is typically initiated in suspected IE before organism identification, with consideration of factors such as prior antibiotic exposure, whether the involved valve is native or prosthetic, and whether infection is community- or hospital-acquired [8,9]. Blood culture remains the most useful diagnostic test for IE and for pathogen identification. Culture-negative IE has been frequently reported and may be partly related to antibiotic use before blood culture collection and to limited capacity to detect fastidious or intracellular organisms, particularly in developing countries [8,10].

Despite advances in diagnostic methods and treatment regimens, mortality and complication-related sequelae remain relatively high [11]. Children with IE may develop complications such as heart failure, systemic embolization, and renal failure, with reported mortality rates ranging from 1% to 5%, and higher rates among those with complications [3,12]. Certain microorganisms, including Staphylococcus aureus, are associated with higher mortality. However, the presence of CHD does not necessarily imply a worse prognosis in children with IE [3]. Recurrence rates are estimated at approximately 5%, with risk factors related to host characteristics, antibiotic treatment, and surgical outcomes [3]. Due to limited published data on pediatric IE in the Middle East in general, and in Iraq in particular, this study aimed to describe patient demographics, clinical presentation, blood culture results, causative organisms, antimicrobial susceptibility patterns, management approaches, and the association with CHD.

METHODS

Study design

A descriptive retrospective study was conducted using the databases of the University of Basrah, College of Medicine, and Basrah Specialized Cardiac Hospital (a tertiary referral hospital in Basrah, Iraq) between January 2022 and December 2024. Medical records of patients younger than 18 years with a definite or possible diagnosis of infective endocarditis were reviewed. Collected data included demographics, underlying medical conditions, medical history, presenting complaints, echocardiographic and microbiological findings, treatment plans, procedures, and outcomes.

Cases were classified as definite or possible infective endocarditis based on the modified Duke criteria. Major criteria included positive blood cultures with typical microorganisms and echocardiographic evidence of endocardial involvement. Minor criteria included predisposing cardiac conditions, fever ≥38°C, vascular phenomena, immunologic phenomena, and microbiological evidence not fulfilling major criteria [7,13].

For microbiological assessment, at least two separate blood culture sets were obtained from each patient. A total of 30 blood culture sets were collected, with a median of 2 sets per patient. Each set consisted of two bottles obtained from separate venipuncture sites. Blood cultures were collected before initiation of antibiotic therapy whenever clinically possible. Culture-negative infective endocarditis was defined as the absence of microbial growth after 5 days of incubation, in accordance with the laboratory's routine protocol; extended incubation and additional testing for fastidious organisms were not available. Antimicrobial susceptibility testing (AST) was performed using the disk diffusion method and interpreted according to Clinical and Laboratory Standards Institute (CLSI) guidelines in use at the time of testing (2022–2023). Prior antibiotic exposure within 7 days before admission was documented when available.

Statistical analysis

Statistical analysis were performed using SPSS version 22.0 for Windows (SPSS Inc.; Chicago, IL, USA). Categorical variables were presented as counts and percentage, and continuous variables

were summarized as mean ± standard deviation. No inferential statistical tests were performed because the study was purely descriptive.

Ethical approval

The study was approved by the Ethics Committee of the University of Basrah, College of Medicine, and by the administration of Basrah Specialized Cardiac Center (approval date: 21 November 2024). Permission to access archived hospital records was granted by the hospital administration. Because this was a retrospective review of existing medical records, the requirement for written informed consent from patients' families was waived by the ethics committee. Verbal consent was obtained from families who were contacted to clarify missing information or obtain additional clinical details. All data were handled confidentially and anonymized to protect patient privacy.

RESULTS

During the study period, a total of 37 cases of infective endocarditis (IE) were reported and referred to Basrah Specialized Cardiac Hospital. However, 19 cases involved patients older than 18 years and were therefore excluded. In addition, 3 cases were excluded because they did not meet the modified Duke criteria required for a diagnosis of definite or possible IE (Table 1). According to the modified Duke criteria, 11 patients (73.3%) met criteria for definite infective endocarditis, while 4 patients (26.7%) were classified as possible infective endocarditis. Among definite cases, echocardiographic evidence of vegetation was present in all 11 patients, and 9 of them had positive blood cultures fulfilling major microbiological criteria. In the possible IE group, diagnosis was based on a combination of minor criteria, including persistent fever and predisposing congenital heart disease, along with supportive echocardiographic findings, without meeting full major criteria (Table 2).

Records were thoroughly reviewed through hospital files and, when needed, direct contact with patients' families. The study population included 5 males (33.3%) and 10 females (66.7%). The mean age at diagnosis was 7.6 years, with the youngest and oldest being 1 year and 16 years respectively. Patients were subdivided into four age categories: <2 years, 2–6 years, 7–12 years, and 13–18 years. Most cases (53.3%) occurred in the 7-12-year age group, while 20% were in the 2-6 year range, and 13.3% were in each of the 13-18-year and <2-year categories. Regarding geographic distribution, the highest number of cases were reported from the northern Basrah and Maysan (26.7% each), followed by central Basrah (20%). Western Basrah accounted for 13.3%, while southern Basrah and Dhi Qar governorates reported the fewest cases (6.7% each) (Table 1).

TABLE 1. Demographics and geographical distribution of patients

	Frequency	Percentage (%)
Gender		
Male	5	33.3
Female	10	66.7
Age (years)	Mean = 7.6	SD = 4.48
<2	2	13.3
2-6	3	20.0
7-12	8	53.3
13-18	2	13.3
Location		
Center of Basrah	3	20.0
South of Basrah	1	6.7
North of Basrah	4	26.7
West of Basrah	2	13.3
Maysan	4	26.7
Dhi Qar	1	6.7

SD: Standard deviation

Regarding patients' presenting complaints, a variety of symptoms were reported. Prolonged fever was the most common symptom, observed in 80.0% (n = 12) of cases, followed by shortness of breath (46.7%). Other symptoms were reported less frequently, either alone or in association with the main complaints (Table 3).

A substantial proportion of patients (80.0%) had pre-existing congenital heart disease (CHD), while 20.0% (n = 3) had no underlying congenital cardiac anomalies, although 2 of them reported having valve prolapse. Among those with CHD, ventricular septal defect (VSD) was the most prevalent condition, present in 40% of cases. Tetralogy of Fallot (TOF) and patent ductus arteriosus (PDA) were identified as single etiologies in 13.3% and 6.7% of cases, respectively. Some patients had mixed and complex forms of CHD. Pulmonary atresia with VSD (PA/VSD) was present in 13.3% of cases. One patient (6.7%) had complex CHD including PA/VSD, a right-to-left shunt (R–L shunt), a tortuous right-to-left shunt, nonconfluent pulmonary artery branches (PABs), and major aortopulmonary collateral arteries (MAPCAs) (Table 4). Six of 15 patients had previous surgical interventions.

Transthoracic echocardiography demonstrated vegetations in 11 patients (73.3%). The most common site was the ventricular septal defect margin (n = 5), followed by the tricuspid valve (n = 3), mitral valve (n = 2), and pulmonary valve/right ventricular outflow tract conduit (n = 1). Vegetation size ranged from 4 to 12 mm (median, 7 mm). Moderate to severe

TABLE 2. Classification according to modified Duke criteria

Classification		Frequency	Percentage
Definite IE		11	73.3%
Possible IE		4	26.7%
Patient ID	**Major criteria**	**Minor criteria**	**Diagnosis**
P1	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD Pyrexia > 38°C	Definite IE
P2	Positive echocardiographic findings PLUS positive blood culture		Definite IE
P3	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD	Definite IE
P4	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD Pyrexia > 38°C	Definite IE
P5	Positive echocardiographic findings PLUS positive blood culture	Pyrexia > 38°C	Definite IE
P6	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD	Definite IE
P7	Positive echocardiographic findings PLUS positive blood culture	Pyrexia > 38°C	Definite IE
P8	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD	Definite IE
P9	Positive echocardiographic findings PLUS positive blood culture	Preexisting CHD	Definite IE
P10	Positive echocardiographic findings	Preexisting CHD Pyrexia > 38°C Glomerulonephritis	Definite IE
P11	Positive echocardiographic findings	Preexisting CHD Pyrexia > 38°C Splenic infraction	Definite IE
P12	Positive blood culture	Preexisting CHD	Possible IE
P13		Preexisting CHD Pyrexia > 38°C Valvular regurgitation	Possible IE
P14		Preexisting CHD Pyrexia > 38°C Valvular regurgitation	Possible IE
P15		Preexisting CHD Pyrexia > 38°C Pericardial effusion	Possible IE

valvular regurgitation was observed in 4 patients (26.7%). No intracardiac abscesses were documented. One patient developed evidence of systemic embolization. None of the cases involved prosthetic valves; however, 6 patients had prior surgical shunts or repairs.

As an essential step for diagnosis, blood cultures were obtained for all patients. Cultures were positive in 66.7% (n = 10), while 33.3% (n = 5) were culture-negative. Among culture-positive cases, the most frequently isolated organism was *Staphylococcus aureus* (33.3%, n =5), followed by *Streptococcus agalactiae* (13.3%, n = 2). Other identified pathogens included *Staphylococcus epidermidis*, *Staphylococcus haemolyticus*, and *Burkholderia cepacia,* each accounting for 6.7% of cases (Table 5). Among the 10 positive isolates, 8/10 (80%) demonstrated resistance to third-generation cephalosporins, including ceftriaxone. All *Staphylococcus aureus* isolates were susceptible to vancomycin. Methicillin-resistance *Staphylococcus aureus* (MRSA), defined as resistance to methicillin (detected by oxacillin or cefoxitin testing), was identified in 2 of the 5 *S. aureus* isolates. No vancomycin-resistant organisms were detected.

Most patients received empiric dual antibiotic therapy, most commonly ceftriaxone plus vancomycin (46.7%), followed by vancomycin plus meropenem (20.0%). Two patients (13.3%) received triple therapy with ceftriaxone, vancomycin, and rifampin. One patient (6.7%) received empiric quadruple therapy. Antibiotic regimens were subsequently tailored to one or two agents based on culture and susceptibility results.

TABLE 3. Clinical presentation and outcome of patients

	Frequency	Percentage (%)
Clinical presentation		
Fever	12	80.0
Shortness of breath	7	46.7
Cough	1	6.7
Chest pain	3	20.0
Poor appetite	3	20.0
Fatigue	1	6.7
Cyanosis	3	20.0
Vomiting	1	6.7
Dizziness	2	13.3
Headache	1	6.7
Abdominal pain	2	13.3
Abdominal distension	1	6.7
Sweating	2	13.3
Outcome		
Improved	12	80.0
Referred for surgery in another hospital	2	13.3
Dead	1	6.7

TABLE 4. Types of underlying congenital heart disease

Presence of CHD	Frequency	Percentage (%)
VSD	6	40.0
TOF	2	13.3
PA / VSD	2	13.3
PDA	1	6.7
Complex CHD	1	6.7
No CHD (Native valves)	3	20.0

CHD: Congenital heart disease, VSD: Ventricular septal defect, TOF: Tetralogy of Falot, PDA: Patent ductus arteriosus, PA: Pulmonary atresia

TABLE 5. Blood culture results among the study patients

	Frequency	Percentage (%)
Culture		
Positive	10	66.7
Negative	5	33.3
Positive culture results		
Staphylococcus aureus	5	33.3
Streptococcus agalactiae	2	13.3
Staphylococcus epidermidis	1	6.7
Staphylococcus haemolyticus	1	6.7
Burkholderia cepacia	1	6.7

The median duration of hospitalization was 23.5 days (18-28 days). The shortest hospital stay was 5 days and the longest was 40 days. The patient who died within 24 hours of admission was excluded from the length-of-stay analysis. Regarding in-hospital outcomes, 80.0% (n = 12) improved clinically and were discharged. One patient (6.7%) died within 1 day of hospitalization, and 2 patients (13.3%) were referred to another hospital for surgical intervention. One patient (6.7%) experienced recurrence of infective endocarditis two years after the initial diagnosis. Follow-up data were obtained through hospital medical records and direct family contact. Recurrence was confirmed by fulfillment of the modified Duke criteria, with repeat positive blood cultures and echocardiographic evidence of vegetation (Table 3).

DISCUSSION

During the early antibiotic era, the epidemiology of IE was similar in both high- and low-income countries [14,15]. limited research output from developing countries and the predominance of single-center reports make contemporary comparisons difficult. in developing countries report only a few

TABLE 6. Antibiotic susceptibility profile of bacterial isolates

	Number of isolates	Ampicillin	Ceftriaxone	Vancomycin	Clindamycin	Gentamicin	Meropenem	Linezolid	Methicillin	Imipenem	Trimethoprim-sulfamethoxazole
Staphylococcus aureus	5	R	R	S	S	R	S	S	2/5 R	NT	NT
Streptococcus agalactiae	2	R	S	S	R	S	S	S	NT	NT	NT
Staphylococcus epidermidis	1	R	R	S	S	R	S	NT	S	NT	NT
Staphylococcus haemolyticus	1	R	R	S	S	NT	R	NT	S	NT	NT
Burkholderia cepacia	1	R	R	S	NT	R	NT	S	NT	R	R

*R: Resistant, S: Susceptible, NT: Not tested

cases, accounting for <0.5% of total cardiology admissions [16]. Over eight decades of microbiological data in pediatric IE, two organism groups have predominated: viridans group streptococci and Staphylococcus aureus. The relative predominance of one over the other has varied over time. Because congenital heart disease (CHD) is the most common predisposing factor for IE, trends in incidence and microbiologic etiology have also changed with evolving management strategies. In the presurgical era, viridans group streptococci were the predominant pathogens, accounting for 45%–65% of cases, whereas Staphylococcus aureus accounted for approximately 20%. In the early surgical era, the proportion of viridans group streptococci declined, with a corresponding increase in Staphylococcus aureus cases [17]. In the era of transcatheter interventions, incidence has been reported to be higher. Overall, these observations suggest that the shift toward Staphylococcus aureus may be related to healthcare exposure and invasive interventions, rather than exclusively community-acquired infection.

Given the small sample size (n = 15) and the retrospective single-center design, this study represents a descriptive review of the local epidemiology of pediatric IE over a three-year period. Our data showed a higher proportion of female patients (2:1), which is consistent with a study from the American University of Beirut Medical Center reporting 59% female cases [18]. Nevertheless, differences in sample size, study design, and time period should be considered when comparing results. The mean age at diagnosis was 7.6 years, which is consistent with prior reports, including Rashed et al. (2023) and Liew et al. [5,19]. Most patients in our cohort were 7-12 years of age, which contrasts with studies from nearby countries, such as the report from Al Zahra Hospital in Isfahan, Iran (Ahmadi and Daryushi, 2014), where most cases occurred in children younger than 2 years [20]. This difference may be related to age-specific exposures in school-aged children (7-12 years), including increased exposure to infections and microorganisms, as well as dental procedures and poor oral hygiene, particularly in the setting of underlying CHD [10].

When exploring geographical distribution, the highest number of cases originated from northern Basrah and Maysan governorate, which are mostly considered rural areas. Lower socioeconomic status and living conditions in these regions might be a contributing factor. Despite the limited availability of data and information regarding the studied population, there are some studies that support the hypothesis of a higher incidence of IE in low socioeconomic backgrounds [21]. The occurrence of IE in patients with CHD as the most common predisposing factor was highlighted in almost all clinical studies. This finding is consistent with our results showing 12 out of 15 patients (80%) were previously diagnosed with CHD. The most prevalent condition was VSD (40%), followed by TOF (13.3%). Three patients 20% had no CHD; however, two patients had valve prolapse and only one had no reported structural cardiac abnormality.

Several studies similarly report VSD as the most common underlying condition [10,12,20], whereas others report TOF as the most common lesion [18,22-24]. The reason for this variation might lie behind TOF being less survivable than VSD without surgical intervention and the high cost of surgical procedures outside the country as they're not routinely performed locally [6]. In addition, late presentation of VSD in some cases may contribute. The advancement of CHD treatment with surgical techniques is also a contributing factor for IE infection as 40% (n = 6) of patients in this study had previous procedures, which is consistent with reports from Yale School of Medicine [17] and supports the need for careful postoperative monitoring.

Among presenting symptoms, prolonged fever was the most common complaint, occurring in 80% of patients, with or without accompanying symptoms. The wide range of conditions that are present with fever has made it a lot more challenging for early detection of IE cases and therefore a high index of suspicion and appropriate investigations are essential for accurate diagnosis, as emphasized in multiple studies [1,3].

The median length of hospitalization was 23.5 days (median equals the mean), with the shortest period being 5 days and the longest being 40 days (IQR 18-28 days). One patient (6.7%) died within one day of hospitalization which was not included in the analysis. This somehow corresponds with the guidelines which indicate that patients might need 4-6 weeks of intravenous antibiotics treatment for proper eradication [25]. The results were higher than the study reported by the Department of Cardiology at Children's Hospital Boston, Harvard Medical School, where the mean length of stay was 10 days [26]. This long hospitalization might have a psychological impact on the patients and their families' well-being. The long term effects of this on the efficacy of treatment and on the morbidity and mortality made it necessary for researchers to explore new treatment methods that shortens the length of hospital stay such as the use of partial oral treatment (POET) which showed reduction in the median of hospitalization to 8 days with an associated lower rate of relapses with no change in mortality [27]. This could be tried with older children to minimize the psychological effects and for better outcomes.

Regarding the results of blood cultures, which are the most crucial step for a definitive diagnosis

and appropriate treatment plan. In our cohort, blood cultures were positive in 66.7% of cases. Similar proportions have been reported in several studies, with culture-positive cases exceeding culture-negative cases [5,18–20]. In contrast, some studies have reported higher rates of culture-negative IE [8]. In our cohort, 33.3% (n=5) were culture-negative. Culture-negative results are commonly attributed to antibiotic exposure before blood culture collection, which can lead to false-negative cultures. In our setting, results may also be influenced by the routine laboratory protocol of five days of incubation, as extended incubation or additional testing for fastidious organisms are not routinely performed in our locality. Therefore, these limitations may affect the observed proportion culture-negative IE cases.

Microbiologic analysis of culture-positive cases identified five bacterial species, with *Staphylococcus aureus* being the most common pathogen encountered and predominating the list. Although, infections with *Staphylococcus aureus* and the viridans group of streptococcus species had run side by side with one predominating over the other at different times and in different regions, there was no evidence of the viridans group of streptococci among our samples.

Similar findings were reported at the Jakaya Kikwete Cardiac Institute in Tanzania, where Staphylococcus aureus was the predominant isolate [8]. This differs from studies reporting predominance of viridans group streptococci [5,19]. One possible explanation is advances in CHD management, as the increasing incidence of *Staphylococcus aureus* has been linked to surgical interventions and healthcare-associated acquisition, as noted above. In contrast, viridans group streptococci are typically community-acquired and are more often associated with native-valve endocarditis in patients with rheumatic or congenital heart disease [14].

Antimicrobial susceptibility testing (AST) results were available for 10 isolates. Overall, 8/10 isolates demonstrated resistance to ceftriaxone, including 5/5 *Staphylococcus aureus,* 1/1 *Staphylococcus epidermidis,* 1/1 *Staphylococcus haemolyticus* and 1/1 *Burkholderia cepacia.* All isolates (10/10) remained susceptible to vancomycin, as there was no detected resistance towards it. These findings support the need for antimicrobial stewardship programs to limit inappropriate broad-spectrum antibiotic use. The high resistance to third-generation cephalosporins suggests that empiric use of these agents should be reconsidered in our setting.

With regards to the outcome of patients, most of them (80%) showed improvement. The mortality rate was 6.7%, which is within the range reported globally (5%–20%) [5,6,20]. One patient (6.7%) experienced recurrence two years after initial improvement.

CONCLUSION

Our study concludes that infective endocarditis predominantly affects children with CHD and may substantially impact quality of life because of prolonged hospitalization and clinical fragility, particularly among those who have undergone surgical interventions. *Staphylococcus aureus* was the most frequently isolated organism. Given the high antimicrobial resistance observed, we recommend implementing structured antimicrobial stewardship programs at our center and locally to limit unnecessary broad-spectrum antibiotic use.

Despite its limitations, this study provides insight into disease characteristics, microbiologic patterns, and treatment practices in a resource-limited setting. Future studies should include larger, multicenter cohorts with improved data documentation and long-term follow-up.

Conflict of interest

The authors declare no conflict of interest.

Financial support

The authors declare this research received no specific grant from any funding agency in the public, commercial, or not-for-profit sectors.

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