ORIGINAL ARTICLE

Candidemia in cancer: A retrospective analysis of risk profiles, treatment approaches and outcomes in critical and non-critical care settings

Seemal Aslam, Madiha Ghulam, Ali Anjum, Hamayal Masood

Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore Pakistan

ABSTRACT

Background: Candidemia is a significant contributor to morbidity and mortality in cancer patients. This study aimed to compare the clinical characteristics, species distribution, risk factors, complications, and outcomes of candidemia between intensive care unit (ICU) and non-ICU settings

Material and Methods: This retrospective study was conducted at a tertiary care oncology hospital in Lahore over a three-year period (January 2020–December 2022). A total of 175 cancer patients with blood culture–confirmed candidemia were included. Patients were stratified into ICU and non-ICU groups to compare demographic characteristics, species distribution, risk factors, complications, and clinical outcomes.

Results: *Candida tropicalis* (40.6%) was the most frequently isolated species, followed by *Candida albicans* (34.3%). Common risk factors included recent antibiotic use (98.3%) and central venous catheterization (72%). ICU patients were significantly older (median age 42 vs. 26 years, $p = 0.007$) and experienced higher in-hospital mortality (77.3% vs. 43.1%, $p < 0.001$). No particular *Candida* species was associated with increased mortality. Recent chemotherapy within 14 days was significantly linked to higher mortality ($p = 0.045$).

Conclusion: Candidemia in cancer patients is associated with high mortality, particularly among ICU admissions. The predominance of non-albicans species and adverse outcomes in critically ill patients emphasize the need for early recognition and timely, targeted antifungal therapy.

Keywords: Antifungal therapy, Cancer, Candidemia, Intensive care unit, Mortality, Non-albicans *Candida*

BACKGROUND

Candida species are commensal yeasts capable of causing invasive infections with potentially severe clinical consequences. Multiple risk factors contribute to the development of invasive candidiasis, including the presence of central venous catheters (CVC), recent exposure to broad-spectrum antibiotics or antifungal agents, administration of chemotherapy, neutropenia, burns, trauma, gastrointestinal surgical procedures, pancreatitis, and total parenteral nutrition (TPN).[1]

Bloodstream infections caused by *Candida* species can result in a range of serious complications. The severity of illness—particularly in immunocompromised individuals such as oncology patients—plays a critical role in the clinical trajectory of candidemia.

Several studies have reported high mortality rates associated with candidemia. For instance, a previous study from our center reported crude mortality in cancer patient ranging from 46% to 58%; however, this analysis did not differentiate outcomes between ICU and non-ICU patients.[2] Recent data from oncology centers report a rising proportion of non-albicans *Candida* species among cancer-associated candidemia cases, underscoring changing epidemiology and treatment challenges.[3] In addition, large retrospective analyses over the past decade confirm persistently high mortality rates in cancer patients afflicted by *Candida* bloodstream infections, despite antifungal therapy.[4]

These findings highlight the need for studies comparing candidemia characteristics and outcomes among cancer patients in critical care versus non-critical care settings — a gap that the present study seeks to fill.

MATERIAL AND METHODS

This retrospective observational study was conducted jointly by the Microbiology Section and the Department of Internal Medicine at Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC),

Correspondence: Dr. Seemal Aslam, Senior Instructor Infectious Diseases, Department of Internal Medicine, Shaukat Khanum Memorial Cancer Hospital and Research Centre, Lahore Pakistan

Email: seemalaslam@skm.org.pk

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Lahore, a tertiary care oncology facility. The study protocol was reviewed and granted exempt status by the Institutional Review Board (IRB) of Shaukat Khanum Memorial Cancer Hospital and Research Centre (SKMCH&RC), Lahore (IRB Exemption No. EX-21-02-25-01, dated March 28, 2025), as it involved retrospective analysis of anonymized patient data, and authors had no conflict of interest. Since this was a retrospective study, no formal sample size calculation was performed. Instead, all consecutive cancer patients with at least one blood culture positive for *Candida* species during the study period (January 2020–December 2022) were included in the final analysis. Data were extracted from the electronic medical record system and the microbiology laboratory database. A standardized data collection form was used to record demographic characteristics, underlying malignancy type, comorbidities, laboratory-confirmed *Candida* species, antifungal susceptibility results, risk factors (such as CVC use, antibiotic/chemotherapy exposure, neutropenia, TPN, corticosteroid use, recent surgery), treatment details (empirical and definitive antifungal therapy, catheter removal, hemodialysis), and clinical outcomes (candidemia clearance, in-hospital mortality, loss to follow-up). Duplicate cultures from the same infection episode were excluded to avoid overrepresentation. An automated blood culture system (Bact/Alert) was utilized for the detection of bloodstream infections. Samples exhibiting yeast on Gram staining were sub cultured onto solid agar media. Following growth, species identification was performed using matrix-assisted laser desorption/ionization time-of-flight mass spectrometry (MALDI-TOF MS), and antifungal susceptibility testing was carried out using the Vitek-2 system.

All cancer patients, irrespective of age, with at least one blood culture positive for *Candida* species during the study period were included. Duplicate cultures from the same clinical episode were excluded to avoid data redundancy and overrepresentation.

Candidemia was defined as a bloodstream infection confirmed by a positive blood culture for *Candida* species. Hepatosplenic candidiasis was identified when CT, MRI, or ultrasound imaging showed compatible lesions in a patient with documented candidemia. Septic thrombophlebitis was diagnosed when radiological studies demonstrated venous thrombosis with associated inflammatory changes in the setting of candidemia. Endocarditis was confirmed through echocardiographic evidence of vegetations together with a positive blood culture for *Candida* species. Endophthalmitis was recognized based on ophthalmologic findings that indicated a fungal intraocular infection. Pancreatitis was identified based on either a biochemical elevation of pancreatic enzymes to at least three times the upper limit of normal or supportive radiological findings. Prolonged and profound neutropenia was defined as an absolute neutrophil count of less than 0.5×10^9/L persisting for more than seven days. Recent chemotherapy was defined as the administration of cytotoxic agents within the preceding 14 days. Recent corticosteroid use referred to the administration of prednisolone (or an equivalent) at a dose of ≥20 mg per day for a duration exceeding 21 days. Recent surgery was defined as gastrointestinal surgery or invasive procedures involving the gastrointestinal tract performed within the past 14 days. Recent antibiotic exposure was defined as the use of antibiotics for more than 48 hours within the preceding 10 days consistent with prior studies evaluating risk factors for candidemia.[5] Recent antifungal use included either therapeutic or prophylactic administration of antifungal agents within the same timeframe. Concomitant bacteremia was defined as a positive bacterial blood culture within 48 hours before or after the positive *Candida* blood culture. Candidemia clearance was defined as the first documented negative blood culture following initiation of antifungal therapy, with no subsequent positive cultures during the admission. In-hospital mortality was defined as death occurring during the same hospital admission in which candidemia was diagnosed. Clinical improvement was characterized by documented resolution of fever, restoration of hemodynamic stability, and negative follow-up blood cultures prior to discharge. Loss to follow-up referred to patients who left the hospital before mycological clearance could be documented.

Data were entered in Microsoft Excel and analyzed using IBM Statistical Package for the Social Sciences (SPSS) Version 20. Continuous variables, including age and time to clearance of candidemia, were assessed for normality using descriptive statistics, histograms, and the Shapiro–Wilk test. Age was normally distributed and was summarized as mean ± standard deviation (SD). Comparisons of age between ICU and non-ICU patients

were performed using the independent-samples t-test, while differences across clinical outcome groups (improved, deceased, lost to follow-up) were assessed using one-way ANOVA, followed by Tukey's HSD test for post-hoc analysis. Time to clearance of candidemia was not normally distributed and was therefore reported as median with interquartile range (IQR). Comparisons between ICU and non-ICU patients for this variable were performed using the Mann–Whitney U test. Frequencies and percentages were calculated for categorical variables such as gender, malignancy type, comorbidities, risk factors, central line presence, antifungal use, and complications. Comparative analyses between ICU and non-ICU patients for categorical variables were conducted using the Chi-square test or Fisher's exact test, as appropriate. A p-value of <0.05 was considered statistically significant.

RESULTS

A total of 175 consecutive cancer patients with culture-confirmed candidemia were included over the study period. Of these, 66 patients (37.7%) were admitted to ICU, while 109 patients (62.3%) received care in non-ICU settings. Patient selection and stratification are illustrated in Figure-I.

The mean age of the study cohort was 32.8 ± 22.1 years. ICU patients were significantly older than non-ICU patients (38.5 ± 19.9 vs. 29.4 ± 22.7 years; mean difference 9.0 years, 95% CI: 2.6–15.5; p = 0.007, independent samples t-test, equal variances not assumed (Table 1). One-way ANOVA demonstrated a significant variation in age across the three clinical outcome groups: deceased, improved, and lost to follow-up (p = 0.014). Post-hoc analysis using Tukey's HSD test indicated that patients who died were significantly older than those who showed clinical improvement, with a mean age difference of 8.8 years (p = 0.026). Gender distribution was comparable between groups, with males comprising 116 (65.9%) patients of the overall cohort (p = 0.2) (Table-I). The prevalence of comorbidities—including diabetes mellitus, hypertension, chronic kidney disease, and ischemic heart disease—did not differ significantly between ICU and non-ICU patients (Table-I).

Patients with solid organ malignancies accounted for 121 (69.1%) of the overall cohort. In contrast, hematologic malignancies were significantly more prevalent among non-ICU patients compared to those in the ICU (39.4%) vs. (16.7%), respectively;(p = 0.001; Table-I).

Among the identified risk factors for candidemia, recent antibiotic use was the most prevalent (98.3%), followed by the presence of a central venous catheter (72%), administration of chemotherapy within the preceding 14 days (48.6%), and neutropenia (42.9%) (Table-I). Of these, only recent chemotherapy use demonstrated a statistically significant difference between ICU and non-ICU patients (p = 0.03; Table-I). Hemodialysis was documented exclusively among ICU patients, reflecting institutional practices; therefore, it was not included in comparative statistical analyses. Similarly, as all ICU patients had CVCs and the interval between catheter placement and onset of candidemia was not recorded, this variable was also excluded from group-wise analysis (Table-I).

Candida tropicalis was the most frequently isolated species, accounting for (40.6%) of cases, followed by *Candida albicans* (34.3%) and *Candida glabrata* (13.1%) (Table-II). Less commonly identified species included *Candida parapsilosis, Candida krusei, Candida lusitaniae,* among others (Table-II). Notably, *Candida auris* was not detected in any patient. The species-specific mortality differences between ICU and non-ICU settings were not statistically significant (p = 0.49; Table-II).

Following the detection of yeast in blood cultures—prior to final species identification and antifungal susceptibility results—empirical antifungal therapy was most commonly initiated with caspofungin, administered to 40.0% of patients. This was followed by amphotericin B deoxycholate (27.4%), fluconazole (9.1%), and voriconazole (4.0%). Notably, 18.9% of patients did not receive any antifungal treatment, predominantly due to early mortality or loss to follow-up shortly after diagnosis.

Among all patients, 99 (56.5%) exhibited concomitant bacteremia, and out of those, 21 (21.0%) had polymicrobial infections involving multiple bacterial species. Among ICU patients, 38 of 66 (57.5%) had concomitant bacteremia, compared to 61 of 109 (55.9%) in the non-ICU group, with no statistically significant difference observed between the two settings (p = 0.48).

The median time to clearance of candidemia for the overall cohort was 10 days (IQR: 7–15). When stratified by place of stay, ICU patients had a median clearance time of 11 days (IQR: 8–15) compared with 9 days

(IQR: 7–15) in non-ICU patients. Although ICU patients demonstrated a trend toward longer clearance times, the difference was not statistically significant (Mann–Whitney U = 3022.5, Z = –1.81, p = 0.071).

Invasive complications were infrequently identified among the study cohort. Hepatosplenic candidiasis was observed in 9 (8.3%) of non-ICU patients and 3 (4.5%) of ICU patients (p = 0.6), while septic thrombophlebitis was reported in 3 (4.5%) of ICU and 3 (2.8%) of non-ICU patients (p = 0.70; Table-III). Other complications, such as endocarditis and endophthalmitis, were not documented in any patient (Table-III). It is important to note that evaluation for these complications was incomplete, with relevant screening performed in only 22–60% of cases, largely due to various clinical and logistical constraints and comparisons between ICU and non-ICU groups should be interpreted with caution.

Table-I: Comparison of demographic details, comorbid conditions, infection profile, and treatment-related interventions between ICU and non-ICU patients. ICU: Intensive Care Unit, TPN: Total Parenteral Nutrition, GI: Gastrointestinal.

Variable	Total (n = 175)	ICU (n = 66)	Non-ICU (n = 109)	p-value
Male Gender, n (%)	116 (65.9%)	37 (56.1%)	79 (72.5%)	0.20
Age, Mean ± SD (years)	32.8 ± 22.1			
Malignancy Type				
– Haematological, n (%)	54 (30.9%)	11 (16.7%)	43 (39.4%)	0.001
– Solid, n (%)	121 (69.1%)	55 (83.3%)	66 (60.6%)	
Diabetes Mellitus, n (%)	24 (13.7%)	8 (12.1%)	16 (14.7%)	0.40
Hypertension, n (%)	13 (7.4%)	6 (9.1%)	7 (6.4%)	0.50
Chronic Kidney Disease, n (%)	8 (4.6%)	4 (6.1%)	4 (3.7%)	0.40
Ischemic Heart Disease, n (%)	6 (3.4%)	3 (4.5%)	3 (2.8%)	0.60
Concomitant Bacteremia, n (%)	99 (56.6%)	38 (57.6%)	61 (56.0%)	0.80
Polymicrobial Bacteremia, n (%)	37 (21.1%)	17 (25.8%)	20 (18.3%)	0.25
Central Line Present, n (%)	126 (72.0%)	63 (100%)	63 (55.0%)	–
TPN Use, n (%)	23 (13.1%)	12 (18.2%)	11 (10.1%)	0.09
Steroid Use, n (%)	16 (9.1%)	6 (9.1%)	10 (9.2%)	0.40
Recent Antibiotics, n (%)	172 (98.3%)	66 (100%)	106 (97.2%)	0.20
Recent Antifungals, n (%)	26 (14.9%)	7 (10.6%)	19 (17.4%)	0.27
Chemotherapy (past 14 days)	85 (48.6%)	25 (37.9%)	60 (55.0%)	0.03
GI Procedure, n (%)	33 (18.9%)	12 (18.2%)	21 (19.3%)	1.00
Pancreatitis, n (%)	3 (1.7%)	1 (1.5%)	2 (1.8%)	1.00
Neutropenia, n (%)	75 (42.9%)	26 (39.4%)	49 (45.0%)	0.50
Hemodialysis, n (%)	25 (14.3%)	25 (37.9%)	0	–
Urine *Candida* Colonisation, n (%)	32 (18.3%)	13 (19.7%)	19 (17.4%)	0.60

Table-I: Distribution of *Candida* species among ICU and non-ICU patients with candidemia, and associated crude mortality.

Candida Species	Total cases = n (%)	ICU =n (%)	ICU mortality =n (%)	Non-ICU = n (%)	Non-ICU mortality = n (%)	p- value
Candida tropicalis	71 (40.6%)	25 (35.2%)	21(84%)	46(64.7%)	21(45.6%)	
Candida albicans	60 (34.3%)	24(40%)	20 (83.3%)	36(60%)	17(47.2%)	
Candida glabrata	23 (13.1%)	12(52.1%)	8(66.6%)	11(47.8%)	6(54.5%)	
Candida parapsilosis	8 (4.6%)	3(37.5%)	0	5(62.5%)	1(20%)	
Candida krusei	2 (1.1%)	0	0	2(100%)	0	
Candida kefyr	1 (0.6%)	0	0	1(100%)	1(100%)	0.49
Candida lusitaniae	4 (2.3%)	0	0	4(100%)	0	
Candida guilliermondii	4 (2.3%)	2(50%)	2	2(50%)	0	
Candida utilis	1 (0.6%)	0		1(100%)	1 (100%)	
Candida pelliculosa	1 (0.6%)	0		1(100%)	0	
Total	175	66(37.7%)		109(62.2%)		

Table-II: Frequency of complications and in-hospital mortality among ICU and non-ICU patients with candidemia.

Variable	Screened patients n (%)	ICU; n (%)	Non-ICU; n (%)	p-value
Hepatosplenic candidiasis	103 (58.8%)	3 (4.5%)	9 (8.3%)	0.60
Endocarditis	105 (60.0%)	0	0	
Endophthalmitis	39 (22.0%)	0	0	
Septic thrombophlebitis	97 (55.4%)	3 (4.5%)	3 (2.8%)	0.70
In-hospital mortality, n (%)	-	51 (77.3%)	47 (43.1%)	<0.001

DISCUSSION

This retrospective study included 175 cancer patients with culture-proven candidemia over three years and aimed to evaluate differences in clinical characteristics and outcomes between critically ill (ICU) and non-ICU patients. High incidence of candidemia in ICU patients may be related to critical illness, use of broad spectrum antibiotics, presence of co morbidities, used of dialysis, CVCs, TPN and many other patient related factors. [6,7]

In our study, while male gender predominated across the cohort, there was no statistically significant difference in gender distribution between the two groups. This is consistent with a multicenter comparative analysis, where ICU vs non-ICU acquired candidemia found no significant difference in gender distributio.[8] In our study, comorbidities such as diabetes mellitus, hypertension, and chronic kidney disease also showed no significant association with ICU admission implying severity. Though this is in contrast to most published literature. A large study conducted over a period 8 years, found cardiovascular diseases and renal dysfunction as independent predictor of severity and mortality.[9] Similarly another Italian study showed that there was high incidence of co morbidities in patients who had candidemia and were being admitted to ICU due to their critical illness.[10] Our lack of association could be due to significantly smaller sample size in both cohorts. However, a significant age difference was observed, with ICU patients being notably older, indicating an age-related predisposition to critical illness among patients with candidemia. We also found that age was meaningfully related to patient outcomes. On average, patients who died were significantly older than those who improved. The difference in average age between these two groups was about 8.8 years, and this difference was statistically significant ($p = 0.026$). This suggests that older age may be linked to a higher risk of death in cancer patients with candidemia.

We observed many known classic risk factors of fungemia in our study cohort. It has been well documented and studied that prolonged neutropenia, prophylactic therapy with antifungals, central catheter placement, total parenteral nutrition, recent chemotherapy and concomitant bacteremia are known risk factors for invasive candidiasis.[11] In this analysis, recent antibiotic use was present in 172 (98.3%), antifungal use in 26 (14.9%), chemotherapy within the preceding 14 days in 85 (48.6%), neutropenia in 75 (42.9%), hemodialysis in 25 (14.3%), and urinary colonization with *Candida* species in 32 (18.3%). No novel risk factors were identified. Among all these risk factors, only chemotherapy in the previous 14 days was significantly associated with mortality Chemotherapy disrupts the mucosal barrier and significantly increases the risk of invasive candidiasis.[12,13] Additionally, its immunosuppressive effects and associated toxicities may contribute to greater infection severity and higher crude mortality as observed in our cohort.

Among the fungal isolates, *Candida albicans* accounted for 60 (34.3%) cases, while non-albicans *Candida* species were responsible for 115 (65.7%) cases. *Candida tropicalis* was the most frequently isolated species, representing 71 (40.6%) isolates. This distribution is likely influenced by the widespread use of fluconazole prophylaxis in chemotherapy patients, a practice well established in the prevention of invasive fungal infections which results in low incidence of *Candida albicans* infection.[14-16] However,post-COVID-19 surveillance has also reported an increased incidence of *Candida parapsilosis*, *Candida glabrata*, along with *Candida tropicalis*, probably related to increased use of broad spectrum antifungals.[17] These trends emphasize the importance of developing antifungal stewardship to be use based on local epidemiological data and susceptibility patterns.[18]

Concomitant bacteremia was observed in 99 (56.5%) patients, and 37 (21.1%) had polymicrobial bloodstream infections involving more than one bacterial species. The absence of a significant difference in the rates of concomitant and polymicrobial bacteremia between ICU and non-ICU groups may reflect consistent infection control practices across both settings. However, the markedly higher mortality among ICU patients suggests that factors specific to this subgroup, such as hemodialysis requirement (37.9%) and universal CVC placement, indicate greater clinical severity. These findings suggest that mortality cannot be attributed solely to fungemia but may also reflect the cumulative burden of critical illness. Additionally, the presence of sepsis, a known independent predictor of mortality, may have further contributed to adverse outcomes. Among non-survivors, *Candida tropicalis* was the predominant species (59.2%), though it remains unclear whether mortality was directly attributable to the organism itself or compounded by underlying malignancy, immunosuppression, and critical care

interventions. A meta-analysis of 69 studies provided a deeper insight on our results. It showed that recent antibiotic use and central venous catheter were most common risk factors for candidemia and pooled prevalence of *non-albicans Candida* species in cancer patients was around 69% and associated with higher mortality.[19] A recent study from China proposed a predictive nomogram for 30-day mortality in cancer patients with invasive candidiasis, identifying prolonged ICU admission (>3 days), lack of source control, presence of metastatic disease, and bloodstream infection as key predictors of poor outcomes.[20]

In our study, the median time to clearance of candidemia was 10 days (IQR 7–15). ICU patients demonstrated a longer median clearance time (11 days, IQR 8–15) compared with non-ICU patients (9 days, IQR 7–15), although this difference was not statistically significant ($p = 0.071$). These clearance times were longer than those reported in prior studies, such as Garey *et al*. (2006), who noted clearance typically within 3–5 days following antifungal initiation. This discrepancy may reflect the higher burden of critical illness, underlying malignancy, and treatment delays in our cohort. Although early clearance has been associated with improved outcomes, persistent candidemia (typically defined as ≥5 days of positive blood cultures) has been linked to higher mortality (Pappas *et al*., 2016).[21]

This study has several limitations. As a retrospective analysis with a relatively small sample size, its findings may be subject to selection and information biases. The study did not capture details regarding the specific antifungal agents used, antifungal susceptibility profiles, or resistance patterns of the *Candida* species, limiting the ability to draw conclusions about therapeutic effectiveness. Additionally, it did not distinguish between community-acquired and nosocomial candidemia, nor did it assess differences in outcomes between these groups. Key clinical variables, such as severity of illness scores (e.g., APACHE II, SOFA) and the timing of antifungal initiation in relation to the detection of positive blood cultures, were not recorded. These omissions may have influenced observed mortality rates and restricted the interpretation of treatment efficacy. Furthermore, while central venous catheterization is a recognized risk factor, its temporal relationship with the onset of candidemia and its independent contribution to outcomes were not explored in detail, thereby limiting the generalizability of the results. Evaluation for invasive fungal complications, such as endocarditis, endophthalmitis, and hepatosplenic candidiasis, was incomplete in a substantial proportion of patients due to inconsistent screening practices. The limited screening for complications significantly restricts meaningful group-wise comparisons, and the findings should therefore be interpreted descriptively rather than conclusively.

Despite these limitations, the study possesses notable strengths. It focuses on a high-risk, clinically significant population—cancer patients with candidemia—providing valuable insights for both oncological and critical care contexts. The inclusion of a relatively large cohort over a three-year period enhances the reliability of observed trends. By comparing ICU and non-ICU patients, the study elucidates important differences in risk factors, *Candida* species distribution, clinical complications, and outcomes, particularly with respect to mortality. The analysis of variables such as malignancy type and infecting species adds depth to the findings, and the identification of a predominance of non-albicans *Candida* reinforces evolving epidemiological patterns with important therapeutic implications.

CONCLUSION

Candidemia remains a severe infection among cancer patients, with substantially higher mortality in critically ill individuals. Older age and recent chemotherapy were associated with poorer outcomes. The predominance of non-albicans *Candida* species highlights the importance of local epidemiological awareness when selecting empirical antifungal therapy. Strengthening early recognition, timely treatment, and institution-specific antifungal stewardship may help improve outcomes in this high-risk population

CONFLICT OF INTEREST

None

GRANT SUPPORT & FINANCIAL DISCLOSURE

Declared none

AUTHOR CONTRIBUTION

Seemal Aslam: Substantial contributions to study design, acquisition of data, manuscript writing, final approval, accountable for all aspects of publication

Madiha Ghulam: Substantial contributions to acquisition of data, manuscript writing, final approval, accountable for all aspects of publication.

Ali Anjum: Substantial contributions acquisition of data, manuscript writing, final approval, accountable for all aspects of publication.

Hamayal Masood: Substantial contributions acquisition of data, manuscript writing, final approval, accountable for all aspects of publication.

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