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Research Article

Association of Serum C - reactive protein, Albumin, and Random Blood Glucose with Microbiologically Confirmed Candidiasis: A Prospective Observational Study

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Abstract: ***Introduction:*** Candidiasis is a prevalent opportunistic fungal infection in hospitalized and immunocompromised patients. Rising incidence and antifungal resistance emphasize the need for early microbiological diagnosis and identification of associated biochemical abnormalities. Serum C-reactive protein (CRP), albumin, and random blood glucose (RBG) may offer supportive prognostic and diagnostic value.**Objectives:** To determine the prevalence and species distribution of Candida isolates in clinically suspected candidiasis and evaluate associations with serum CRP, albumin, and RBG levels.**Methods:** Prospective observational study of 73 patients with clinically suspected candidiasis. Appropriate specimens were processed using standard microbiological techniques, including Gram stain, germ tube test, and chromogenic media for species identification. Serum CRP, albumin, and RBG were measured concurrently and correlated with culture results. Statistical analysis included descriptive statistics, t-tests, and Pearson correlations ($p < 0.05$ significant).**Results:** Microbiologically confirmed candidiasis was present in 41/73 (56.2%) cases. Candida albicans accounted for 21 (51.2%) isolates, while non-albicans Candida species comprised 20 (48.8%), with C. tropicalis (n=9), C. glabrata (n=6), and C. krusei (n=3) predominant. Confirmed cases demonstrated significantly higher mean CRP (48.6 ± 22.4 vs. 18.3 ± 11.7 mg/L, $p<0.001$), lower albumin (2.8 ± 0.6 vs. 3.6 ± 0.5 g/dL, $p<0.001$), and higher RBG (162.4 ± 58.7 vs. 118.5 ± 42.3 mg/dL, $p=0.002$). CRP showed a strong positive correlation with candidiasis ($r=0.58$, $p<0.001$).**Conclusion:** Elevated CRP, hypoalbuminemia, and hyperglycemia are significantly associated with confirmed candidiasis. These routine biochemical markers may serve as useful adjuncts to culture for early diagnosis and risk stratification in resource-limited settings. Larger multicenter studies are warranted to validate these findings.

Keywords: Candidiasis,Candida albicans, Non-albicans Candida, C-Reactive Protein, Albumin, Blood Glucose, Biomarkers,Mycoses

INTRODUCTION

Candidiasis is one of the most common opportunistic fungal infections encountered in clinical practice and continues to account for substantial healthcare-associated morbidity and mortality worldwide. *Candida* species normally colonize the oral cavity, gastrointestinal tract, skin, and genitourinary tract without causing disease. When host immunity is compromised or the normal microbial flora is disrupted, these commensal organisms can invade tissues and produce infections ranging from superficial mucocutaneous disease to invasive candidiasis and candidemia (Kullberg & Arendrup, 2015; Pappas et al., 2018).

Over the past two decades, invasive candidiasis has become an increasingly important healthcare-associated infection, largely reflecting advances in modern medical care. Greater survival of critically ill patients, together with the expanding use of immunosuppressive therapy, organ transplantation, cancer chemotherapy, invasive medical devices, and intensive care interventions, has increased the number of individuals vulnerable to opportunistic fungal infections. Although antifungal therapy and supportive care have improved considerably, invasive candidiasis is still associated with prolonged hospital stays, substantial healthcare costs, and mortality rates exceeding 40%, particularly when diagnosis and treatment are delayed (Andes et al., 2024; Clancy & Nguyen, 2018). These observations highlight the importance of early recognition and prompt identification of patients at increased risk of infection.

Fungal diseases represent an increasing public health concern, with *Candida* species ranking among the leading causes of fungal bloodstream infections in hospitalized patients. These infections contribute considerably to morbidity, particularly among critically ill individuals receiving intensive care. The incidence of candidiasis varies across geographical regions owing to differences in patient demographics, healthcare practices, antimicrobial exposure, and the availability of diagnostic facilities (Benedict et al., 2019; Bongomin et al., 2017). In many low- and middle-income countries, including India, limited access to rapid diagnostic

techniques delays confirmation of infection and timely initiation of appropriate antifungal therapy, which can negatively affect clinical outcomes (Denning, 2024; World Health Organization, 2022).

The epidemiology of candidiasis has evolved markedly over the past two decades, with a gradual shift in the distribution of clinically significant *Candida* species. Although *Candida albicans* remains the predominant pathogen in many regions, infections caused by non-*albicans Candida* (NAC) species are being reported with increasing frequency. Among these, *Candida tropicalis*, *Candida glabrata*, *Candida parapsilosis*, and *Candida krusei* have emerged as important causes of bloodstream and other invasive fungal infections. This changing species distribution has important therapeutic implications because individual *Candida* species differ in their virulence, antifungal susceptibility patterns, and clinical response to treatment. Consequently, accurate species-level identification is essential for selecting appropriate antifungal therapy and improving patient outcomes (Pfaller & Diekema, 2007; Arendrup, 2014).

Species distribution of *Candida* differs considerably between geographical regions and healthcare settings. While *Candida albicans* remains the predominant pathogen in North America and Europe, several Asian countries have reported a higher prevalence of non-*albicans Candida* species, particularly *Candida tropicalis*. Similar trends have been documented in India, where multicentre surveillance studies identify *C. tropicalis* as one of the leading causes of candidemia and other invasive candidiasis, with isolation rates comparable to or exceeding those of *C. albicans*. These regional differences have important implications for empirical antifungal therapy, infection prevention measures, and antimicrobial stewardship, emphasizing the need for institution-specific epidemiological surveillance (Chakrabarti et al., 2015; Chakrabarti & Sood, 2021; Lamoth et al., 2022).

Host susceptibility plays a central role in the development of candidiasis, often determining whether *Candida* colonization progresses to invasive disease. Patients requiring prolonged intensive care, broad-spectrum antibiotic therapy, central venous or urinary catheterization, mechanical ventilation, renal replacement therapy, major abdominal surgery, organ transplantation, or immunosuppressive treatment are at particularly high risk of invasive candidiasis (Pappas et al., 2016; Andes et al., 2024). Under these conditions, disruption of the normal bacterial microbiota by prolonged antibacterial therapy promotes excessive *Candida* colonization and facilitates tissue invasion. As a result, candidiasis has become a major healthcare-associated infection that requires coordinated management involving clinicians, microbiologists, infection prevention specialists, and antimicrobial stewardship teams.

Diabetes mellitus is a well-recognized risk factor for candidiasis and contributes substantially to the increasing burden of fungal infections worldwide. Persistent hyperglycaemia impairs multiple components of the innate immune response, including neutrophil chemotaxis, phagocytosis, and intracellular killing, while also enhancing the adhesion and proliferation of *Candida* species on epithelial surfaces. Consequently, individuals with diabetes have a higher incidence of oral, vulvovaginal, urinary tract, and invasive candidiasis than the general population (Casqueiro et al., 2012; Geerlings & Hoepelman, 1999). Stress-induced hyperglycaemia is also common in critically ill patients and may further increase susceptibility to opportunistic fungal infections. Careful assessment of these predisposing factors can facilitate early microbiological investigation, timely diagnosis, and appropriate antifungal therapy.

Early diagnosis of candidiasis remains difficult because its clinical manifestations are often nonspecific and frequently overlap with those of bacterial sepsis and other systemic infections. Persistent fever despite broad-spectrum antibiotic therapy, unexplained organ dysfunction, or progressive clinical deterioration may suggest invasive fungal infection, but these features alone are insufficient for a definitive diagnosis. Conventional fungal culture is still regarded as the reference method for confirming candidiasis and identifying the infecting species. However, its diagnostic sensitivity is limited, particularly in patients with a low fungal burden or deep-seated infection, and culture-based identification often requires several days (Clancy & Nguyen, 2018; Pappas et al., 2018). As a result, delayed microbiological confirmation may postpone targeted antifungal therapy and contribute to poorer clinical outcomes.

Several non-culture-based diagnostic methods, including detection of (1→3)-β-D-glucan, mannan antigen, polymerase chain reaction (PCR)-based assays, MALDI-TOF mass spectrometry, and T2Candida technology, have expanded the diagnostic options for invasive candidiasis. These techniques offer faster turnaround times and improved diagnostic performance in selected clinical settings. However, widespread implementation remains challenging in many developing countries because of limited availability, high cost, and the need for specialized laboratory infrastructure and trained personnel (Lamoth et al., 2022; Clancy & Nguyen, 2018). As a result, tertiary care hospitals in resource-limited settings continue to depend largely on conventional microbiological methods supported by routinely available laboratory investigations when evaluating patients with suspected candidiasis.

Serum C-reactive protein (CRP), serum albumin, and blood glucose are routinely assessed in hospitalized patients and provide complementary information on the host response to infection. Among these parameters, CRP is an acute-phase protein synthesized by the liver in

response to pro-inflammatory cytokines and is widely used as a marker of systemic inflammation. Although CRP lacks specificity for fungal infections, persistently elevated concentrations have been associated with severe invasive candidiasis and adverse clinical outcomes. When interpreted alongside microbiological findings and the overall clinical picture, CRP may also be useful for assessing disease severity and monitoring the response to antifungal therapy (León et al., 2016; Pappas et al., 2018).

Serum albumin is routinely measured in hospitalized patients and serves as an indicator of nutritional status, systemic inflammation, and disease severity. Hypoalbuminaemia frequently occurs in critically ill individuals because of reduced hepatic protein synthesis, increased vascular permeability, ongoing inflammatory responses, and poor nutritional status. Low serum albumin concentrations have consistently been linked to prolonged hospital stay, greater disease severity, and increased mortality among patients with severe infections (Vincent et al., 2003; Soeters et al., 2019). Although serum albumin is not specific for candidiasis, it provides valuable prognostic information and reflects the overall clinical condition of patients with invasive fungal infections. When interpreted together with microbiological findings and other laboratory parameters, serum albumin may contribute to a more comprehensive assessment of disease severity.

Blood glucose assessment is a routine component of clinical evaluation and may provide useful information when patients are investigated for suspected candidiasis. Chronic hyperglycaemia associated with diabetes mellitus impairs innate immune defence, promotes *Candida* colonization, and increases susceptibility to both mucosal and invasive infections. In critically ill patients, stress-induced hyperglycaemia is also common and has been associated with adverse clinical outcomes irrespective of pre-existing diabetes. Because random blood glucose testing is inexpensive, rapid, and widely available, it may help identify patients at increased risk of candidiasis when interpreted alongside microbiological findings and other routinely performed laboratory investigations (Casqueiro et al., 2012; Geerlings & Hoepelman, 1999).

Routine measurement of serum CRP, serum albumin, and blood glucose forms part of the standard evaluation of hospitalized patients. However, evidence describing their combined association with microbiologically confirmed candidiasis remains limited. Most available studies have concentrated on candidemia, critically ill patients, or individual inflammatory biomarkers, providing little information on the combined clinical relevance of these routinely available laboratory parameters across different forms of candidiasis and clinical specimens. Indian data are particularly scarce despite the increasing burden of fungal infections and the changing epidemiology of non-*albicans Candida* species (Chakrabarti et al., 2015; Chakrabarti & Sood, 2021). These gaps in the literature emphasize the need for institution-specific studies that evaluate local epidemiological patterns while exploring the potential role of routinely available biochemical markers in the early clinical assessment of patients with suspected candidiasis.

The present prospective observational study was conducted to determine the prevalence and species distribution of *Candida* isolates recovered from clinically suspected cases of candidiasis in a tertiary care teaching hospital. The study also evaluated the association of microbiologically confirmed candidiasis with routinely measured biochemical parameters, including serum C-reactive protein (CRP), serum albumin, and random blood glucose levels. Correlation of these accessible biochemical markers with conventional microbiological findings may support early clinical assessment, facilitate risk stratification, and assist in timely therapeutic decision-making, particularly in resource-limited healthcare settings where access to advanced fungal diagnostic techniques remains limited.

Primary Objective

To determine the association between microbiologically confirmed candidiasis and serum biochemical markers.

Secondary Objectives

- Species distribution
- Demographic profile
- Risk factors
- Relationship with biochemical parameters

MATERIALS AND METHODS

Study Design This was a prospective observational study conducted in the Department of Microbiology in collaboration with the Departments of Medicine, Obstetrics & Gynaecology, and Biochemistry departments of a tertiary care hospital of Eastern India.

Study Duration The study was carried out over a period of 12 months (from January 2025 to December 2025).

Sample Size A total of 73 clinically suspected cases of candidiasis were enrolled in the study.

Inclusion Criteria

- Patients of all age groups and both sexes with clinical suspicion of candidiasis (oral thrush, esophageal candidiasis, vulvovaginal candidiasis, cutaneous candidiasis, urinary tract infection, respiratory tract infection, fungemia, or invasive candidiasis).
- Patients from whom appropriate clinical specimens were received for microbiological processing.
- Willingness to provide informed consent (or assent where applicable).

Exclusion Criteria

- Patients already on antifungal therapy for more than 48 hours at the time of sampling.
- Patients with incomplete clinical or laboratory data.
- Contaminated or improperly collected specimens.

Ethical Consideration The study protocol was approved by the Institutional Ethics Committee. Written informed consent was obtained from all participants (or their legal guardians) before enrolment.

MATERIAL & METHODS

Specimen Collection Appropriate clinical specimens including urine, blood, sputum, high vaginal swabs, pus, wound swabs, cerebrospinal fluid, peritoneal fluid, and other relevant samples were collected under aseptic conditions following standard protocols.

Microbiological Processing All specimens were processed according to standard microbiological techniques.

- Direct microscopic examination was performed using Gram staining and 10% KOH mount.
- Specimens were inoculated on Sabouraud Dextrose Agar (SDA) with and without chloramphenicol and incubated at 37°C for 24–72 hours.
- Yeast colonies were identified by colony morphology, Gram stain, germ tube test, and chromogenic media (CHROM agar Candida) for presumptive species identification.
- Further species confirmation was done using conventional methods including sugar assimilation and fermentation tests where necessary.

Biochemical Parameters The following biochemical parameters were estimated from venous blood samples collected at the time of microbiological sampling:

- Serum C-reactive protein (CRP) — measured by immunoturbidimetric method.
- Serum albumin — measured by bromocresol green method.
- Random blood glucose (RBS) — measured by glucose oxidase-peroxidase method.

All biochemical tests were performed using automated analyzers and quality-controlled procedures.

Data Collection A structured proforma was used to record demographic details, clinical history, risk factors, microbiological findings, and biochemical parameters for each patient.

Statistical Analysis Data were entered into Microsoft Excel and analyzed using SPSS software version 25.0.

- Descriptive statistics were expressed as mean ± standard deviation for continuous variables and frequencies/percentages for categorical variables.
- Chi-square test or Fisher's exact test was used to compare categorical variables.
- Independent t-test or Mann-Whitney U test was applied for comparison of continuous variables between groups.
- Pearson's or Spearman's correlation was used to assess the relationship between biochemical parameters and candidiasis.
- A p-value of < 0.05 was considered statistically significant.

RESULTS

A total of 73 clinically suspected cases of candidiasis were enrolled in the study. Of these, 41 patients (56.2%) were confirmed to have candidiasis by microbiological culture, while the remaining 32 (43.8%) were culture-negative.

Table 1: Demographic Profile of Study Participants

Parameter	Confirmed Candidiasis (n=41)	Culture Negative (n=32)	Total (n=73)
Age (Mean ± SD)	48.6 ± 18.4 years	45.2 ± 17.9 years	47.1 ± 18.1
Male	22 (53.7%)	15 (46.9%)	37 (50.7%)
Female	19 (46.3%)	17 (53.1%)	36 (49.3%)

Species Distribution Among the 41 culture-positive isolates, *Candida albicans* was the most common species, accounting for 21 isolates (51.2%), followed by non-albicans *Candida* (NAC) species in 20 isolates (48.8%). The distribution of NAC species was as follows:

- ***C. tropicalis* — 9 (22.0%)**
- ***C. glabrata* — 6 (14.6%)**
- ***C. krusei* — 3 (7.3%)**
- ***C. parapsilosis* — 2 (4.9%)**

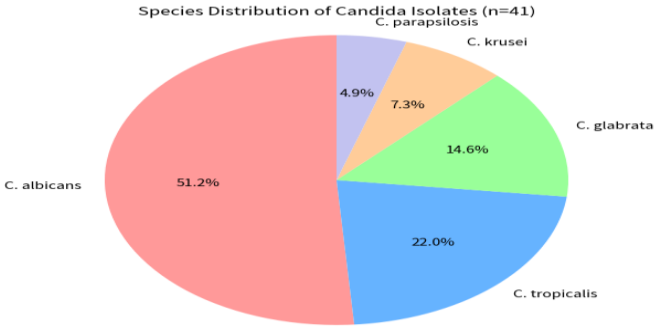

Fig-1 Species Distribution of Candida Isolates (n = 41)

Specimen-wise Positivity The highest culture positivity was observed in urine samples (18/41, 43.9%), followed by high vaginal swabs (9/41, 22.0%), blood (6/41, 14.6%), pus/wound swabs (5/41, 12.2%), and sputum (3/41, 7.3%).

Biochemical Parameters Patients with microbiologically confirmed candidiasis demonstrated significantly altered biochemical profiles compared to culture-negative patients (Table 2).

Table 2: Comparison of Biochemical Markers

Biochemical Parameter	Confirmed Candidiasis (n=41)	Culture Negative (n=32)	p-value
Serum CRP (mg/L)	48.6 ± 22.4	18.3 ± 11.7	<0.001
Serum Albumin (g/dL)	2.8 ± 0.6	3.6 ± 0.5	<0.001
Random Blood Glucose (mg/dL)	162.4 ± 58.7	118.5 ± 42.3	0.002

There was a strong positive correlation between serum CRP levels and confirmed candidiasis (Pearson's $r = 0.58$, $p < 0.001$). A significant negative correlation was observed between serum albumin levels and candidiasis ($r = -0.52$, $p < 0.001$). Random blood glucose also showed a moderate positive correlation ($r = 0.41$, $p = 0.002$).

Comparison between *C. albicans* and Non-albicans *Candida* Patients with non-albicans *Candida* infections had slightly higher mean CRP levels (52.3 ± 24.1 mg/L) compared to *C. albicans* (45.2 ± 20.8 mg/L), though the difference was not statistically significant ($p = 0.312$). Serum albumin was lower in NAC infections (2.6 ± 0.7 g/dL vs 2.9 ± 0.5 g/dL, $p = 0.089$), while random blood glucose levels were comparable between the two groups.

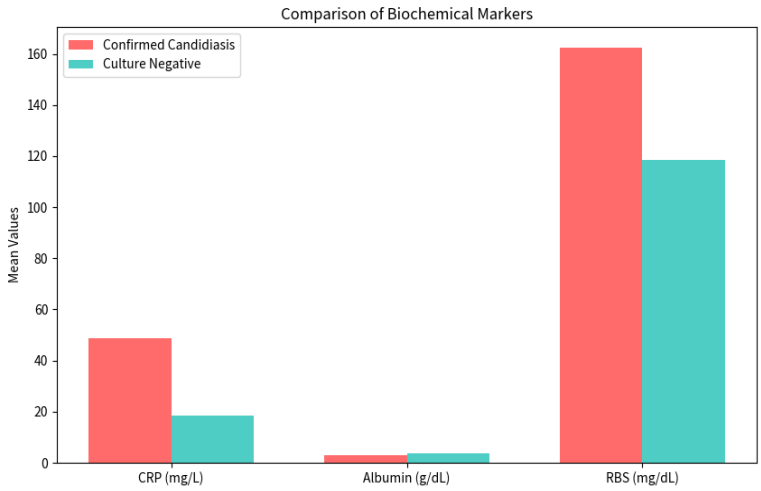

Fig-2 Bar Graph – Comparison of Biochemical Markers (Confirmed vs Culture Negative)

Risk Factor Analysis The most common associated risk factors among culture-positive patients were broad-spectrum antibiotic use (68.3%), diabetes mellitus (61.0%), central venous catheterization (43.9%), and prolonged hospitalization (>7 days) (53.7%).

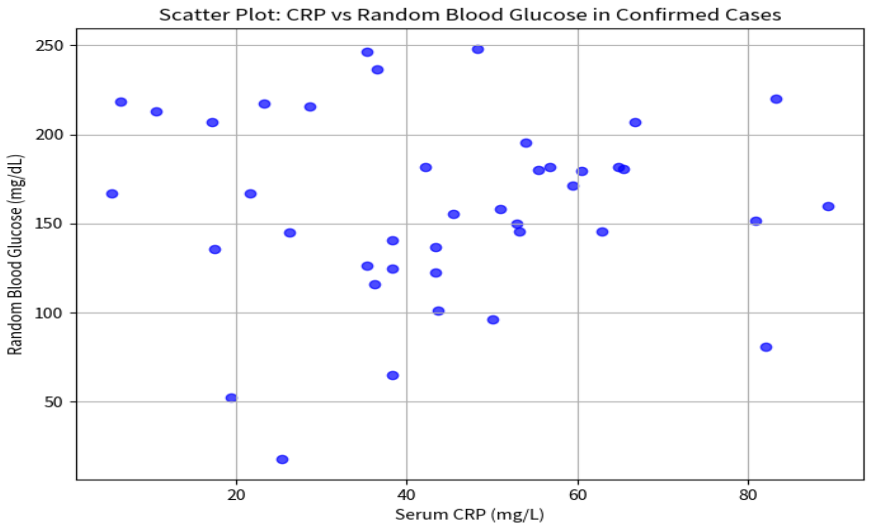

Fig-3 Scatter Plot – Correlation between CRP and Random Blood Glucose (Confirmed Cases)

In summary, more than half of the clinically suspected cases had microbiologically confirmed candidiasis with a nearly equal distribution of *C. albicans* and non-albicans species. Significantly elevated CRP, reduced serum albumin, and higher random blood glucose levels were strongly associated with confirmed infection, highlighting the potential utility of these routine biochemical parameters as supportive diagnostic and prognostic markers.

DISCUSSION

The present study found a high prevalence of microbiologically confirmed candidiasis (56.2%) among 73 clinically suspected cases. Candida albicans accounted for 51.2% of isolates, while non-albicans Candida (NAC) species constituted 48.8%, with C. tropicalis being the most common NAC species. This near-equal distribution reflects the ongoing global epidemiological shift toward NAC species reported in recent studies.

Patients with confirmed candidiasis showed significantly higher serum CRP (48.6 ± 22.4 mg/L vs 18.3 ± 11.7 mg/L, $p<0.001$), lower serum albumin (2.8 ± 0.6 g/dL vs 3.6 ± 0.5 g/dL, $p<0.001$), and higher random blood glucose levels (162.4 ± 58.7 mg/dL vs 118.5 ± 42.3 mg/dL, $p=0.002$) compared to culture-negative patients. These findings indicate a strong association between altered biochemical parameters and candidiasis.

The elevated CRP reflects systemic inflammation, while hypoalbuminemia may result from inflammatory response or underlying illness. Hyperglycemia, both a risk factor and consequence, promotes Candida growth and impairs host immunity. These observations are consistent with previous reports linking these markers with invasive fungal infections.

Limitations of the study include its single-center nature and modest sample size. Antifungal susceptibility testing was not performed.

The study highlights that routine biochemical markers (CRP, albumin, and blood glucose) can serve as useful adjuncts to culture for early suspicion and management of candidiasis in resource-limited settings. Larger multicentric studies are recommended to validate these findings.

CONCLUSION

This study showed a high prevalence (56.2%) of microbiologically confirmed candidiasis among clinically suspected cases, with nearly equal distribution of *Candida albicans* (51.2%) and non-albicans *Candida* species. Elevated CRP, low serum albumin, and hyperglycemia were significantly associated with confirmed infection.

Routine biochemical markers along with culture can aid in early diagnosis and better management of candidiasis. Larger multicenter studies are needed to validate these findings.

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Conflict of Interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this manuscript.

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