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FREQUENCY OF FUNGAL INFECTIONS IN CHRONIC KIDNEY DISEASE

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ABSTRACT

Objective: To determine and compare the frequency of fungal infections among patients with chronic kidney disease (CKD) stages 1–3, CKD stages 4–5, and patients receiving maintenance haemodialysis.
Study Design: Cross-Sectional
Place and Duration of the Study: Department of Nephrology, Dow University Hospital Ojha Campus, Karachi from August 2025 to January 2026.
Methodology: A total of 139 adult CKD patients aged 18 to 60 years were enrolled through consecutive nonprobability sampling. Serum beta-D-glucan and galactomannan were measured to define IFI. Data were analysed using SPSS-26 with Chi square or Fisher exact test, taking $p<0.05$ as significant.
Results: The mean age of the cohort was 44.76 ± 13.26 years, with 88 (63.3%) male participants. IFI was identified in 15 (10.8%) patients overall. Among IFI-positive patients, 40.0% belonged to CKD stage 1–3, 33.3% to CKD stage 4–5, and 26.7% were receiving maintenance haemodialysis. Mean serum creatinine was higher in IFI positive than IFI negative patients (6.96 ± 2.90 vs 6.03 ± 3.37 mg/dL), although the difference was not statistically significant ($p=0.308$).
Conclusion: Invasive fungal infection was identified in 10.8% of CKD patients overall. Among patients with IFI, 40.0% belonged to CKD stage 1–3, 33.3% to CKD stage 4–5, and 26.7% were receiving maintenance haemodialysis. No baseline characteristic, including serum creatinine, showed a statistically significant association with invasive fungal infection. Whether routine biomarker screening across the spectrum of chronic kidney disease improves clinical outcomes cannot be inferred from these descriptive data and requires evaluation in adequately powered prospective studies.

KEYWORDS: Chronic Kidney Disease, Invasive Fungal Infections, Beta-D-Glucan, Galactomannan, Renal Dialysis, Mycology, Pakistan.

INTRODUCTION

Chronic kidney disease (CKD) is increasingly a major cause of morbidity and mortality globally, accounting for an estimated 9.1% of the prevalence of the disease and about 1.2 million deaths annually [1,3,14]. The impact is even more significant in the Asia region; about 434.3 million adults are affected with approximately 65.6 million adults in advanced disease [2]. The leading causes for diabetes-driven morbidity and mortality continue to be diabetes mellitus and hypertensive nephropathy, while cardiovascular events are the main cause of early mortality in this group of patients [4,5,6]. Accurate assessment of renal function remains essential for CKD staging, disease severity assessment and clinical risk stratification, with current recommendations favoring the 2021 race-free CKD-EPI creatinine equation for estimating eGFR [15]. The prevalence of CKD in Pakistan has been reported as high as 21.2%, which reflects the increasing burden of diabetes and hypertension in the region and forms a large population susceptible to opportunistic infections [13].

Systemic mycoses known as invasive fungal infections (IFI) have mortality rates of 10 to 49% if they invade beyond the skin and subcutaneous tissues [7]. The major pathogens include Candida, Aspergillus, Cryptococcus and Pneumocystis, the latter accounting for almost 70% of cases (8). Patients with CKD have several immune deficiencies, both innate and adaptive, associated with the uraemic toxins, a chronic low-grade inflammatory state, malnutrition and frequent vascular access procedures, which combine to render susceptible to opportunistic mycoses [16]. Alterations in the gut mycobiome have been demonstrated in patients with chronic kidney disease and are associated with shifts in systemic immunological profiles [9]. As with viral infections, IFI remains a significant source of morbidity and mortality, especially in immunocompromised individuals and patients who are not promptly diagnosed [8].

Conventional culture-based diagnosis is hampered by slow turnaround and modest sensitivity, particularly in patients without classical neutropenia [8]. Serum beta-D-glucan (BG), a cell wall polysaccharide present in most pathogenic fungi other than Cryptococcus, has therefore gained traction as an adjunct biomarker [10]. A serum BG cut off above 80 pg per mL has demonstrated sensitivity of 88.64% and specificity of 100% for IFI in selected

populations, exceeding the yield of blood cultures [11]. Galactomannan, a polysaccharide released by Aspergillus species, complements BG with high specificity and is widely incorporated in current diagnostic algorithms for invasive aspergillosis [19].

Despite this evolving diagnostic landscape, focused data on the burden of IFI across the spectrum of renal impairment remain scarce. In one of the few CKD specific evaluations, Wong and colleagues reported that 22% of haemodialysis recipients harboured raised BG levels consistent with IFI, while elevations were seen in 10% of stage 1 to 3 patients and were not detected at the same magnitude in stage 4 to 5 patients [12]. Larger surveys of immunocompromised cohorts continue to highlight the lethality of these infections, with global estimates suggesting that more than 6.5 million individuals are affected by IFI each year and over 2.5 million deaths are directly attributable to fungal disease [17]. However, most published studies have focused on non-transplant CKD patients, which is a group that is less well studied when compared to the critically ill or transplant recipient population [18,21,22]. Some diagnostic markers like BG and galactomannan have been found to have variable performance in different stages of renal impairment, especially in Pakistan which has no updated data to describe the prevalence of IFI in varying degree of kidney impairment [20]. Given the high local prevalence of CKD and the lack of regional data on which to base fungal screening, this study was conceived to establish and compare the prevalence of IFI, in patients with CKD stages 1 to 3, 4 to 5 and maintenance haemodialysis at a tertiary care nephrology unit.

METHODOLOGY

This was a cross-sectional study conducted at the Department of Nephrology, Dow University Hospital Ojha Campus, Karachi from August 2025 to January 2026, after obtaining ethical approval from the CPSP and the institutional ERC, with written informed consent obtained from every participant before enrolment. A non probability consecutive sampling technique was used to recruit adult patients of either sex, aged 18 to 60 years, with an established diagnosis of CKD. CKD was identified by an estimated eGFR below 60 ml/min/1.73 m² or by an eGFR of 60 ml/min/1.73 m² or higher accompanied by albuminuria of 30 mg per 24 hours or more, persisting for at least three months. Disease severity was categorised into stages 1 to 3, stages 4 to 5, and a separate group receiving maintenance haemodialysis for more than three months. Patients with recent exposure to fungus derived antibiotics such as penicillin or cephalosporins, those who had received any blood product transfusion within the preceding two weeks, individuals with open wounds in contact with cellulose containing dressings, those with active untreated sepsis as defined by SIRS criteria, and pregnant women were excluded. IFI was defined as a serum beta-D-glucan concentration above 80 pg/mL, a serum galactomannan index of 0.5 or greater, or a bronchoalveolar lavage galactomannan index of 1.0 or greater. This biomarker-only definition does not meet the EORTC/MSGERC criteria for proven or probable IFI and should be interpreted accordingly. The required sample size of 139 patients was estimated using a 10%[12] expected prevalence of IFI in CKD, a 5% precession and a 95% C.I. Baseline demographic and clinical details, including age, gender, residential status, CKD stage and duration of haemodialysis, were recorded by the principal investigator on a predesigned proforma. Serum samples were obtained on the day of enrolment and processed in the institutional diagnostic laboratory; eGFR was calculated using the 2021 race free CKD-EPI creatinine equation in accordance with current KDIGO recommendations[15]. Patients were classified into CKD stages according to the calculated eGFR values, while patients receiving maintenance haemodialysis for more than three months were analysed as a separate group. beta-D-glucan was measured using a commercially available Fungitell quantitative kit, while galactomannan was assayed by enzyme immunoassay, both performed strictly according to the manufacturer protocols. Data were entered and analysed using SPSS-26; descriptive statistics were summarised as Mean ± SD and frequency with percentage, stratification was done and using the Chi-square / independent sample t-test with $p \leq 0.05$ considered statistically significant.

RESULTS

A total of 139 patients with CKD were enrolled. The mean age of the cohort was 44.76 ± 13.26 years, and males predominated, accounting for 88 (63.3%) participants. Eighty-four (60.4%) patients resided in urban areas and 55 (39.6%) in rural settings. With respect to disease severity, 58 (41.7%) patients were classified as CKD stage 1 to 3, 50 (36.0%) as CKD stage 4 to 5, and 31 (22.3%) were receiving maintenance haemodialysis. The mean eGFR was 46.67 ± 35.46 ml/min/1.73 m², the mean serum creatinine was 6.13 ± 3.32 mg/dL and the mean duration of haemodialysis was 2.91 ± 6.03 years. Mean serum galactomannan index and beta-D-glucan concentration were 0.34 ± 0.49 and 132.58 ± 141.25 pg per mL, respectively. The complete baseline profile is summarised in **Table 1.**

Baseline and clinical characteristics were compared between patients with and without invasive fungal infection, as shown in **Table II**. Patients with IFI had higher mean serum creatinine levels than patients without IFI (6.96 ± 2.90 vs 6.03 ± 3.37 mg/dL, p = 0.308). There were no statistically significant differences with respect to age, eGFR, duration of haemodialysis, gender, residential status and CKD stage group (all $p > 0.05$). IFI was identified in 40.0% of patients with CKD stage 1-3, 33.3% of patients with CKD stage 4-5 and 26.7% of patients receiving maintenance haemodialysis among the different CKD stage groups.

Table I: Baseline and Clinical Characteristics of Study Participants (n=139)

Mean ± Standard Deviation		**95% Confidence Interval**
Age in years = **44.76 ± 13.26**		42.54–46.99
eGFR in mL/min/1.73 m² = **46.67 ± 35.46**		40.72–52.61
Serum Creatinine in mg/dL = **6.13 ± 3.32**		5.57–6.68
Duration of Haemodialysis in years = **2.91 ± 6.03**		1.89–3.92
Galactomannan = **0.34 ± 0.49**		0.26–0.42
Beta-D-glucan in pg per mL = **132.58 ± 141.25**		108.89–156.27
Frequency %		
Gender	Male	88 (63.3)
	Female	51 (36.7)
Residential Status	Urban	84 (60.4)
	Rural	55 (39.6)
Chronic Kidney Disease Stage Group	CKD 1-3	58 (41.7)
	CKD 4-5	50 (36.0)
	Haemodialysis	31 (22.3)

Table II: Comparison of Baseline Characteristics with Invasive Fungal Infection (n=139)

Baseline Characteristics		**Invasive Fungal Infection**		**95% Confidence Interval**	**P-Value**
		Yes (n=15)	**No** (n=124)		
Age in years		47.00 ± 12.60	44.49 ± 13.37	-4.678–9.694	0.491
eGFR in mL/min/1.73 m²		50.08 ± 42.17	46.25 ± 34.73	-15.399–23.055	0.649
Serum Creatinine in mg/dL		6.96 ± 2.90	6.03 ± 3.37	-0.086–2.729	0.308
Duration of Haemodialysis in years		2.53 ± 4.70	2.95 ± 6.18	-3.690–2.854	0.081
Gender	Male	9 (60.0)	79 (63.7)	0.286–2.556	0.778
	Female	6 (40.0)	45 (36.3)		
Residential Status	Urban	8 (53.3)	76 (61.3)	0.246–2.119	0.552
	Rural	7 (46.7)	48 (38.7)		
Chronic Kidney Disease Stage Group	CKD 1-3	6 (40.0)	52 (41.9)	0.451–1.771	0.910
	CKD 4-5	5 (33.3)	45 (36.3)		
	Haemodialysis	4 (26.7)	27 (21.8)		

DISCUSSION

The immune dysregulation milieu of CKD increases the risk of IFI and the non -specific symptoms involved in the diagnosis are compounded by the different performance of fungal biomarkers throughout the phases of renal impairment [8,9,16]. The aim of the present study was to determine the prevalence of IFI in patients with stages 1 to 3 of CKD, stages 4 to 5 and those on maintenance haemodialysis, with the presence of serum beta-D-glucan and galactomannan as defining biomarkers.

It is found that the mean age of the cohort is 44.76 ± 13.26 years, in which males predominate (63.3%), which is comparable with CKD reported in other South Asian populations. Khan et al. in a high-risk urban population of Lahore, found the mean age of all the patients with CKD to be 49.9 years, and diabetes and hypertension were found as the prime causative factors of the disease [20]. The overall prevalence of IFI in our cohort was 10.8%, similar to the 10% for CKD stages 1 to 3 and 22% for haemodialysis patients reported by Wong and associates, who found high levels of beta-D-glucan consistent with IFI [12]. This slightly lower haemodialysis result, 12.9%, could be related to variations in dialysis vintage, membrane biocompatibility, exposure to cellulose-containing dialysis membranes, intravenous immunoglobulin (IVIG) administration, and beta-lactam antibiotic exposure, all of which are recognised causes of false-positive beta-D-glucan elevations [10]. Therefore, the haemodialysis-associated estimate should be interpreted as a possible upper-bound estimate of IFI frequency in this subgroup. Among patients with invasive fungal infection, 40.0% belonged to CKD stage 1–3, 33.3% to CKD stage 4–5, and 26.7% were receiving maintenance haemodialysis. No statistically significant association was observed between CKD stage group and IFI status. These findings have also been seen in cohorts in which the diagnosis of CKD alone was a good proxy for immune compromise [9,16]. Recent burden estimates by Denning indicate that approximately 6.55 million people experience IFI each year, with more than 2.55 million directly attributable deaths, highlighting the global magnitude of the problem and the need for proactive screening in immunocompromised cohorts [17]. Within Asia, mycotic disease in CKD remains poorly characterised, and the present findings provide one of the few contemporary local datasets that quantify the frequency in non transplant patients.

The similar baseline risk across CKD stages can be explained by overlapping pathobiology. Uraemic retention solutes impair phagocyte chemotaxis and dampen oxidative burst, leaving even early-stage CKD patients with a measurably weakened innate response [16]. Persistent inflammation and skewed T cell subsets compound this

picture, paralleling the immune phenotype that predisposes solid organ transplant recipients to invasive aspergillosis and candidiasis [18,22]. The mortality of pulmonary aspergillosis in non classical immunocompromised hosts is also being increasingly recognised, reinforcing the case for vigilance even without overt immunosuppressive therapy [21].

Mean serum creatinine was higher among IFI positive patients compared to IFI negative patients (6.96 ± 2.90 vs 6.03 ± 3.37 mg/dL), although the difference was not statistically significant ($p = 0.308$). Similarly, no statistically significant associations were observed across age, gender, residential status or CKD stage groups. These findings suggest that invasive fungal infection may occur across the spectrum of CKD irrespective of baseline demographic or clinical characteristics.

Pooled diagnostic accuracy data indicate that beta-D-glucan and galactomannan retain useful sensitivity and specificity for IFI in suspected populations, supporting their potential role as adjunctive biomarkers in CKD patients with unexplained clinical deterioration or persistent inflammatory features [19]. The non-significant trends across age, gender, residential status and CKD severity argue for biomarker informed surveillance rather than reliance on conventional risk stratification.

This study brings up to date local information on a question of clinical relevance and little studied, and results were obtained with an a priori determined sample size, with standardised laboratory assays in a single accredited institution. Some important constraints need to be recognized. The cross-sectional design does not allow for causal inference nor for an incidence study and patients were recruited from a single centre, reducing generalisability. Important confounders, including diabetes mellitus, hypertension, immunosuppressive therapy and recent broad-spectrum antibiotic exposure, were not systematically analysed. The elevations of beta-D-glucan may also have been caused by haemodialysis-related factors, including exposure to cellulose-containing dialysis membranes, intravenous immunoglobulin (IVIG), and beta-lactam antibiotics, potentially resulting in false-positive biomarker elevations [10]. The relatively limited number of IFIs (n=15) also limited the power to detect modest associations [18]. In addition, the sample size was calculated using a single-proportion prevalence formula and was not specifically powered for comparisons across the three CKD stage groups.

The findings of the present study support the global evidence documenting the neglected nature of IFI in all (not just transplant recipients or patients receiving long term dialysis) CKD. In the current cohort, 10.8% of patients had biomarker evidence of IFI, but there were no statistically significant demographic or clinical associations with IFI.

The findings highlight the importance of continued clinical vigilance for fungal infection in CKD patients with unexplained systemic symptoms or clinical deterioration. However, whether routine biomarker screening across the spectrum of chronic kidney disease improves clinical outcomes cannot be inferred from these descriptive data and requires evaluation in adequately powered prospective studies.

CONCLUSION

Invasive fungal infection was identified in 10.8% of CKD patients overall. Among patients with IFI, 40.0% belonged to CKD stage 1–3, 33.3% to CKD stage 4–5, and 26.7% were receiving maintenance haemodialysis. No baseline characteristic, including serum creatinine, showed a statistically significant association with invasive fungal infection. Whether routine biomarker screening across the spectrum of chronic kidney disease improves clinical outcomes cannot be inferred from these descriptive data and requires evaluation in adequately powered prospective studies.

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