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URINARY FUNGAL INFECTION AMONG DECOMPENSATED CHRONIC LIVER DISEASE PATIENTS

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Abstract

BACKGROUND: *Fungal urinary tract infection (FUTI) is a growing concern among patients with chronic illnesses, yet its risk factors remain incompletely understood.*

OBJECTIVE: *To determine the frequency of urinary fungal infection among decompensated chronic liver disease patients.*

METHODOLOGY: *This cross-sectional study included 148 patients, comprised 148 DCLD subjects were explored for urinary fungal infection. Associations between FUTI and variables such as age, gender, Child-Pugh class, obesity, and disease duration were assessed using chi-square tests, with $p < 0.05$ considered significant.*

RESULTS: The urinary fungal infection was observed in 90 (60.8%) subjects. The *FUTI prevalence was highest in the 18-29 and 60-70 year groups (22.2% each), but no statistically significant association was observed with age ($p=0.70$). Gender showed a strong association ($p<0.01$), with females comprising 73.3% of cases. Child-Pugh classification was significantly related to FUTI ($p<0.01$), with Class B patients more frequently affected (70.0%) than Class C (30.0%). Obesity was also significantly linked to FUTI ($p<0.01$), with 67.8% of obese individuals infected. Disease duration showed no significant association ($p=0.87$).*

CONCLUSION: *Female gender, obesity, and Child-Pugh Class B were significantly associated with FUTI in chronic liver disease patients, whereas age and disease duration were not. Targeted screening and preventive measures for these high-risk groups may help reduce infection burden.*

INTRODUCTION

Chronic liver disease (CLD) patients are at high risk of developing infections that lead to life-threatening conditions, such as sepsis and hepatic encephalopathy (HE) [1]. Such patients are at risk of infections for multiple reasons, including a dysfunctional immune response; increased permeability of the intestines, which causes alterations in the quantity and quality of the gut microbiota; and genetic predisposition, which contributes to the pathological translocation of fungal organisms from the gut to systemic circulation [2]. The onset of fungal infections has been linked to the occurrence of multiple complications, for example, acute kidney injury (AKI), HE, and

multiorgan failure, all of which confers long- and short-term mortality. Fungal infections lead to a rise in the risk of mortality at any liver disease stage, either compensated or decompensated, and include acute or chronic liver failure as well [3]. A study conducted by Hamid A, et al to determine the frequency of fungal urinary tract infection among patient with chronic liver disease and found that 141 patients (59.7%) of CLD had fungal UTI [4]. Another similar type of study was conducted by Kumani L, et al and revealed that 141 of 156 (90.3%) CLD patients had urine culture positivity for fungal pathogen [5]. Different fungi can cause systemic life-threatening infections and can present dilemmas in diagnosis and management. Liver cirrhosis is defined as a state of immune dysfunction which impairs the ability of the body's natural defense system to clear microorganisms, cytokines, and endotoxins from the circulation. The pathogenesis of this immune dysfunction in cirrhosis is multifactorial [6]. The liver has 90% of the reticuloendothelial cells in the form of kupffer and sinusoidal endothelial cells that play a key role in clearing organisms. In cirrhosis of the liver, there is shunting of the portal blood flow away from the liver and a reduced number of reticuloendothelial cells resulting in fewer bacteria and endotoxin clearing from the circulation. Cirrhotic patients have reduced neutrophil mobilization, their phagocytic activity and antigenpresenting HLA-DR molecules on monocytes [7]. Additional factors that add to this immunodeficiency in cirrhotic patients include malnutrition, immunosuppressive drugs and the use of alcohol [8]. Common pathogens such as Mycobacterium tuberculosis, Cryptococcus neoformans, Clostridium difficile, Listeria monocytogenes and Vibrio vulnificus are more virulent in patients with cirrhosis as compared to the general population. About one-third of non-human immunodeficiency virus, cryptococcoma cases are seen in patients having chronic liver disease and is proven to be an independent predictor for 30 days mortality as compared to those having acquired immunodeficiency syndrome [8]. The clinical significance of fungal organisms isolated from cirrhotic patients is still not fully known especially in decompensated Chronic Liver Disease Patients. Fungal infections may increase the morbidity and mortality in liver cirrhosis and using potent antifungal drugs in these patients is difficult due to compromised hepatic and renal functions. Prevention, early detection and proper management of these infections in cirrhotic patients can help in improving survival. This study aimed to determine the frequency of urinary fungal infection among decompensated chronic liver disease patients. As studies are available in chronic liver disease patients no such study has ever been conducted in decompensated chronic liver disease.

PATIENTS AND METHODS:

The cross sectional study was started from 22 Feb, 2025 to 22 May, 2025 after the approval of synopsis from CPSP at Department of Gastroenterology, Liaquat University Hospital Hyderabad. All the subjects attended inpatient or outpatient department of gastroenterology, Liaquat University of medical health Sciences, Jamshoro fulfilling our eligibility criteria were included in this study through non probability consecutive sampling.

The inclusion criteria were the diagnosed cases of DCLD for more than 1 year both male and female gender having age between 18 - 70 years, willing to provide informed consent and presented with complain of frequency and urgency or urine and pain and/or burning with urination

The exclusion criteria were the diabetes mellitus for more than one year and were confirmed either FBS > 126mg/dl on two different occasions or HBA1c > 6.5 and the patients already on Antifungal drugs or history of usage in last 2 weeks.

Urinary fungal infection was labeled as the Patient presented with the complains of frequency and urgency or urine and pain and/or burning with urination (assessed clinically) and confirmed on urine DR showing > 102 CFU fungi/ml or yeast in collected non voided urine samples or 105 CFU fungi/ml in a collected voided urine sample.

Decompensated chronic liver disease patients was labeled as positive if there was presence of any two of the following which assessed clinically (ascites, jaundice, hematemesis and/or melena) and hematology (thrombocytopenia and prolonged prothrombin time) and confirmed on ultrasonographic findings showing coarse echo texture of liver, irregular margins, increased portal

vein diameter > 13mm, splenomegaly (bipolar diameter > 13cm).

By taken the prevalence of F. UTI in DCLD i.e. 6.6% (from pilot study), margin of error = 4%, confidence interval = 95%, then a tleast a sample of 148 were recruited.

Written informed consent from the participants was taken. Demographic details which include age, height, weight, BMI, duration of disease, hypertension and child class (B/C) was noted and recorded on the approved proforma. Urine sample of all patients was collected by staff nurse and sent to laboratory for analysis. The outcome variable i.e. fungal urinary tract infection was noted as per operational definition.

Data was entered and analyzed by using SPSS statistical package version. Shapiro-Wilk test was applied to check the normality of quantitative data like age, height, weight, BMI and duration of disease. If data follows normality (P-value > 0.05), mean and standard deviation was calculated otherwise median (IQR) was reported. Frequencies and percentages were reported for categorical variables like gender, hypertension, and child class and outcome variable i.e. fungal urinary tract infection. The stratification with respect to age, BMI, duration of disease and child class was done. Post-stratification chi-square/ fisher exact test was applied to see the difference among strata's. P-value less than and equal to 0.05 was taken as significant.

RESULTS: Out of 148 participants, the largest proportion of patients were in the 40-49 year age group (22.3%), followed closely by those aged 50-59 years and 60-70 years (21.6% each). The 18-29 year group comprised 19.6%, while 14.9% were aged 30-39 years. Females constituted the majority of the study population (63.5%), whereas males accounted for 36.5%.

Regarding obesity status, 55.4% of patients were classified as obese, while 44.6% were non-obese. The duration of disease ranged from 1 to ≥10 years, with 29.7% having 1-3 years, 25.0% having 4-6 years, 22.3% having 7-9 years, and 23.0% having duration of 10 years or more.

Based on Child-Pugh classification, 61.5% of patients were in Class B and 38.5% were in Class C. The urinary fungal infection was detected in 60.8% of cases, while 39.1% had no fungal infection.

Table 01 shows the demographical profile while Table 02 represents the statistical stratification of urinary fungal infection in relation to different study variables.

The mean ± SD and median for age (in years) was 58.52 ± 8.82. The skewness and kurtosis statistic for age is -0.07 and -0.58, and for BMI is -0.55 and -0.73 whereas the median for age (yrs) and BMI (kg/m2) is 60.00, 7.700 and 31.00. The p-value for age and BMI on Shapiro-Wilk test reveals p=0.05, p<0.01 and p<0.01 respectively.

TABLE 1: THE DEMOGRAPHICAL AND CLINICAL PARAMETERS OF STUDY POPULATION

PARAMETER	FREQUENCY (n=148)	PERCENTAGE (%)
AGE (yrs)		
18-29	29	19.6
30-39	22	14.9
40-49	33	22.3
50-59	32	21.6
60-70	32	21.6
GENDER		
Male	54	36.5
Female	94	63.5
OBESITY		

Yes	76	55.4
No	66	44.6
DURATION OF DISEASE (years)		
1-3	44	29.7
4-6	37	25.0
7-9	33	22.3
≥10	34	23.0
CHILD-PUGH CLASS		
B	91	61.5
C	57	38.5
URINARY FUNGAL INFECTION		
Yes	90	60.8
No	58	39.1

TABLE 2: THE OCCURRENCE OF URINARY FUNGAL INFECTION IN RELATION TO DIFFERENT STUDY VARIABLES

	URINARY FUNGAL INFECTION n = 146 (%)			
AGE (years)	Yes	No	Total	P-value
18-29	20	09	29	0.70**
	(22.2%)	(15.5%)	(19.6%)	
30-39	14	08	22	
	(15.6%)	(13.8%)	(14.9%)	
40-49	17	16	33	
	(18.9%)	(27.6%)	(22.3%)	
50-59	19	13	32	
	(21.1%)	(22.4%)	(21.6%)	
60-70	20	12	32	
	(22.2%)	(20.7%)	(21.6%)	
GENDER				
Male	24	30	54	<0.01*
	(26.7%)	(51.7%)	(36.5%)	
Female	66	28	94	
	(73.3%)	(48.3%)	(63.5%)	
CHILD-PUGH CLASS				
B	63	28	91	<0.01*
	(70.0%)	(48.3%)	(61.5%)	
C	27	30	57	
	(30.0%)	(51.7%)	(38.5%)	
OBESITY				
Yes	61	21	82	<0.01*
	(67.8%)	(36.2%)	(55.4%)	
No	29	37	66	

	(32.2%)	(63.8%)	(44.6%)	
DURATION OF DISEASE (years)				
1-3	29	15	44	
	(32.2%)	(25.9%)	(29.7%)	
4-6	22	15	37	
	(24.4%)	(25.9%)	(25.0%)	
7-9	19	14	33	0.87**
	(21.1%)	(24.1%)	(22.3%)	
>10	20	14	34	
	(22.2%)	(24.1%)	(23.0)	

*Statistically significant;
**Statistically non-significant

DISCUSSION:

In the present study, the distribution of fungal urinary tract infection (FUTI) across age groups did not demonstrate a statistically significant association ($p = 0.70$). Although the highest proportion of FUTI cases was observed among participants aged 18-29 years and 60-70 years (22.2% each), the prevalence was relatively uniform across age categories. This finding contrast with previous studies where older age has been reported as a risk factor due to immune senescence and increased comorbidities. [9, 10] The relatively even age distribution in our study population may explain the absence of a significant trend.

Gender, however, showed a strong and statistically significant association with FUTI ($p < 0.01$), with females representing 73.3% of cases. This is consistent with established epidemiological evidence, where shorter urethral length, hormonal factors, and higher susceptibility to periurethral colonization contribute to increased UTI incidence among women. [11] However, some investigations, particularly in critically ill or catheterized populations, have reported a reduced gender disparity, with males showing comparable or even higher infection rates, likely due to prolonged catheterization and comorbid urological conditions. The present study's higher female predominance may therefore reflect both community-acquired risk factors and gender-specific healthcare exposures, whereas the variability in other reports could be attributed to differences in patient populations, healthcare practices, and diagnostic criteria.

Similarly, a significant association was found between Child-Pugh classification and FUTI ($p < 0.01$). Patients in Class B had a higher prevalence of infection compared to those in Class C. While advanced liver disease (Class C) is associated with immune dysfunction, the higher infection rates in Class B may be attributed to the larger number of Class B patients in our series or better survival in this stage allowing more time for infection to develop. This pattern warrants further investigation into host immune status and hospitalization frequency at different stages of liver disease. [12]

Obesity was also significantly linked with FUTI ($p < 0.01$), with 67.8% of obese individuals affected. Obesity is known to alter immune responses, promote chronic inflammation, and increase urinary stasis, all of which may predispose to infection. Our results align with prior studies demonstrating obesity as an independent risk factor for urinary tract infections in both community and hospital settings. [13]

Interestingly, the duration of disease was not significantly associated with FUTI ($p = 0.87$). This suggests that chronicity alone may not be a major determinant of infection risk, and that other factors such as nutritional status, metabolic control, and comorbidities may play a more pivotal role.[14]

Overall, our findings reinforce the significance of gender, liver disease severity, and obesity as key determinants of FUTI in patients with chronic illness, while age and disease duration appear to have less influence in this cohort. These insights highlight the importance of targeted preventive strategies, particularly for high-risk subgroups such as obese female patients with intermediate-stage liver disease.

CONCLUSION: This study highlights that female gender, Child-Pugh class, and obesity are significant determinants of fungal urinary tract infection in patients with chronic illness, whereas age and disease duration show no significant association. The predominance of FUTI among females, obese individuals, and those with moderate liver disease (Class B) underscores the need for targeted screening and preventive strategies in these high-risk groups. Early identification of high-risk individuals, particularly females, obese patients, and those with moderate liver disease, along with targeted preventive strategies such as regular screening, patient education, and optimized clinical monitoring, is recommended to reduce the burden of FUTI and improve patient outcomes.

LIMITATION OF THE STUDY:

This study has certain limitations that should be considered when interpreting the findings. First, its cross-sectional design precludes establishing a causal relationship between identified risk factors and FUTI. Second, the study was conducted at a single center, which may limit the generalizability of results to broader populations. Third, the reliance on age group ranges rather than exact ages may have reduced the precision of age-related associations. Additionally, certain potential confounders, such as prior antibiotic use, catheterization history, immunosuppressive therapy, and glycemic control, were not assessed, which could influence infection risk. Finally, the relatively modest sample size may have limited the statistical power to detect associations with less prevalent factors, such as specific age categories or disease duration.

AUTHOR'S CONTRIBUTION:

Collection and acquisition of data & grammatical corrections	Dr. Laiba Khan
Concept & design of study & proof read	Jazba Khan Mari
Drafting the article and finalizing the manuscript	Dr. Riaz Hussain Awan
Revising critically and make it suitable for final format	Dr. Muhammad Aqib Shaikh
Acquisition of data and grammatical review	Dr. Qandeel Jamali
Drafting the article and finalizing the manuscript	Dr. Ayesha Sajid
Revision of the manuscript	Dr. Moiz muhammad Shaikh
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