Original Article

Impact of elevated urine leukocyte and bacteria count per high-power field on the in-hospital outcome of patients with liver cirrhosis

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Background: Liver cirrhosis is prone to the development of urinary tract infection (UTI). Urine culture is a golden standard for the diagnosis of UTI, but it is often missing in routine clinical practice. Urinalysis may be an alternative. This study aimed to evaluate the prevalence of abnormal urinalysis and its impact on the in-hospital outcome of liver cirrhosis.

Method: Cirrhotic patients (n=2,067) who were admitted between July 2010 and June 2014 and underwent urinalyses were retrospectively enrolled. A urine leukocyte count of >4.33 and/or a urine bacteria count of >975 per high-power field were defined as abnormal urinalysis. Receiver-operator characteristic (ROC) curve analysis was performed to identify the capacity of urine leukocyte and bacteria count per high-power field for predicting the in-hospital death. The area under the ROC curve (AUROC) was calculated.

Results: The prevalence of elevated urine leukocyte and bacteria count per high-power field was 25.8% and 6.7%, respectively. The AUROC of urine leukocyte and bacteria count per high-power field for predicting the in-hospital death were 0.600 (P=0.015) and 0.600 (P=0.014), respectively. The best cut-off value of urine leukocyte per high-power field was 8.19 with a sensitivity of 34.5% and a specificity of 84.8%. The best cut-off value of urine bacteria per high-power field was 142.04 with a sensitivity of 38.6% and a specificity of 84.19%.

Conclusions: Abnormal urinalysis is common in liver cirrhosis and may be a predictor for the in-hospital death.

Keywords: Infection; liver cirrhosis; urinalysis; urine culture; death

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Introduction

Bacterial infection is one of the most significant complications in patients with decompensated liver cirrhosis (1). Spontaneous bacterial peritonitis (SBP) and urinary tract infection (UTI) are the most common types of bacterial infections in cirrhotic patients (2). The proportion of UTI in all bacterial infections is 20–25% (3), and the most common bacteria that cause UTI are Escherichia coli (4). Bacterial infections confer to a 4-fold increase in the mortality of cirrhosis (5). However, it remains unclear whether or not UTI increases the risk of mortality in cirrhotic patients (6).

The golden standard for diagnosis of UTI is a urine culture with significant colony counts of a single organism in a sterile manner (7). However, urine culture is not frequently used in clinical practice, especially in outpatient settings (8), for several reasons. First, a urine culture is time consuming requiring 48 hours for the growth and identification of the pathogen and additional 48–72 hours for determining its antimicrobial susceptibility. Second, a large number of cirrhotic patients with UTI are asymptomatic so that a urine culture is often not obtained (9). Third, the clinicians often use their clinical judgment rather than the standard diagnostic criteria for bacterial infections (10).

By comparison, urinalysis, microscopy, and bedside urine dipsticks are readily and rapidly available, which allows the clinicians to initiate empiric treatment for suspected UTI while awaiting urine culture results (11). Fernandez *et al.* also put forward that uncountable leukocytes can be used as a basis for the diagnosis of UTI, even without the urine culture result (1).

Considering that urine culture is hardly available in the clinical setting, the present study aimed to analyze the results of routine urinalysis, exploring the prevalence of abnormal urinalysis and its effect on the in-hospital outcome of cirrhotic patients.

Methods

Patients

All patients with liver cirrhosis who were consecutively admitted to our hospital between July 2010 and June 2014 and underwent urinalyses at their admission were potentially eligible, but patients with hepatocellular carcinoma and other malignancies were excluded. The study protocol was approved by the ethic committee of our hospital. The number of ethical approval was k (2017) 02. Patients' informed consents were waived. Demographic data, clinical presentation, regular laboratory tests, Child-Pugh class, and model for end-stage liver diseases (MELD) score were also collected.

Urinalyses

A clean-catch midstream urine specimen was taken to undergo the urinalyses. Data regarding urine leukocyte and bacteria count per high-power field were collected. Their reference ranges were 0.1–4.33 and 0.1–975, respectively. We defined the results of abnormal urinalysis as a urine leukocyte count per high-power field of >4.33 and/or a urine bacteria count per high-power field of >975. If two or more urinalyses were performed, the highest urine leukocyte and bacteria count per high-power field were selected.

Statistical analyses

Continuous data were expressed as the mean ± standard deviation and the median with minimum and maximum and were compared by non-parametric Mann-Whitney-Wilcoxon tests. Categorical data were expressed as the frequency (percentage) and were compared by Chi-square test. In all comparisons, a P value of <0.05 was considered statistically significant. Risk factors associated with elevated urine leukocyte and bacteria count per high-power field were assessed by logistic regression analyses. Statistically significant variables shown in univariate analyses were entered into the multivariate analyses. Odds ratios (ORs) and 95% confidence intervals (CIs) were calculated. Receiver-operator characteristic (ROC) curve analyses were performed to identify the capacity of the urine leukocyte and bacteria count per high-power field in predicting the in-hospital mortality. Areas under the ROCs curve (AUROCs) with 95% CIs were calculated. The best cut-off value was selected as the sum of sensitivity and specificity was the maximum. Sensitivity, specificity, positive likelihood ratio (PLR), negative likelihood ratio (NLR), positive predictive value (PPV), and negative predictive value (NPV) with 95% CIs were reported. SPSS statistics 17.0.0 and MedCalc version 11.4.2.0 were employed for all statistical analysis.

Results

Patients

A total of 2,067 cirrhotic patients underwent the urinalyses, of whom 2,056 had the data regarding urine leukocyte

count per high-power field (*Table 1*) and 2,031 had the data regarding urine bacteria count per high-power field (*Table 2*).

Urine leukocyte count per high-power field

The prevalence of elevated urine leukocyte count per high-power field was 25.8% (530/2,056). Elevated urine leukocyte count per high-power field was significantly associated with female, etiology of liver diseases, older age, higher blood urea nitrogen (BUN), and lower albumin (ALB), potassium, and gamma-glutamyl transpeptidase (GGT) (*Table 1*). Logistic regression multivariate analysis demonstrated that female (P<0.0001, OR =4.71), ALB (P<0.0001, OR =0.97), and BUN (P<0.0001, OR =1.05) were independently associated with elevated urine leukocyte count per high-power field (*Table 3*).

Elevated urine leukocyte count per high-power field was significantly associated with higher in-hospital mortality. In ROC analysis, the AUROC of urine leukocyte count per high-power field for predicting the in-hospital death was 0.600 (95% CI: 0.579–0.622, P=0.015) (*Figure 1*). The best cut-off value of urine leukocyte count per high-power field was 8.19, with a sensitivity of 34.5% (95% CI: 22.5–48.1%) and a specificity of 84.8% (95% CI: 83.1–86.3%). PLR and NLR were 2.27 (95% CI: 1.6–3.2) and 0.77 (95% CI: 0.6–1.0), respectively. PPV and NPV were 6.2% (95% CI: 3.8–9.4%) and 97.8% (95% CI: 97.0–98.4%), respectively.

Urine bacteria count per high-power field

The prevalence of elevated urine bacteria count per high-power field was 6.7% (137/2,031). Elevated urine bacteria count per high-power field was significantly associated with female, etiology of liver diseases, higher age and BUN, and lower red blood cells, hemoglobin, and ALB (*Table 2*). Logistic regression multivariate analysis demonstrated that female (P<0.0001, OR =3.73), age (P=0.027, OR =1.02), and ALB (P=0.019, OR =0.96) were independently associated with elevated urine bacteria count per high-power field (*Table 4*).

Elevated urine bacteria count per high-power field was significantly associated with higher in-hospital mortality. In ROC analysis, the AUROC of urine bacteria count per high-power field for predicting the in-hospital death was 0.600 (95% CI: 0.578–0.622, P=0.014) (*Figure 2*). The best cut-off value of urine bacteria count per high-power field was 142.04, with a sensitivity of 38.6% (95% CI: 26.0–52.4%) and a specificity of 84.19% (95% CI: 82.5–85.8%). PLR and NLR were 2.44 (95% CI: 1.8–3.4) and 0.73 (95% CI: 0.6–0.9), respectively. PPV and NPV were 6.6% (95% CI: 4.2–9.8%) and 97.9% (95% CI: 97.1–98.6%), respectively.

Discussion

We here demonstrate on a large single-center cohort a high prevalence of elevated urine leukocyte and bacteria count per high-power field of 25.8% and 6.7%, respectively. In addition, these simple screening tests predicted the in-hospital death with a moderate diagnostic accuracy. Although their sensitivity was low, they showed an excellent specificity of >80%.

Urinalysis represents a non-invasive, technically simple, and economic screening tool (12). Lee *et al.* suggested that the presence of at least 5 urine leukocyte counts per high-power field from urine specimen should be pyuria, which was observed in 67% (165/247) of patients(13). Cantey *et al.* pointed that urinalysis was positive if >10 leukocytes per oil immersion field were seen (14). Gieteling *et al.* indicated that the presence of ≥10 leucocytes per high-power field should be helpful for a diagnosis of UTI (15). Thus, urinalysis, such as urine leukocyte and bacteria count per high-power field, may be helpful to establish a rapid diagnosis of UTI in the absence of urine culture. If possible, empirical antibiotic treatment can be rapidly guided by abnormal urinalyses.

The prevalence of UTI in liver cirrhosis patients is 20–25%, which is confirmed on our cohort (3). We included a large number of cirrhotic patients over a 4-year period of time. Therefore, our data may be more generalizable.

The association between UTI and severity of liver dysfunction remained controversial. Previous studies demonstrated that the occurrence of UTI was associated with Child-Pugh score (9,16) and ascites (6,17). By contrast, our and Amato *et al.*'s (18) studies demonstrated that the prevalence of UTI was not significantly associated with liver disease severity. This discrepancy might be explained by the heterogeneity in the sample size, the patient characteristics and the use of diuretics.

It is generally accepted that patients with cirrhosis are susceptible to the development of infectious diseases and that bacterial infection may aggravate the deterioration of patients' conditions, even leading them to death (19). Our study found a significant association between abnormal urinalysis (i.e., elevated urine leukocyte and/or bacteria count per high-power field count) and in-hospital mortality

Table 1 Comparison between normal versus abnormal urine leukocyte count per high–power field in regular urine tests

Variables	Total (n=2,056)			Normal (n=1,526)			Abnormal (n=530)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Sex (male/female), n (%)	2,056	1,357 (66.0%)/ 699 (34.0%)		1,526	1,135 (74.4%)/ 391 (25.6%)		530	222 (41.9%)/ 308 (58.1%)		<0.0001
Age (years)	2,056	56.51±12.14	55.96 (6.20–89.23)	1,526	56.09±11.92	55.65 (6.20–89.23)	530	57.73±12.70	57.25 (14.37–86.84)	0.002
Etiology of liver diseases, n (%)	2,056			1,526			530			<0.0001
HBV		592 (28.8%)			443 (29.0%)			149 (28.1%)		0.688
HCV		134 (6.5%)			86 (5.6%)			48 (9.1%)		0.006
HBV + HCV		14 (0.7%)			8 (0.5%)			6 (1.1%)		0.215
Alcohol		482 (23.4%)			405 (26.5%)			77 (14.5%)		<0.0001
HBV + Alcohol		155 (7.5%)			133 (8.7%)			22 (4.2%)		0.001
HCV + Alcohol		23 (1.1%)			17 (1.1%)			6 (1.1%)		0.973
HBV + HCV + Alcohol		3 (0.1%)			1 (0.1%)			2 (0.4%)		0.165
Others		210 (10.2%)			129 (8.5%)			81 (15.3%)		<0.0001
Unknown		443 (21.5%)			304 (19.9%)			139 (26.2%)		0.002
Ascites, n (%)	2,039			1,516			523			0.635
No		1,034 (50.7%)			764 (50.4%)			270 (51.6%)		0.628
Mild		270 (13.2%)			197 (13.0%)			73 (14.0%)		0.575
Moderate to severe		735 (36.0%)			555 (36.6%)			180 (34.4%)		0.368
HE, n (%)	2,039			1,516			523			0.538
No		1,895 (92.9%)			1,407 (92.8%)			488 (93.3%)		0.702
Grade I–II		119 (5.8%)			88 (5.8%)			31 (5.9%)		0.918
Grade III–IV		25 (1.2%)			21 (1.4%)			4 (0.8%)		0.266

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Total (n=2,056)			Normal (n=1,526)			Abnormal (n=530)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Laboratory tests										
RBC (10^{12}/L)	2,033	3.13±0.84	3.06 (0.90–6.80)	1,512	3.15±0.85	3.10 (0.90–6.80)	521	3.09±0.79	3 (1.10–5.90)	0.331
Hb (g/L)	2,035	95.18±29.37	94 (23–218)	1,514	95.50±30.12	94 (23–218)	521	94.24±27.09	92 (29–176)	0.557
WBC (10^{9}/L)	2,036	5.24±3.89	4.20 (0.30–46.10)	1,515	5.15±3.75	4.10 (0.50–33)	521	5.50±4.27	4.40 (0.30–46.10)	0.140
PLT (10^{9}/L)	2,033	100.65±82.27	78 (10–1,278)	1,512	100.71±83.83	77 (11–1,278)	521	100.47±77.65	79 (10–545)	0.823
TBIL (μmol/L)	2,027	40.83±65.33	22.10 (2–903)	1,508	40.71±62.16	22.40 (2–679.10)	519	41.19±73.85	21.50 (2.40–903)	0.435
ALB (g/L)	1,990	32.19±6.87	32.20 (0.40–52.80)	1,483	32.59±6.82	32.60 (0.40–52.80)	507	1.03±6.87	30.80 (12.40–52.10)	<0.0001
ALT (U/L)	2,023	42.46±79.20	27 (4–1,460)	1,505	42.56±80.31	27 (5–1,460)	518	42.19±75.98	26 (4–1,064)	0.607
AST (U/L)	2,023	58.53±92.46	37 (7–1,399)	1,505	56.12±76.77	36 (7–1,366)	518	65.53±127.38	37 (9–1,399)	0.445
Ammonia (umol/L)	948	50.47±41.93	42 (8–480)	707	50.88±42.28	43 (8–480)	241	49.27±40.95	42 (8–236)	0.443
ALP (U/L)	2,021	115.74±99.36	87 (12.80–980)	1,504	115.01±99.09	87.25 (12.80–980)	517	117.87±100.21	86 (17–889)	0.852
PT (second)	1,996	16.36±4.54	15.40 (10.50–94.60)	1,480	16.26±4.03	15.40 (10.70–62.80)	516	16.65±5.77	15.40 (10.50–94.60)	0.981
APTT (second)	1,994	43.17±10.34	41.80 (21.90–181)	1,479	42.76±8.91	41.70 (26.90–181)	515	44.34±13.60	42 (21.90–181)	0.148
INR	1,993	1.35±0.56	1.22 (0.76–13.40)	1,478	1.33±0.48	1.22 (0.76–7.96)	515	1.39±0.76	1.22 (0.76–13.40)	0.902
GGT (U/L)	2,019	115.89±202.22	50 (5–4,562)	1,502	121.50±216.86	51 (6–4,562)	517	99.62±150.90	47 (5–1,486)	0.037
BUN (mmol/L)	1,990	7.54±6.13	5.81 (1.58–62.45)	1,474	7.20±5.38	5.74 (1.58–61.88)	516	8.52±7.82	6.07 (1.72–62.45)	0.004
Cr (μmol/L)	1,990	82.17±106.60	59 (15–1,473)	1,474	76.57±91.49	60 (21–1473)	516	98.16±140	58.80 (15–1,069)	0.993
K (mmol/L)	2,014	4.04±0.53	4 (2.26–8.28)	1,498	4.05±0.52	4 (2.26–6.85)	516	4.01±0.56	3.96 (2.27–8.28)	0.015
Na (mmol/L)	2,014	138.40±4.40	139 (116.30–160.80)	1,498	138.40±4.16	138.90 (121–152.40)	516	138.37±5.06	139 (116.30–160.80)	0.443
Ca (mmol/L)	983	2.10±0.22	2.10 (1.05–2.94)	720	2.10±0.22	2.11 (1.05–2.89)	263	2.09±0.21	2.09 (1.35–2.94)	0.186

Table 1 *(continued)*

Table 1 *(continued)*

Variables	Total (n=2,056)			Normal (n=1,526)			Abnormal (n=530)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Child–Pugh class, n (%)	1,912			1,427			485			0.467
A		690 (36.1%)			515 (36.1%)			175 (36.1%)		0.998
B		896 (46.9%)			677 (47.4%)			219 (45.2%)		0.383
C		326 (17.1%)			235 (16.5%)			91 (18.8%)		0.246
Child–Pugh score	1,912	7.54±2.04	7 (5–15)	1,427	7.51±2	7 (5–15)	485	7.63±2.16	7 (5–14)	0.490
MELD score	1,936	7.50±7.39	6.14 (–9.67–54.94)	1,433	7.29±6.70	6.17 (–8.25–42.04)	503	8.12±9.07	6.11 (–9.67–54.94)	0.769
HPF–WBC (HPF)	2,056	24.25±255.62	1.46 (0.02–8,946.90)	1,526	1.25±1.02	0.92 (0.02–4.28)	530	90.49±497.90	10.95 (4.43–8,946.90)	<0.0001
HPF–Bacteria (HPF)	2,031	272.53±1,107.03	7.13 (0.07–15,329.21)	1,506	106.16±538.29	3.98 (0.07–9,608.11)	525	749.75±1,899.42	42.19 (0.32–15,329.21)	<0.0001
Death, n (%)	2,056	58 (2.8%)		1,526	35 (2.3%)		530	23 (4.3%)		0.014

ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Ca, calcium ion; Cr, creatinine; GGT, gamma–glutamyl transpeptidase; Hb, hemoglobin; HE, hepatic encephalopathy; HPF, high–power field; INR, international normalized ratio; K, potassium; MELD, model for end stage liver disease; Na, sodium ion; PLT, platelet; PT, prothrombin time; Pts, patients; RBC, red blood cell; TBIL, total bilirubin; WBC, white blood cell.

Table 2 Comparison between normal versus abnormal urine bacteria count per high–power field in regular urine tests

Variables	Total (n=2,031)			Normal (n=1894)			Abnormal (n=137)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Sex (male/female), n (%)	2,031	1,342 (66.1%)/ 689 (33.9%)		1,894	1,298 (68.5%)/ 596 (31.5%)		137	44 (32.1%)/ 93 (67.9%)		<0.0001
Age (years)	2,031	56.46±12.15	55.96 (6.20–89.23)	1,894	56.16±12.13	55.66 (6.20–89.23)	137	60.73±11.63	61.02 (30.30–85.38)	<0.0001
Etiology of liver diseases, n (%)	2,031			1,894			137			0.001
HBV		583 (28.7%)			546 (28.8%)			37 (27.0%)		0.649
HCV		133 (6.5%)			125 (6.6%)			8 (5.8%)		0.728
HBV + HCV		14 (0.7%)			12 (0.6%)			2 (1.5%)		0.243
Alcohol		476 (23.4%)			453 (23.9%)			23 (16.8%)		0.057
HBV + Alcohol		155 (7.6%)			153 (8.1%)			2 (1.5%)		0.005
HCV + Alcohol		23 (1.1%)			23 (1.2%)			0 (0.0%)		0.398
HBV + HCV + Alcohol		3 (0.1%)			3 (0.2%)			0 (0.0%)		1.000
Others		209 (10.3%)			189 (10.0%)			20 (14.6%)		0.086
Unknown		435 (21.4%)			390 (20.6%)			45 (32.8%)		0.001
Ascites, n (%)	2,014			1,878			136			0.308
No		1,021 (50.7%)			953 (50.7%)			68 (50.0%)		0.867
Mild		268 (13.3%)			255 (13.6%)			13 (9.6%)		0.183
Moderate to Severe		725 (36.0%)			670 (35.7%)			55 (40.4%)		0.264
HE, n (%)	2,014			1,879			135			0.146
No		1,870 (92.9%)			1,749 (93.1%)			121 (89.6%)		0.133
Grade I–II		119 (5.9%)			106 (5.6%)			13 (9.6%)		0.058
Grade III–IV		25 (1.2%)			24 (1.3%)			1 (0.7%)		1.000

Table 2 *(continued)*

Table 2 *(continued)*

Variables	Total (n=2,031)			Normal (n=1894)			Abnormal (n=137)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Laboratory tests										
RBC (10^{12}/L)	2,008	3.13±0.84	3.06 (0.93–6.78)	1,876	3.14±0.84	3.08 (0.93–6.78)	132	2.98±0.81	2.88 (1.25–5.57)	0.028
Hb (g/L)	2,008	95.13±29.33	93 (23–218)	1,876	95.56±29.40	94 (23–218)	132	88.97±27.73	86 (29–159)	0.011
WBC (10^{9}/L)	2,008	5.24±3.90	4.20 (0.30–46.10)	1,876	5.25±3.92	4.20 (0.50–46.10)	132	5.17±3.72	4.20 (0.30–26.30)	0.661
PLT (10^{9}/L)	2,008	100.70±82.38	77.50 (10–1278)	1,876	101.10±83.23	78 (10–1278)	132	94.99±69.23	74.50 (13–443)	0.641
TBIL (μmol/L)	2,003	40.56±64.85	22 (2–903)	1,869	39.99±64.12	22.20 (2–903)	134	48.58±74.14	20.70 (5.30–383.20)	0.827
ALB (g/L)	1,967	32.22±6.84	32.20 (0.40–52.80)	1,837	32.33±6.85	32.40 (0.40–52.80)	130	30.60±6.48	30.50 (15.20–47.30)	0.004
ALT (U/L)	1,999	42.49±79.62	27 (4–1,460)	1,865	42.17±77.74	27 (4–1460)	134	46.94±102.54	24 (7–748)	0.186
AST (U/L)	1,999	58.35±92.63	37 (7–1,399)	1,865	57.04±82.75	37 (7–1366)	134	76.56±180.47	36 (10–1,399)	0.801
Ammonia (μmol/L)	1,999	58.35±92.63	37 (7–1,399)	1,865	57.04±82.75	37 (7–1366)	134	76.56±180.47	36 (10–1,399)	0.801
ALP (U/L)	903	52.05±42.15	43 (9–480)	847	51.68±42.05	43 (9–480)	56	57.70±43.63	48 (9–236)	0.241
PT (second)	1,973	16.35±4.51	15.40 (10.50–94.60)	1,838	16.35±4.56	15.40 (10.50–94.60)	135	16.39±3.76	15.50 (11.50–38.90)	0.598
APTT (second)	1,968	42.96±8.87	41.80 (21.90–152.70)	1,834	42.92±8.84	41.80 (21.90–152.70)	134	43.53±9.31	41.50 (28–81.70)	0.610
INR	1,970	1.35±0.56	1.22 (0.76–13.40)	1,835	1.35±0.57	1.22 (0.76–13.40)	135	1.34±0.43	1.23 (0.84–4.13)	0.615
GGT (U/L)	1,994	115.94±203.16	50 (5–4,562)	1,860	117.91±208.15	50 (5–4,562)	134	88.59±110.11	51.50 (8–709)	0.348
BUN (mmol/L)	1,967	7.55±6.14	5.82 (1.58–62.45)	1,835	7.48±6.05	5.80 (1.58–62.45)	132	8.53±7.28	6.25 (1.95–44.34)	0.035
Cr (μmol/L)	1,967	81.72±105.07	59 (15–1,473)	1,835	81.35±103.68	60 (15–1,473)	132	86.99±123.10	56 (29–919)	0.301
K (mmol/L)	1,992	4.04±0.53	4 (2.26–8.28)	1,858	4.04±0.53	4 (2.27–8.28)	134	3.96±0.47	3.96 (2.26–5.38)	0.075
Na (mmol/L)	1,992	138.38±4.56	139 (83–160.80)	1,858	138.42±4.50	139 (83–160.80)	134	137.85±5.37	138.90 (116.30–148)	0.484
Ca (mmol/L)	970	2.10±0.22	2.10 (1.05–2.94)	895	2.09±0.22	2.10 (1.05–2.94)	75	2.12±0.20	2.10 (1.76–2.62)	0.341

Table 2 *(continued)*

Table 2 *(continued)*

Variables	Total (n=2,031)			Normal (n=1894)			Abnormal (n=137)			P value
	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	No. Pts available	Mean ± SD or frequency (percentage)	Median (range)	
Child–Pugh class, n (%)	1,891			1,764			127			0.516
A		685 (36.2%)			643 (36.5%)			42 (33.1%)		0.444
B		884 (46.7%)			825 (46.8%)			59 (46.5%)		0.946
C		322 (17.0%)			296 (16.8%)			26 (20.5%)		0.285
Child–Pugh score	1,891	7.54±2.04	7 (5–15)	1,764	7.52±2.03	7 (5–15)	127	7.83±2.18	8 (5–14)	0.149
MELD score	1,915	7.46±7.35	6.11 (–9.67–54.94)	1,787	7.43±7.31	6.12 (–9.67–54.94)	128	7.90±7.93	6.11 (–4.56–35.30)	0.795
HPF–WBC (HPF)	2,031	24.50±257.18	1.44 (0.02–8,946.90)	1,894	10.69±74.88	1.35 (0.02–2,417.09)	137	215.38±932.64	14.09 (0.20–8,946.90)	<0.0001
HPF–Bacteria (HPF)	2,031	272.53±1,107.03	7.13 (0.07–15,329.21)	1,894	56.18±139.60	5.58 (0.07–965.90)	137	3,263.51±2,890.99	2,213.55 (992.68–15,329.21)	<0.0001
Death, n (%)	2,031	57 (2.8%)		1,894	47 (2.5%)		137	10 (7.3%)		0.004

ALB, albumin; ALP, alkaline phosphatase; ALT, alanine aminotransferase; APTT, activated partial thromboplastin time; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Ca, calcium ion; Cr, creatinine; GGT, gamma–glutamyl transpeptidase; Hb, hemoglobin; HE, hepatic encephalopathy; HPF, high–power field; INR, international normalized ratio; K, potassium; MELD, model for end stage liver disease; Na, sodium ion; PLT, platelet; PT, prothrombin time; Pts, patients; RBC, red blood cell; TBIL, total bilirubin; WBC, white blood cell.

Table 3 Univariable and multivariable logistic analysis of abnormal urine leukocyte count per high–power field

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
HCV as an etiology of liver diseases				
Sex	4.03 (3.27–4.96)	<0.0001	4.76 (3.77–6.00)	<0.0001
Age	1.01 (1.00–1.02)	0.007	0.99 (0.98–1.00)	0.071
HCV	0.60 (0.42–0.87)	0.006	0.77 (0.51–1.15)	0.195
ALB	0.97 (0.95–0.98)	<0.0001	0.97 (0.95–0.98)	<0.0001
GGT	0.99 (0.99–1.00)	0.032	1.00 (0.99–1.00)	0.311
BUN	1.03 (1.02–1.05)	<0.0001	1.05 (1.03–1.06)	<0.0001
K	0.85 (0.70–1.02)	0.086		
Alcohol as an etiology of liver diseases				
Sex	4.03 (3.27–4.96)	<0.0001	4.64 (3.62–5.95)	<0.0001
Age	1.01 (1.00–1.02)	0.007	0.99 (0.98–1.00)	0.085
Alcohol	2.13 (1.63–2.78)	<0.0001	1.13 (0.83–1.55)	0.436
ALB	0.97 (0.95–0.98)	<0.0001	0.97 (0.95–0.98)	<0.0001
GGT	0.99 (0.99–1.00)	0.032	1.00 (0.99–1.00)	0.322
BUN	1.03 (1.02–1.05)	<0.0001	1.05 (1.03–1.06)	<0.0001
K	0.85 (0.70–1.02)	0.086		
HBV + Alcohol as an etiology of liver diseases				
Sex	4.03 (3.27–4.96)	<0.0001	4.74 (3.75–6.01)	<0.0001
Age	1.01 (1.00–1.02)	0.007	0.99 (0.98–1.00)	0.080
HBV + Alcohol	2.21 (1.39–3.50)	0.001	1.16 (0.71–1.89)	0.563
ALB	0.97 (0.95–0.98)	<0.0001	0.97 (0.95–0.98)	<0.0001
GGT	0.99 (0.99–1.00)	0.032	1.00 (0.99–1.00)	0.260
BUN	1.03 (1.02–1.05)	<0.0001	1.05 (1.03–1.06)	<0.0001
K	0.85 (0.70–1.02)	0.086		

ALB, albumin; BUN, blood urea nitrogen; GGT, gamma–glutamyl transpeptidase; HBV, hepatitis B virus; HCV, hepatitis C virus; K, potassium.

of cirrhotic patients. Indeed, in our patients, 23 of 58 deaths had an elevated urine leukocyte count per high-power field. Similarly, a retrospective observational cohort study also demonstrated an association of UTI with increased short-term mortality in patients with advanced cirrhosis (6). Despite the direct contribution of UTI to the risk of death in cirrhotic patients remained uncertain, abnormal urinalysis might be a predictor of worse prognosis. Evidence suggested that 42% of advanced liver disease patients with UTI have systemic inflammatory response syndrome (20) and that UTI is a strong reason for progressive renal failure in cirrhosis (21).

Our study had some limitations. First, we recorded urine leukocyte count per high-power field of >4.33. Abnormal urinalysis is not exactly equal to positive urine culture (22). Thus, our study could not accurately identify the diagnosis of UTI. Second, there was a potential risk of urine specimens' contamination. Third, the symptoms related to UTI (i.e., fever, urinary frequency, and urinary urgency) were missing.

In conclusion, an elevated urine leukocyte and/or

Table 4 Univariable and multivariable logistic analysis of abnormal urine bacteria count per high–power field

Variables	Univariable analysis		Multivariable analysis	
	OR (95% CI)	P	OR (95% CI)	P
Sex	4.60 (3.18–6.67)	<0.0001	3.73 (2.50–5.58)	<0.0001
Age	1.03 (1.02–1.05)	<0.0001	1.02 (1.00–1.03)	0.027
HBV + Alcohol	5.93 (1.45–24.19)	0.013	2.34 (0.56–9.82)	0.245
ALB	0.96 (0.94–0.99)	0.005	0.96 (0.93–0.99)	0.019
RBC	0.79 (0.64–0.99)	0.037	1.33 (0.81–2.19)	0.262
Hb	0.99 (0.99–1.00)	0.013	0.99 (0.98–1.00)	0.095
BUN	1.02 (0.99–1.05)	0.062		

ALB, albumin; BUN, blood urea nitrogen; Hb, hemoglobin; HBV, hepatitis B virus; RBC, red blood cell.

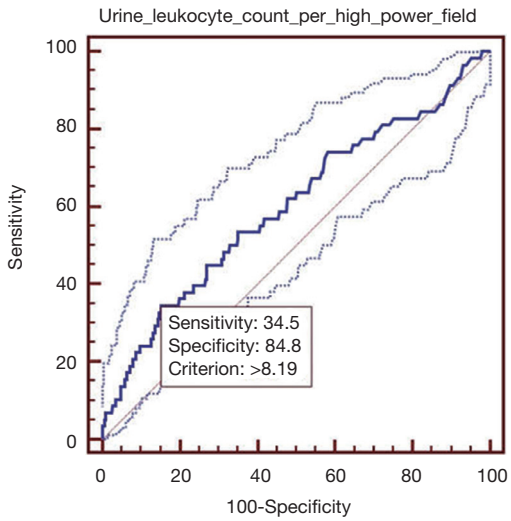

Figure 1 ROC analysis of the urine leukocyte count per high-power field for predicting the in-hospital mortality. ROC, receiver-operator characteristic.

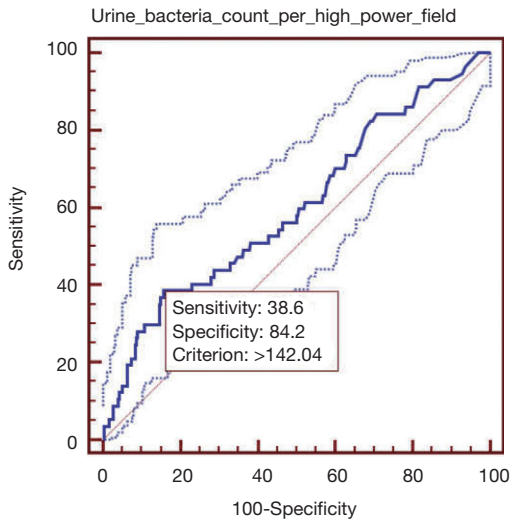

Figure 2 ROC analysis of the urine bacteria count per high-power field for predicting the in-hospital mortality. ROC, receiver-operator characteristic.

bacteria count per high-power field may be an adjuvant diagnostic criterion for UTI and should be a predictor for the in-hospital death in patients with liver cirrhosis. In future, some novel noninvasive screening tools for liver damage, such as M30 levels (23), or for liver fibrosis, such as transient elastography (24), should be combined with UTI to further evaluate the disease progression and outcome of liver cirrhosis.

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Footnote

Conflicts of Interest: All authors have completed the ICMJE uniform disclosure form (available at http://dx.doi.org/10.21037/jphe.2017.08.02). The authors have no conflicts of interest to declare.

Ethical Statement: The authors are accountable for all

aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013).The study protocol was approved by the ethic committee of our hospital. The number of ethical approval was k (2017) 02. Patients' informed consents were waived.

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