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Original Article

Association between type 2 diabetes mellitus and Klebsiella pneumoniae colonization: construction of nomogram model

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Abstract: Objective: To investigate the association between the basic and clinical characteristics of patients with type 2 diabetes mellitus (T2DM) and their susceptibility to Klebsiella pneumoniae colonization (KPC). Additionally, a clinical prediction model was developed to identify high-risk patients for KPC. Methods: Data from 486 T2DM patients who visited Shanghai Fifth People's Hospital from December 2020 to December 2022 were retrospectively collected. Patients were classified into the KPC group and normal group based on their Klebsiella pneumoniae test results. Differences between the two groups were analyzed using t-test and chi-square test. Logistic regression was performed to identify factors influencing KPC susceptibility in T2DM patients, with odds ratios (ORs) calculated. A clinical prediction model was constructed using a nomogram and evaluated through the area under the receiver operating characteristic (ROC) curve (AUC), Hosmer-Lemeshow test, calibration curve, and decision curve analysis (DCA). Results: Of the 486 T2DM patients, 124 were found to have KPC, with a colonization rate of 25.51%. Logistic regression analysis revealed that hospitalization within the past six months, elevated white blood cell count, decreased hemoglobin, and elevated ferritin levels were independent risk factors for KPC. Thyroid and liver function indicators were also associated with KPC susceptibility. The clinical prediction model achieved an AUC of 0.74 (95% CI: 0.68-0.80). The calibration curve indicated no significant differences between observed and predicted values, suggesting that the model effectively identifies high-risk KPC patients. Conclusion: T2DM patients are at an increased risk of secondary KPC. Identifying key risk factors for KPC in T2DM patients has significant clinical implications for early identification, targeted interventions, and individualized treatment strategies.

Keywords: Type 2 diabetes mellitus, Klebsiella pneumoniae, colonization, clinical prediction model

Introduction

Type 2 diabetes mellitus (T2DM) is a chronic metabolic disorder characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia [1]. With rapid global economic development and lifestyle changes, T2DM has become a critical public health challenge, with increasing prevalence and associated mortality [2]. Representing more than 90% of all diabetes cases, T2DM significantly impacts patients' quality of life and life expectancy due to its severe complications [3]. Studies have established T2DM as a major risk factor for cardiovascular diseases, including heart disease and stroke [4]. Furthermore, prolonged hyperglycemia contributes to chronic kidney disease, retinopathy, neuropathy, and other debilitating complications [5].

Klebsiella pneumoniae (KP), a gram-negative bacterium, is widely present in both community and healthcare settings and is known for its high pathogenicity and multidrug resistance [6]. Recent research highlights diabetes as a key risk factor for KP infections [7]. This underscores the complex interplay between T2DM and infection risk, emphasizing the need for effective prevention and intervention strategies.

Chronic hyperglycemia in T2DM patients often leads to complications such as immune dysfunction, microvascular damage, and neuropa-

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thy. These pathological changes increase susceptibility to infections by opportunistic pathogens like KP [8]. The altered microenvironment in diabetic patients, characterized by acidosis and nutrient-rich tissue fluids, facilitates KP colonization and proliferation.

In some T2DM patients, KP can be detected in urine, stool, or respiratory tract samples without manifesting clinical symptoms, a condition termed KPC. Secondary KPC is associated with higher risks of infection and worse clinical outcomes. KPC in T2DM patients not only leads to localized infections, such as pneumonia and urinary tract infections, but may also disseminate systemically through the bloodstream, resulting in severe complications such as sepsis and endophthalmitis [9].

Early identification and management of KPC are crucial for preventing diabetes-related infections and reducing associated morbidity. However, clinicians currently lack effective predictive tools for assessing the risk of KP colonization in T2DM patients. This limitation hampers timely intervention and personalized treatment, highlighting the urgent need for improved risk prediction models and tailored management strategies.

This study aims to comprehensively investigate the association between the clinical status of T2DM and KPC by analyzing demographic and clinical characteristics in T2DM patients. A clinical prediction model was developed using multiple regression analysis to identify high-risk T2DM patients with KPC. This model is expected to provide clinicians with a practical tool to identify individuals at high risk of KPC, enabling targeted preventive measures to reduce infection rates and improve patient outcomes. In addition, this study aims to provide insights into the underlying mechanisms of T2DM and KPC, offering theoretical support for diabetes prevention and treatment strategies.

Materials and methods

Patient population

This retrospective study included 486 T2DM patients admitted to Shanghai Fifth People's Hospital from December 2020 to December 2022.

Inclusion criteria: (1) Diagnosed with T2DM according to the Chinese Guidelines for the Prevention and Treatment of Type 2 Diabetes (2020) [10]; (2) Aged 18-75 years; (3) Absence of severe underlying diseases or cancer; (4) No obvious clinical symptoms of KP infection; (5) Availability of complete clinical data.

Exclusion criteria: (1) Pregnancy or nursing; (2) Use of antibiotics or immunomodulatory drugs within the past two weeks; (3) Presence of severe complications or comorbidities; (4) History of mental illness.

Fecal samples were collected from all participants for KP culture. Patients with positive culture results were assigned to the KPC group, while those with negative results were classified as the normal group. Ethical approval was obtained from the Ethics Committee of Shanghai Fifth People's Hospital.

Data collection

Demographic and clinical data collected included: General demographics: age, sex, BMI, T2DM duration, history of hypertension, smoking, alcohol consumption, and hospitalization within six months. Clinical indicators: white blood cell count (WBC), neutrophil count (NC), hemoglobin (Hb), fasting blood glucose (FBG), alanine aminotransferase (ALT), aspartate aminotransferase (AST), creatinine (Cr), uric acid (UA), ferritin, fructosamine, thyroid-stimulating hormone (TSH), fasting insulin (FINS), and fasting C-peptide (FCP).

Statistical analysis

Quantitative variables were expressed as mean ± standard deviation and compared using independent samples t-tests. Qualitative variables were expressed as frequencies and percentages, with differences analyzed using Pearson's chi-square test. Logistic regression analysis assessed the association between various factors and the risk of T2DM combined with KPC, providing odds ratios (ORs) and 95% confidence intervals (CIs). Variables with $P < 0.05$ in univariate logistic regression were included in the multivariate logistic regression analysis. Variance inflation factors (VIF) were calculated to assess collinearity in multivariate models. Statistical analyses were conducted

using SPSS (version 27.0) and R (version 4.2.1). All tests were two-sided, with $P < 0.05$ considered statistically significant.

Model development and evaluation

The original dataset was randomly divided into a training set and an internal test set using a 7:3 ratio based on a random number method. Additionally, the case collection period was extended by six months to collect an external test set. A total of 96 patients were included in the external test set from January 2023 to June 2023. The training and test sets were assessed for balance. Logistic regression analysis was performed on the training set, and variables with $P < 0.10$ were included in the construction of the nomogram and the Receiver Operating Characteristic (ROC) curve.

The area under the ROC curve (AUC) was used to evaluate the discriminatory power of the prediction model. The Hosmer-Lemeshow goodness-of-fit test and calibration curve were employed to assess the model's calibration. Decision curve analysis (DCA) was conducted, with treatment decision threshold probabilities as the horizontal axis and net benefit as the vertical axis, to evaluate the clinical utility of the prediction model across different thresholds. In addition, the accuracy, sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated to comprehensively assess the model's performance.

Results

General information

A total of 486 T2DM patients were included in the study. Based on KP test results, 362 patients were assigned to the normal group, while 124 patients were assigned to the KPC group, corresponding to a KPC rate of 25.51% (**Table 1**). The mean age of the normal and KPC groups was 62.66 ± 14.09 years and 62.83 ± 13.66 years, respectively, with no significant difference (P=0.905). The proportion of males was similar in both groups (55.25% vs. 54.03%, P=0.814). The mean BMI values for the normal and KPC groups were 24.70 ± 3.59 and 24.52 ± 3.70, respectively, with no significant difference (P=0.633) (**Table 1**).

Difference analysis between the two groups

Among the normal group, 28 patients (7.73%) had been hospitalized within six months, compared to 23 patients (18.55%) in the KPC group, showing a significant difference ($P < 0.001$) (**Table 1**). The WBC level was significantly higher in the KPC group (6.51 ± 2.13) compared to the normal group (5.79 ± 1.77, $P < 0.001$). The Hb level was lower in the KPC group (131.90 ± 15.75) than that in the normal group (136.22 ± 16.95, P=0.013). Additionally, significant differences were observed for UA (P=0.039), ferritin ($P < 0.001$), and TSH (P=0.040) between the two groups. However, no significant differences were found in T2DM duration, hypertension, smoking, alcohol consumption, neutrophil count, FBG, ALT, AST, Cr, fructosamine, or fasting C-peptide (all $P > 0.05$).

Logistic regression analysis

Univariate logistic regression identified several potential risk factors for KPC, including hospitalization within six months, elevated WBC, decreased Hb, elevated ferritin, and elevated TSH (**Table 2**). Multivariate logistic regression further confirmed that hospitalization within six months significantly increased the risk of KPC (OR=3.00, 95% CI: 1.54-5.82, P=0.001). Elevated WBC (OR=1.22, 95% CI: 1.08-1.38, P=0.001), decreased Hb (OR=0.98, 95% CI: 0.97-0.99, P=0.022), and elevated ferritin (OR=1.01, 95% CI: 1.01-1.01, $P < 0.001$) were also identified as independent risk factors.

Construction of clinical prediction model

All participants were randomly divided into a training set and a test set. The clinical prediction model was developed based on the results of multivariate logistic regression analysis using the training set data. The model included the following predictors: hospitalization within six months, WBC, Hb, ALT, AST, and ferritin. These predictors were visualized in a nomogram (**Figure 1**).

Balance check between training and validation sets

To ensure the statistical comparability of the training and test sets, the raw data were split

Table 1. Difference analysis between normal group and KPC group

Variables	Total (n=486)	Normal group (n=362)	KPC group (n=124)	Statistic	*P*
Age, Mean ± SD	62.70 ± 13.97	62.66 ± 14.09	62.83 ± 13.66	t=-0.12	0.905
Sex, n (%)				χ^2=0.06	0.814
Female	219 (45.06)	162 (44.75)	57 (45.97)		
Male	267 (54.94)	200 (55.25)	67 (54.03)		
BMI, Mean ± SD	24.65 ± 3.62	24.70 ± 3.59	24.52 ± 3.70	t=0.48	0.633
Course of T2DM, Mean ± SD	12.00 ± 8.34	11.58 ± 7.79	13.21 ± 9.72	t=-1.69	0.093
Hypertension, n (%)				χ^2=0.31	0.579
No	226 (46.50)	171 (47.24)	55 (44.35)		
Yes	260 (53.50)	191 (52.76)	69 (55.65)		
Smoking, n (%)				χ^2=0.61	0.436
No	388 (79.84)	286 (79.01)	102 (82.26)		
Yes	98 (20.16)	76 (20.99)	22 (17.74)		
Drinking, n (%)				χ^2=1.01	0.315
No	449 (92.39)	337 (93.09)	112 (90.32)		
Yes	37 (7.61)	25 (6.91)	12 (9.68)		
Hospitalized within six months, n (%)				χ^2=11.50	< 0.001
No	435 (89.51)	334 (92.27)	101 (81.45)		
Yes	51 (10.49)	28 (7.73)	23 (18.55)		
WBC, Mean ± SD	5.98 ± 1.90	5.79 ± 1.77	6.51 ± 2.13	t=-3.38	< 0.001
NC, Mean ± SD	3.54 ± 1.57	3.48 ± 1.47	3.72 ± 1.85	t=-1.26	0.210
Hb, Mean ± SD	135.11 ± 16.75	136.22 ± 16.95	131.90 ± 15.75	t=2.49	0.013
FBG, Mean ± SD	7.84 ± 3.18	7.72 ± 3.09	8.21 ± 3.39	t=-1.52	0.130
ALT, Mean ± SD	21.88 ± 16.00	21.12 ± 16.20	24.09 ± 15.27	t=-1.78	0.075
AST, Mean ± SD	19.24 ± 12.94	18.61 ± 13.11	21.07 ± 12.29	t=-1.82	0.069
Cr, Mean ± SD	77.08 ± 29.78	78.32 ± 30.98	73.45 ± 25.75	t=1.72	0.086
UA, Mean ± SD	305.84 ± 96.04	310.60 ± 100.37	291.97 ± 80.89	t=2.08	0.039
Ferritin, Mean ± SD	302.15 ± 214.76	266.59 ± 196.37	405.96 ± 232.57	t=-5.98	< 0.001
Fructosamine, Mean ± SD	409.53 ± 109.78	412.72 ± 111.62	400.21 ± 104.09	t=1.09	0.274
TSH, Mean ± SD	2.63 ± 2.06	2.51 ± 2.05	2.96 ± 2.05	t=-2.06	0.040
Fasting C-peptide, Mean ± SD	0.63 ± 0.45	0.65 ± 0.47	0.59 ± 0.35	t=1.26	0.209

Abbreviations: KPC, Klebsiella pneumoniae colonization; SD, standard deviation; BMI, body mass index; T2DM, type 2 diabetes mellitus; WBC, white blood cell; NC, neutrophil cell; Hb, hemoglobin; FBG, fasting blood glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; UA, uric acid; TSH, thyroid stimulating hormone.

into a 7:3 ratio, and the two groups were compared for differences in basic and clinical features. The results showed no significant differences (P > 0.05), confirming that the two groups were balanced (**Table 3**).

Difference analysis and regression analysis of training set

In the training set, significant differences between the normal and KPC groups were observed for hospitalization within six months (P=0.001), WBC (P=0.029), ALT (P=0.045) and ferritin (P < 0.001) (**Table 4**). Regression analysis revealed that the following factors were associated with an increased risk of KPC: Hospitalization within six months (OR=4.26, 95% CI: 1.91-9.48, P < 0.001); High WBC levels (OR=1.19, 95% CI: 1.03-1.37, P=0.015); Elevated ALT levels (OR=1.02, 95% CI: 1.01-1.04, P=0.012); Elevated ferritin levels (OR=1.01, 95% CI: 1.01-1.01, P < 0.001) (**Table 5**).

Model evaluation

The ROC curve of the prediction model yielded an AUC value of 0.74 (95% CI: 0.68-0.80) (**Figure 2A**), indicating good discriminatory power. The Hosmer-Lemeshow goodness-of-fit test (P=0.650) and the calibration curve showed no significant differences between observed and predicted values, confirming

Table 2. Logistic regression analysis of T2DM patients with KPC

Variables	Univariate Logistic regression					Multivariate Logistic regression				
	β	S.E.	Z	*P*	OR (95% CI)	β	S.E.	Z	*P*	OR (95% CI)
Hospitalized within six months										
No					1.00 (Reference)					1.00 (Reference)
Yes	1.00	0.30	3.29	< 0.001	2.72 (1.50-4.92)	1.10	0.34	3.24	0.001	3.00 (1.54-5.82)
WBC	0.20	0.06	3.60	< 0.001	1.22 (1.10-1.37)	0.20	0.06	3.20	0.001	1.22 (1.08-1.38)
Hb	-0.02	0.01	-2.47	0.014	0.98 (0.97-0.99)	-0.02	0.01	-2.29	0.022	0.98 (0.97-0.99)
Ferritin	0.01	0.00	5.94	< 0.001	1.01 (1.01-1.01)	0.01	0.00	5.69	< 0.001	1.01 (1.01-1.01)
TSH	0.10	0.05	2.05	0.041	1.11 (1.01-1.22)	0.09	0.06	1.68	0.093	1.10 (0.98-1.23)

Abbreviations: KPC, Klebsiella pneumoniae colonization; T2DM, type 2 diabetes mellitus; OR, odds ratio; CI, confidence interval; WBC, white blood cell; NC, neutrophil cell; Hb, hemoglobin; TSH, thyroid stimulating hormone.

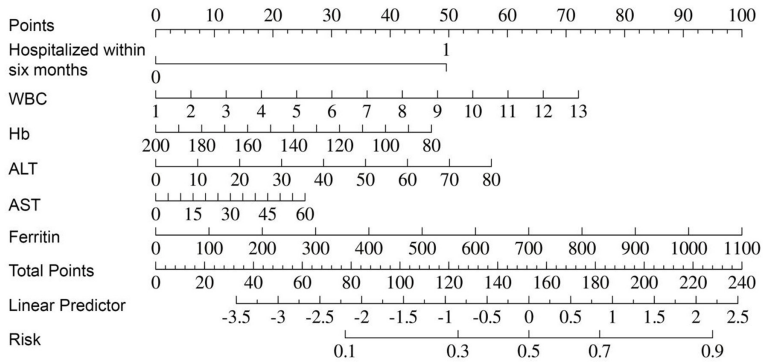

Figure 1. A nomogram of the clinical predictive model.

good model calibration (**Figure 2D**). Decision curve analysis (DCA) demonstrated that the model provided a positive net benefit for patients within a threshold probability range of 0.1-1.0 (**Figure 2G**).

Model validation

The internal validation set included 146 T2DM patients, of whom 36 were KPC-positive, resulting in a KPC rate of 24.66%. The AUC of the internal test set was 0.76 (95% CI: 0.66-0.86) (**Figure 2B**). The Hosmer-Lemeshow goodness-of-fit test (P=0.290) and the calibration curve results showed that the model fits well (**Figure 2E**). DCA indicated a positive net benefit within the probability range of 0.1-1.0 (**Figure 2H**).

The external test set included 96 patients, of whom 25 were KPC-positive, corresponding to a KPC rate of 26.04%. The external test set's AUC was 0.75 (95% CI: 0.62-0.87) (**Figure 2C**). The Hosmer-Lemeshow goodness-of-fit test result was 0.078 (**Figure 2F**). The DCA results showed that the model provided good net returns within the threshold probability range of 0.2-1.0 (**Figure 2I**).

Confusion matrix analysis of the training, internal test, and external test sets

In the training set, the clinical prediction model demonstrated an accuracy of 0.65 (95% CI: 0.59-0.70). Sensitivity and specificity were 0.59 (95% CI: 0.53-0.65) and 0.82 (95% CI: 0.74-0.90), respectively. Positive predictive value (PPV) and negative predictive value (NPV) were 0.90 (95% CI: 0.86-0.95) and 0.41 (95% CI: 0.34-0.48), respectively (**Table 6**).

In the internal test set, the accuracy was 0.63 (95% CI: 0.55-0.71). Sensitivity and specificity were 0.57 (95% CI: 0.48-0.67) and 0.81 (95% CI: 0.68-0.93), respectively. PPV and NPV were 0.90 (95% CI: 0.83-0.97) and 0.38 (95% CI: 0.27-0.49), respectively.

For the external test set, the model exhibited an accuracy of 0.80 (95% CI: 0.71-0.88). Sensitivity, specificity, PPV, and NPV were 0.85 (95% CI: 0.76-0.93), 0.68 (95% CI: 0.50-0.86), 0.88 (95% CI: 0.81-0.96), and 0.61 (95% CI: 0.43-0.79), respectively (**Table 6**).

Discussion

T2DM is a chronic metabolic disease characterized by insulin resistance and impaired insulin secretion, leading to persistent hyperglycemia [11]. T2DM accounts for over 90% of diabetes cases and damages multiple organs, including the kidneys, cardiovascular system, nervous system, and eyes. It also increases susceptibility to infections [12]. Hyperglycemia impairs immune defenses by reducing alveolar macrophages' recognition and adhesion abilities and restricting lysozyme synthesis, which weakens antibacterial functions [13]. Additionally, hyperglycemia compromises immune cell phagocytosis, further reducing infection resistance [14].

This study identified several risk factors associated with KPC in T2DM patients: hospitalization within the past six months, elevated WBC levels, reduced Hb levels, and increased ferritin and TSH levels. A clinical prediction model was constructed based on these factors and demonstrated good predictive performance.

Recent hospitalization is a well-recognized risk factor for healthcare-associated infections due to increased exposure to resistant pathogens [15]. Reports indicate that KP infections account for approximately one-third of Gram-negative bacterial infections in hospitalized patients, with a high risk of developing drug-resistant strains [16, 17]. In T2DM patients, the microenvironmental changes, including acidic tissue fluids and nutrient abundance, facilitate

Table 3. Balance check between training and testing sets

Variables	Total (n=486)	test (n=146)	train (n=340)	Statistic	*P*
Age, Mean ± SD	62.70 ± 13.97	61.71 ± 14.85	63.13 ± 13.58	t=-1.03	0.303
Sex, n (%)				χ^2=0.00	0.967
No	219 (45.06)	66 (45.21)	153 (45.00)		
Yes	267 (54.94)	80 (54.79)	187 (55.00)		
BMI, Mean ± SD	24.65 ± 3.62	24.83 ± 3.82	24.57 ± 3.53	t=0.72	0.470
Course of T2DM, Mean ± SD	12.00 ± 8.34	12.09 ± 8.64	11.96 ± 8.22	t=0.16	0.875
Hypertension, n (%)				χ^2=0.00	0.983
No	226 (46.50)	68 (46.58)	158 (46.47)		
Yes	260 (53.50)	78 (53.42)	182 (53.53)		
Smoking, n (%)				χ^2=0.72	0.396
No	388 (79.84)	120 (82.19)	268 (78.82)		
Yes	98 (20.16)	26 (17.81)	72 (21.18)		
Drinking, n (%)				χ^2=0.17	0.677
No	449 (92.39)	136 (93.15)	313 (92.06)		
Yes	37 (7.61)	10 (6.85)	27 (7.94)		
Hospitalized within six months, n (%)				χ^2=1.41	0.235
No	435 (89.51)	127 (86.99)	308 (90.59)		
Yes	51 (10.49)	19 (13.01)	32 (9.41)		
WBC, Mean ± SD	5.98 ± 1.90	5.97 ± 1.93	5.98 ± 1.89	t=-0.08	0.936
NC, Mean ± SD	3.54 ± 1.57	3.54 ± 1.60	3.55 ± 1.56	t=-0.04	0.968
Hb, Mean ± SD	135.11 ± 16.75	136.87 ± 16.67	134.36 ± 16.75	t=1.52	0.130
FBG, Mean ± SD	7.84 ± 3.18	7.57 ± 2.99	7.96 ± 3.25	t=-1.22	0.221
ALT, Mean ± SD	21.88 ± 16.00	22.48 ± 15.57	21.62 ± 16.20	t=0.55	0.586
AST, Mean ± SD	19.24 ± 12.94	18.94 ± 13.00	19.37 ± 12.93	t=-0.33	0.739
Cr, Mean ± SD	77.08 ± 29.78	76.10 ± 30.18	77.50 ± 29.64	t=-0.48	0.633
UA, Mean ± SD	305.84 ± 96.04	293.68 ± 92.92	311.06 ± 97.02	t=-1.83	0.067
Ferritin, Mean ± SD	302.15 ± 214.76	310.34 ± 211.84	298.64 ± 216.21	t=0.55	0.582
Fructosamine, Mean ± SD	409.53 ± 109.78	418.63 ± 103.60	405.62 ± 112.24	t=1.20	0.231
TSH, Mean ± SD	2.63 ± 2.06	2.74 ± 2.00	2.58 ± 2.09	t=0.77	0.444
Fasting C-peptide, Mean ± SD	0.63 ± 0.45	0.62 ± 0.45	0.64 ± 0.45	t=-0.46	0.642

Abbreviations: KPC, Klebsiella pneumoniae colonization; SD, standard deviation; BMI, body mass index; T2DM, type 2 diabetes mellitus; WBC, white blood cell; NC, neutrophil cell; Hb, hemoglobin; FBG, fasting blood glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; UA, uric acid; TSH, thyroid stimulating hormone.

KP colonization. Once colonized, KP may disseminate via the bloodstream, causing complications like sepsis and endophthalmitis [9]. Hospitalization also disrupts normal microbiota and often involves exposure to broad-spectrum antibiotics, further increasing the likelihood of KPC in T2DM patients [18].

Elevated WBC levels in T2DM patients were associated with increased susceptibility to KPC. As a marker of immune response, high WBC levels often reflect infection [19]. However, chronic inflammation - a hallmark of T2DM - can impair immune system function, reducing its ability to combat infections [11]. Elevated WBC levels may thus represent both immune system activation due to KP infection and an underlying dysfunction, increasing the risk of KPC [20].

This study found that decreased Hb levels correlated with a higher risk of KPC. Diabetic nephropathy, a common microvascular complication of T2DM, damages kidney function, leading to reduced erythropoietin secretion and subsequent anemia [21, 22]. Lower Hb levels may signal advanced T2DM, which is more susceptible to bacterial infections. While the

Table 4. Differential analysis of training set

Variables	Total (n=340)	Normal group (n=252)	KPC group (n=88)	Statistic	*P*
Age, Mean ± SD	63.13 ± 13.58	63.54 ± 13.85	61.95 ± 12.77	t=0.94	0.346
Sex, n (%)				χ^2=0.02	0.881
Female	153 (45.00)	114 (45.24)	39 (44.32)		
Male	187 (55.00)	138 (54.76)	49 (55.68)		
BMI, Mean ± SD	24.57 ± 3.53	24.63 ± 3.52	24.39 ± 3.59	t=0.55	0.582
Course of T2DM, Mean ± SD	11.96 ± 8.22	11.88 ± 7.79	12.18 ± 9.39	t=-0.27	0.788
Hypertension, n (%)				χ^2=0.05	0.824
No	158 (46.47)	118 (46.83)	40 (45.45)		
Yes	182 (53.53)	134 (53.17)	48 (54.55)		
Smoking, n (%)				χ^2=1.21	0.271
No	268 (78.82)	195 (77.38)	73 (82.95)		
Yes	72 (21.18)	57 (22.62)	15 (17.05)		
Drinking, n (%)				χ^2=0.85	0.357
No	313 (92.06)	234 (92.86)	79 (89.77)		
Yes	27 (7.94)	18 (7.14)	9 (10.23)		
Hospitalized within six months, n (%)				χ^2=10.71	0.001
No	308 (90.59)	236 (93.65)	72 (81.82)		
Yes	32 (9.41)	16 (6.35)	16 (18.18)		
WBC, Mean ± SD	5.98 ± 1.89	5.85 ± 1.79	6.36 ± 2.11	t=-2.19	0.029
NC, Mean ± SD	3.55 ± 1.56	3.57 ± 1.49	3.48 ± 1.75	t=0.41	0.682
Hb, Mean ± SD	134.36 ± 16.75	135.32 ± 16.96	131.61 ± 15.90	t=1.79	0.074
FBG, Mean ± SD	7.96 ± 3.25	7.85 ± 3.20	8.28 ± 3.39	t=-1.07	0.285
ALT, Mean ± SD	21.62 ± 16.20	20.58 ± 16.41	24.60 ± 15.28	t=-2.01	0.045
AST, Mean ± SD	19.37 ± 12.93	18.62 ± 13.07	21.51 ± 12.33	t=-1.81	0.071
Cr, Mean ± SD	77.50 ± 29.64	78.63 ± 30.86	74.29 ± 25.76	t=1.18	0.238
UA, Mean ± SD	311.06 ± 97.02	316.30 ± 100.35	296.08 ± 85.53	t=1.69	0.092
Ferritin, Mean ± SD	298.64 ± 216.21	268.05 ± 195.98	386.23 ± 246.73	t=-4.07	< 0.001
Fructosamine, Mean ± SD	405.62 ± 112.24	409.35 ± 115.91	394.94 ± 100.86	t=1.04	0.301
TSH, Mean ± SD	2.58 ± 2.09	2.47 ± 2.10	2.88 ± 2.04	t=-1.58	0.115
Fasting C-peptide, Mean ± SD	0.64 ± 0.45	0.65 ± 0.47	0.60 ± 0.37	t=1.09	0.276

Abbreviations: KPC, Klebsiella pneumoniae colonization; SD, standard deviation; BMI, body mass index; T2DM, type 2 diabetes mellitus; WBC, white blood cell; NC, neutrophil cell; Hb, hemoglobin; FBG, fasting blood glucose; ALT, alanine aminotransferase; AST, aspartate aminotransferase; Cr, creatinine; UA, uric acid; TSH, thyroid stimulating hormone.

exact mechanism linking Hb and KPC requires further investigation, this finding suggests that anemia could be a marker for heightened vulnerability to KPC.

This study identified elevated ferritin as a factor associated with increased susceptibility to KPC in T2DM patients. The underlying mechanism may involve multiple pathways and complex interactions. Iron overload, for example, can enhance infection risk by providing bacteria with the iron required for growth [23]. Elevated ferritin levels are not only indicative of iron deficiency anemia but are also linked to various inflammatory, infectious, and oncologic conditions [24]. Ferritin elevation may result in increased free iron availability, facilitating KP growth [25, 26]. As an acute-phase protein, elevated ferritin levels may reflect enhanced inflammatory responses, which could promote KPC [27]. Furthermore, dysregulated iron metabolism may impair immune function, exacerbating infection risk [28]. For T2DM patients, monitoring and regulating ferritin levels could represent a novel strategy for preventing KP infections.

This study also highlighted the potential roles of TSH and liver function (ALT) in KPC susceptibility. Elevated TSH levels may impair immune cell activity, making it more difficult for T2DM patients to eliminate KP, thereby increasing the

Table 5. Logistic regression analysis of training set

Variables	Univariate Logistic regression					Multivariate Logistic regression					
	β	S.E.	Z	*P*	OR (95% CI)	β	S.E.	Z	*P*	OR (95% CI)	VIF
Hospitalized within six months											
No					1.00 (Reference)					1.00 (Reference)	
Yes	1.19	0.38	3.14	0.002	3.28 (1.56-6.88)	1.45	0.41	3.54	< 0.001	4.26 (1.91-9.48)	1.006
WBC	0.14	0.07	2.17	0.030	1.15 (1.01-1.31)	0.18	0.07	2.44	0.015	1.19 (1.03-1.37)	1.039
Hb	-0.01	0.01	-1.78	0.075	0.99 (0.97-1.00)	-0.01	0.01	-1.41	0.158	0.99 (0.97-1.00)	1.013
ALT	0.01	0.01	1.99	0.046	1.02 (1.01-1.03)	0.02	0.01	2.52	0.012	1.02 (1.01-1.04)	1.031
AST	0.02	0.01	1.80	0.072	1.02 (1.00-1.04)	0.01	0.01	1.19	0.232	1.01 (0.99-1.03)	1.024
Ferritin	0.01	0.00	4.26	< 0.001	1.01 (1.01-1.01)	0.01	0.00	4.27	< 0.001	1.01 (1.01-1.01)	1.020

Abbreviations: OR, odds ratio; CI, confidence interval; VIF, variance inflation factor; WBC, white blood cell; Hb, hemoglobin; ALT, alanine aminotransferase; AST, aspartate aminotransferase.

Table 6. Analysis of confusion matrix between training set and test set

Data	AUC (95% CI)	Accuracy (95% CI)	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	Cut off
Training set	0.74 (0.68-0.80)	0.65 (0.59-0.70)	0.59 (0.53-0.65)	0.82 (0.74-0.90)	0.90 (0.86-0.95)	0.41 (0.34-0.48)	0.206
Internal test set	0.76 (0.66-0.86)	0.63 (0.55-0.71)	0.57 (0.48-0.67)	0.81 (0.68-0.93)	0.90 (0.83 - 0.97)	0.38 (0.27-0.49)	0.206
External test set	0.75 (0.62-0.87)	0.80 (0.71-0.88)	0.85 (0.76-0.93)	0.68 (0.50-0.86)	0.88 (0.81-0.96)	0.61 (0.43-0.79)	0.299

Abbreviations: AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value.

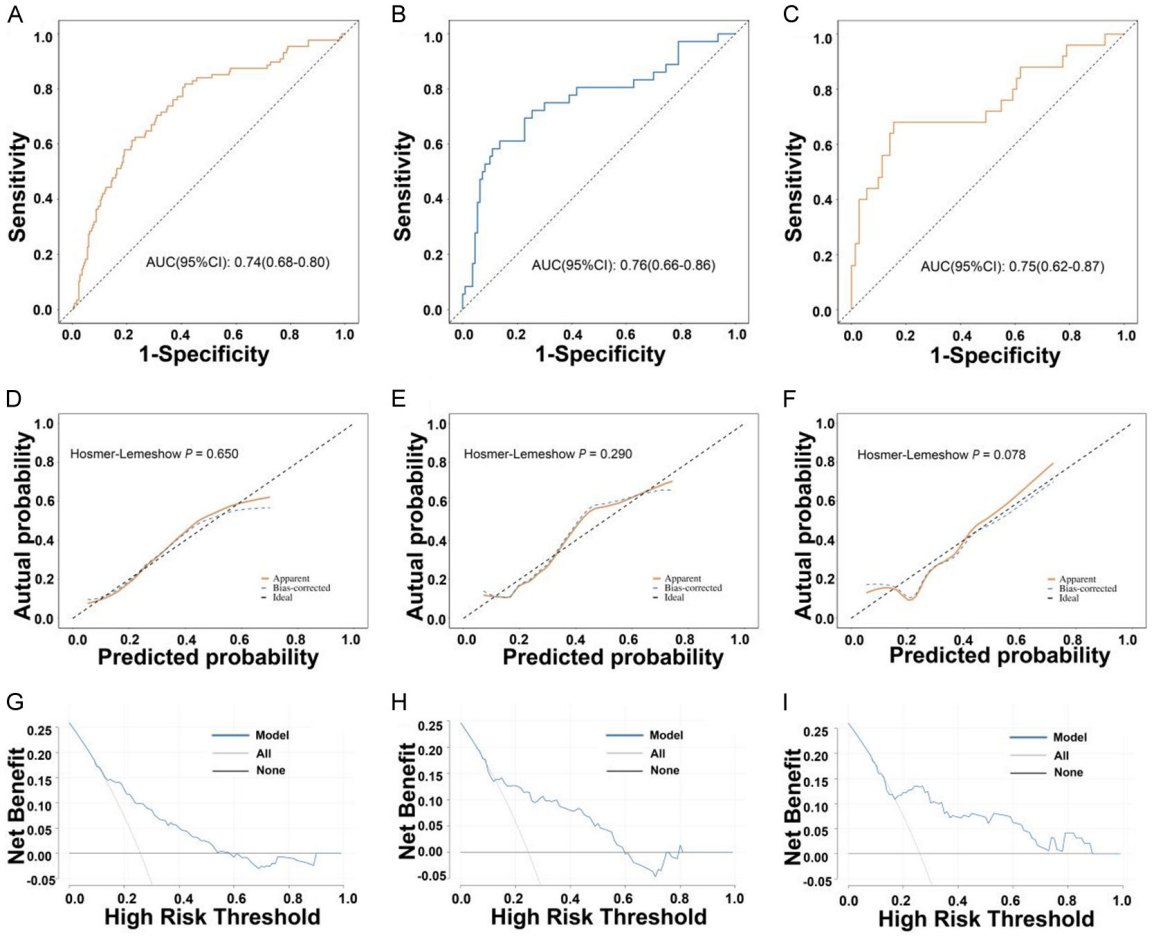

Figure 2. ROC curve, calibration curve, DCA curve of training set and test set. (A, D, G) ROC curve, calibration curve and DCA curve of the training set; (B, E, H) ROC curve, calibration curve and DCA curve of the internal test set. (C, F, I) ROC curve, calibration curve and DCA curve of the external testing set.

risk of colonization [29]. Similarly, elevated ALT levels may indicate liver inflammation or injury, which could compromise detoxification and metabolic functions, ultimately affecting immune responses and antibacterial capacity [30]. Increased KPC susceptibility in T2DM patients likely involves multiple mechanisms, including inflammatory reactions, immune dysfunction, and dysbiosis exacerbated by hyperglycemia. Metabolic abnormalities such as anemia and iron overload may also provide favorable conditions for pathogen growth. These findings offer new insights into the relationship between T2DM and KP colonization and underscore the need to focus on these indicators in future research on bacterial infections.

This study has certain limitations. First, as a retrospective analysis, it relies on previously collected data, which may introduce selection and recall biases. Second, the single-center nature of the study limits the generalizability of its findings. Third, the heterogeneity of T2DM manifestations and the multifactorial nature of KPC underscore the need for cautious interpretation of the results.

Despite these constraints, this study constructed a clinical prediction model for identifying high-risk T2DM patients prone to KPC. This model enables early identification and targeted intervention, such as enhanced surveillance, optimized glucose control, and adjusted antibiotic strategies, reducing infection risks and improving patient outcomes. Moreover, it facilitates the development of individualized treatment plans, enhancing therapeutic effectiveness while minimizing unnecessary medical resource utilization.

In conclusion, this study investigated the association between the basic and clinical characteristics of T2DM patients and their susceptibility to KPC through retrospective analysis. The findings identified hospitalization within the past six months, elevated WBC, decreased Hb, and elevated ferritin as independent risk factors for KPC. Additionally, thyroid and liver function indicators may influence susceptibility.

The clinical prediction model developed in this study demonstrated strong predictive capability in identifying high-risk populations for KPC. These findings provide theoretical insights into the clinical characteristics of T2DM and its relationship with KPC. They can aid clinicians in early identification and intervention for high-risk T2DM patients, enabling personalized treatment and improving patient prognosis.

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Disclosure of conflict of interest

None.

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