

Title:

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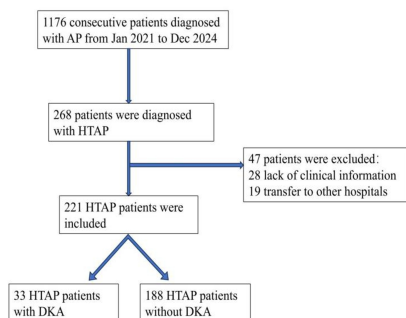
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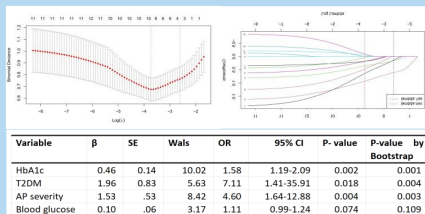
Incidence and Risk factors for diabetic ketoacidosis in hypertriglyceridemia-induced acute pancreatitis patients: A retrospective study

Study population

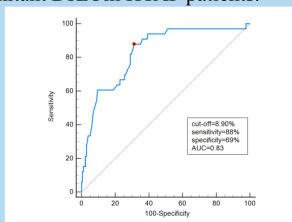


Methods

The LASSO and multivariate logistic analyses were performed to explore risk factors for DKA in HTAP patients.



ROC curve analysis for HbA1c for predicting concomitant DKA in HTAP patients.



Outcomes

1. Severe acute pancreatitis (SAP), type 2 diabetes mellitus (T2DM) history, and elevated HbA1c as independent risk factors for DKA development in HTAP patients.
2. In future, a prospective, multicenter, large-sample studies are needed to validate our findings.

Incidence and risk factors for diabetic ketoacidosis in hypertriglyceridemia-induced acute pancreatitis patients – A retrospective study

Running title: Incidence and Risk factors for diabetic ketoacidosis in hypertriglyceridemia-induced acute pancreatitis patients

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Abbreviations: DKA, diabetic ketoacidosis; HTAP, hypertriglyceridemia-induced acute pancreatitis; HbA1c, hemoglobin A1c; hemoglobin A1c, low-density lipoprotein cholesterol; PCT, procalcitonin; TC, total cholesterol; total cholesterol, aspartate aminotransferase; CRP, C-reactive protein; RDW, red cell distribution width; MCTSI,

modified CT severity index; T2DM, type 2 diabetes mellitus; type 2 diabetes mellitus, severe acute pancreatitis; LASSO, least absolute shrinkage and selection operator; TG, triglyceride; AP, acute pancreatitis; DM, diabetes mellitus; SAP, severe acute pancreatitis.

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Conflict of interest: The authors have no conflicts of interest to declare.

Data availability statements: The data underlying this article is available under petition to the correspondence author.

Ethics approval: This study was performed in accordance with the guidelines of the Declaration of Helsinki, and all protocols were approved by the Institutional Review Board (IRB) of Zhengzhou People's Hospital (No. 202109–59).

Patient consent: The institutional review boards (IRB) of the Zhengzhou People's Hospital were informed and agreed the study and the requirement to obtain written informed consent was waived.

Artificial intelligence: The authors declare that they did not use artificial intelligence (AI) or any AI-assisted technologies in the elaboration of the article.

Lay summary

Diabetic ketoacidosis (DKA) is a serious diabetes complication. Why it occurs, particularly in patients with severe pancreas inflammation caused by hypertriglyceridemia, is not fully understood. This study in Chinese patients aimed to find out how often DKA happens with hypertriglyceridemia-induced acute pancreatitis (HTAP) and identify key risk factors. Researchers studied medical records of 221 HTAP patients treated between 2021 and 2024. By comparing the patient group that developed DKA with the group that did not, they examined relevant factors such as test results and disease severity. About 15% (33 out of 221) of HTAP patients developed DKA. Patients with DKA were more likely to have comorbid type 2 diabetes, presented with more severe pancreatitis, and had a longer hospital stay. Analysis pinpointed three main factors significantly increasing DKA risk: having severe pancreas inflammation, a history of type 2 diabetes mellitus, and poor long-term blood glucose control (elevated HbA1c levels). DKA occurs relatively frequently in HTAP patients, and emergency physicians should maintain vigilance against this condition. Early identification of such high-risk patients may facilitate the prevention of DKA.

Abstract

Background and aims: The occurrence of diabetic ketoacidosis (DKA), along with its risk factors and pathophysiological mechanisms, remains incompletely understood, this study aimed to evaluate the clinical features of DKA in patients with hypertriglyceridemia-induced acute pancreatitis (HTAP) and identify independent risk factors for the development of DKA in a Chinese cohort.

Methods: Patients diagnosed with HTAP from January 2021 to December 2024 were retrospectively enrolled. They were divided into the DKA group and the non-DKA group. Demographic data, clinical features, admission laboratory findings, and clinical courses were compared between the two groups. The least absolute shrinkage and selection operator (LASSO) and multivariate logistic regression

analyses were performed to explore independent risk factors for DKA development.

Results: A total of 221 HTAP patients were enrolled, of whom 14.9% (33 patients) had concomitant DKA. blood glucose, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-C), neutrophil count (NEUT%), procalcitonin (PCT), total cholesterol (TC), aspartate aminotransferase (AST), C-reactive protein (CRP), red cell distribution width (RDW), and modified CT severity index (MCTSI) - all showed statistically significant differences between two groups ($p < 0.05$) in baseline characteristics comparison. Additionally, patients in the DKA group were more likely to have a type 2 diabetes mellitus (T2DM), severe acute pancreatitis (SAP) and longer hospital stays. The LASSO regression and multivariate logistic analysis identified SAP, T2DM history, and elevated HbA1c as independent risk factors for DKA development in HTAP patients.

Conclusion: In patients with HTAP, the relatively high incidence of DKA demands the attention of emergency clinicians. HTAP patients with SAP, a history of T2DM and poor HbA1c control should be considered high-risk for developing DKA. However, prospective, multicenter, large-sample studies will be needed in the future to validate our findings.

Keywords: Diabetes mellitus. Hypertriglyceridemia-induced acute pancreatitis. Diabetic ketoacidosis.

1. Introduction

Acute pancreatitis (AP) is a prevalent gastrointestinal emergency encountered in clinical settings [1]. Hypertriglyceridemia-induced acute pancreatitis (HTAP) is defined as AP triggered by serum triglyceride (TG) levels exceeding 11.30 mmol/L or levels ranging from 5.65 to 11.30 mmol/L in the presence of chylomicronemia. With rising living standards and dietary habit modifications, HTAP incidence has shown a consistent upward trend. Notably, recent evidence indicates that hypertriglyceridemia (HTG) has replaced alcohol as the second most common etiology of AP [2].

Diabetic ketoacidosis (DKA), a life-threatening acute metabolic complication of

diabetes mellitus (DM), is characterized by ketoacidosis, ketonuria, and hyperglycemia. Management typically requires intensive care unit (ICU) admission for intravenous insulin therapy and fluid resuscitation [3]. Studies indicate that patients with AP complicated by DKA face significantly higher mortality rates than those with AP alone. However, since abdominal pain—a shared initial symptom of both conditions—often leads to an initial AP diagnosis, DKA recognition is frequently delayed. Early diagnosis and intervention in such cases are crucial for improving outcomes. The association between DKA, AP, and hypertriglyceridemia has been documented in case reports since 1980 [4,5]. The rising incidence of HTAP has led to a corresponding increase in such case reports in recent years. However, isolated case studies provide limited insight into the actual prevalence or natural progression of DKA in HTAP patients.

Previous studies have mostly enrolled patients with AP of all etiologies as subjects. Compared with AP of other etiologies, HTAP has a higher propensity to develop DKA [6]. However, current research specifically targeting HTAP remains relatively limited, and its research objectives have mainly focused on comparisons of clinical characteristics and outcomes [7,8]. In particular, the occurrence of DKA, its risk factors, and pathophysiological mechanisms have not yet been fully elucidated. On the other hand, many earlier studies were conducted based on small sample sizes, and the incidence rates estimated and research findings derived therefrom may be limited in terms of reliability. This retrospective study aims to: (1) clarify the incidence and clinical features of DKA in HTAP patients; (2) identify potential risk factors for the development of DKA in this population to facilitate early clinical identification and intervention.

2. Methods

2.1 Patient selection

We conducted a retrospective review of medical records for patients admitted to the Zhengzhou People's hospital between January 2021 and December 2024. This study

was performed in accordance with the guidelines of the Declaration of Helsinki, and all protocols were approved by the Institutional Review Board (IRB) of Zhengzhou People's hospital (No. 202109–59). We present this article in accordance with the STROBE reporting checklist (supplementary table 1).

2.2 Inclusion and Exclusion criteria

Diagnosis of AP based on the Atlanta criteria, i.e., meeting at least two of the following three criteria:(I) Abdominal pain consistent with AP;(II) Serum amylase activity ≥ 3 times the upper limit of normal; (III) Characteristic findings of AP on computed tomography (CT). Diagnosis of HTAP as defined by either a pre-treatment serum TG level ≥ 11.30 mmol/L, or a serum TG level of 5.65–11.30 mmol/L accompanied by lipid turbidity [9]. DKA was diagnosed in accordance with the consensus guidelines of the American Diabetes Association (ADA) [10], which require meeting the following criteria: 1) plasma glucose > 13.9 mmol/L; 2) positive serum or urine ketones; 3) arterial pH < 7.3 , serum bicarbonate < 10 mmol/L and anion gap (AG) > 10 mmol/L. Based on this, all enrolled patients were divided into two groups: the HTAP with DKA group and the HTAP without DKA group.

Exclusion criteria:(I) Age < 18 years; (II) History of chronic pancreatitis or pancreatic tumor; (III) Pregnant women; (IV) Incomplete clinical data; (V) AP caused by other etiologies (e.g., gallstones/microlithiasis, alcohol, autoimmune factors, drug-induced causes).

2.3 Data collection

We documented demographic information (age, sex), body mass index (BMI), and comorbidity history (including diabetes mellitus, hypertension). We also collected admission laboratory test results. Additionally, the Modified Computed Tomography Severity Index (MCTSI) scores [12] were calculated based on enhanced CT images obtained after admission. The severity of AP was graded using the 2012 revised Atlanta Classification [11], which defines: Mild AP (MAP): Characterized by the absence of both organ failure and local or systemic complications; moderately severe AP (MSAP): Defined by transient organ failure (resolving spontaneously within 48 hours) accompanied by local or systemic complications; severe AP (SAP): Marked by persistent organ failure (continuing beyond 48 hours).

2.4 Statistical Analysis

Statistical analyses were performed using IBM SPSS Statistics for Windows, version 24.0 (IBM Corp., Armonk, NY, USA) and R software (version 3.6.1; R Foundation for Statistical Computing, Vienna, Austria). Post-hoc power of the study was estimated using G*Power software. For descriptive statistics analysis, continuous variables are presented as median (interquartile range) and were compared using the Mann Whitney U test. Categorical data were compared using the Chi-square test or Fisher's exact test. In this study, due to the inherent limitation of the relatively low incidence and insufficient number of DKA cases, the LASSO regression method was used to selected relatively important risk factors, thereby achieving variable selection and coefficient shrinkage to avoid overfitting. Subsequently, variance inflation factor (VIF) analysis was utilized to eliminate multicollinearity. Final, multivariate logistical regression analysis was carried out to explore the independent risk factors that contributed to DKA and HTAP's coexistence. The odds ratios (ORs) and 95% confidence intervals (CIs) for the variables were calculated. To estimate the parameters and significance levels more accurately, bootstrap technique and a sample size of 1000 were used. And the Hosmer-Lemeshow test was used to assess the goodness of fit of the model. If the P-value was <0.05 , the result was judged significant.

3. Results

3.1 Patient selection

Figure 1 illustrates the complete patient screening process. During the study period (January 2021 to December 2024), we identified 1,176 consecutive patients with AP, of whom 268 adult patients met the diagnostic criteria for HTAP. After excluding 47 patients due to insufficient clinical data or inter-hospital transfers, our final cohort comprised 221 HTAP cases. Among these, 33 patients (14.9%) were diagnosed with concurrent HTAP and DKA. A post hoc power analysis showed a power of 75% with a medium effect size (Cohen's $d = 0.5$), with using G*Power software.

3.2 Baseline characteristics of the study population.

Table 1 compares baseline demographic and clinical characteristics between HTAP patients with and without DKA at admission. No significant differences were

observed in gender, age, or BMI between the two groups. These clinical parameters - including blood glucose, hemoglobin A1c (HbA1c), low-density lipoprotein cholesterol (LDL-C), neutrophil count (NEUT%), procalcitonin (PCT), total cholesterol (TC), aspartate aminotransferase (AST), C-reactive protein (CRP), red cell distribution width (RDW), and MCTSI - all showed statistically significant differences between two groups ($p < 0.05$). Additionally, a significantly higher proportion of DKA patients had pre-existing diabetes mellitus ($p < 0.05$). The history of diabetes mellitus in all patients is type 2 diabetes mellitus (T2DM). According to the 2012 revised Atlanta Classification, the incidence of SAP was higher in the HTAP with DKA group than in the HTAP-only group. Additionally, the DKA-complicated group had a longer hospital stay. No other significant intergroup differences were observed in the remaining clinical parameters.

3.3 The LASSO and Multivariate logistic analysis of risk factors for concurrent DKA in HTAP

To mitigate the impact of multiple variables on a relatively small sample size, the LASSO regularization ($\alpha = 1$) with 10-fold cross-validation was applied. Based on the analysis of the results of comparison of the baseline demographic and clinical characteristics between two groups, 12 variables were selected to be included in LASSO regression analysis (Figures 2a and 2b). There are nine variables had non-zero coefficients. Considering the limited sample size and clinical experience, we selected only 4 variables with larger coefficients (coefficient ≥ 0.30) into multivariate analysis, namely HbA1c (coefficient = 0.927), T2DM (coefficient = 0.635), blood glucose (coefficient = 0.353), and AP severity (coefficient = 0.465). Variance inflation factor analysis was conducted on these variables. All VIF values were less than 5, indicating that multicollinearity could be excluded (supplementary table 2).

Table 2 presents the risk factors associated with concurrent HTAP and DKA at admission. We identified 3 independent predictors by multivariate logistic regression analysis: (1) pre-existing T2DM (adjusted OR 14.28, 95% CI 1.66-122.57, $p < 0.05$) and (2) elevated HbA1c levels (adjusted OR 1.58, 95% CI 1.19-2.09, $p < 0.01$). (3) AP severity (adjusted OR 4.60, 95% CI 1.64-12.88, $p < 0.01$). The results from bootstrap method show that estimation of parameters were exact and had precision. Notably,

admission blood glucose levels showed no significant association with DKA comorbidity. In addition, The Hosmer-Lemeshow test demonstrated that the model was a good fit ($\chi^2 = 9.794$, $df = 8$, $p = 0.280 > 0.05$). In the ROC curve analysis, when the cut-off value of HbA1c was 8.9%, the AUC for predicting DKA was 0.83 (95%CI: 0.74-0.90), with sensitivity = 0.88 and specificity = 0.69 (Figure 3).

4. Discussion

Abdominal pain, while characteristic of AP, represents a common overlapping symptom in DKA, frequently leading to delayed DKA diagnosis when AP is initially suspected [13]. This diagnostic delay carries significant clinical implications, as concurrent DKA exacerbates hypovolemic shock, amplifies metabolic derangements, and increases both AP severity and mortality risk. Supporting this observation, prior research has demonstrated significantly higher mortality in AP patients with DKA compared to those without this metabolic complication [6]. Moreover, compared with AP caused by other etiologies, HTAP is more likely to be complicated by DKA [14]. This study specifically targets the distinct patient population with HTAP, with the primary aim of systematically elucidating independent risk factors for subsequent development of DKA.

In this single-center retrospective cohort study involving 221 HTAP patients, we found that 33 patients (14.9%) met the diagnostic criteria for DKA, which is close to the incidence rate (10%-14.5%) reported in previous studies [6,7]. Our findings demonstrate that pre-existing T2DM, elevated HbA1c (>8.9%) and AP severity serve as independent risk factors for DKA development in HTAP patients. Compared with previous studies, our study has several strengths: First, it has a relatively large sample size, so the calculated results are more representative and credible; Second, more notably, we employed LASSO regression and the Bootstrap method of Logistic regression to explore the risk factors, and also used VIF analysis to test for multicollinearity among these factors, which renders our results more rigorous and objective. While Quintanilla-Flores et al [7] previously conducted the first comparative study of HTAP patients with versus without DKA, their analysis of 55 cases revealed no significant difference in diabetes prevalence between groups. This discrepancy with our results may reflect their limited sample size. In another study

focusing on DKA occurrence in AP patients of all etiologies, diabetes mellitus (DM) emerged as a critical predictive indicator [14]. Over the past few decades, the prevalence of DM has increased significantly. Diabetes can exacerbate the body's inflammatory response and enhance susceptibility to infectious diseases [15]. A meta-analysis [16] confirmed that diabetic patients face significantly higher risks of both local and systemic complications from AP. The metabolic stress induced by HTAP may precipitate acute diabetic decompensation, potentially triggering the development of DKA in susceptible individuals. HbA1c reflects average blood glucose levels over approximately 3 months. Elevated HbA1c indicates poor glycemic control, which may serve as both a predisposing factor for and consequence of AP and DKA. However, in previous studies, few have focused on the important indicator HbA1c. This bidirectional relationship is particularly evident in patients with poorly controlled DM, which has been established as an independent risk factor for both AP development and DKA progression [17]. Hyperglycemia (plasma glucose >13.9 mmol/L) as one of the diagnostic criteria for DKA. Previous studies have also suggested that hyperglycemia is an independent predictive factor of DKA[24]. However, those studies focused on AP of all etiologies with concurrent T2DM, which differs from the study subject of our research. While our study revealed significantly elevated admission blood glucose levels in HTAP patients with DKA compared to those without DKA, multivariate logistic regression analysis demonstrated that hyperglycemia at presentation did not independently predict DKA occurrence. Initially, we thought this might be due to multicollinearity among hyperglycemia, a history of T2DM, and elevated HbA1c levels; however, VIF analysis showed that this was not the case. On the other hand, this elevation in blood glucose may be termed "stress hyperglycemia," referring to a transient increase in glucose levels during critical illness, which is quite common in many acute pancreatitis patients [18]. A mild-moderate increase in blood glucose concentration in the pancreas may have a protective effect on the pancreas, especially in response to reduced pancreatic blood flow and oxidative stress during pancreatic inflammation. These changes enhance the ability to adapt to stress [19.21], rather than a true reflection of the hyperglycemia seen in DKA. Meanwhile, AP severity shows significant correlation

with DKA occurrence. Previous studies [7,14] demonstrated that acute pancreatitis patients with concurrent DKA exhibited significantly higher Ranson and APACHE II scores, along with prolonged ICU stays. AP severity shows significant correlation with DKA occurrence. Previous studies consistently demonstrated that DKA patients exhibited: A most recently study [20] also revealed a significantly higher incidence of severe pancreatitis in HTAP patients with concurrent DKA compared to those with HTAP alone.

The complex pathophysiological interplay between hypertriglyceridemia, AP, and DKA remains poorly understood and has received limited attention in the medical literature [7,8,20]. This complex pathophysiological interaction has been termed the "enigmatic triangle" due to its intricate mechanistic relationships. The exact role of DKA in this triad remains undetermined, with two apparent research pathways emerging: specifically, whether it primarily functions as: (1) a pathogenic initiator in AP development (DKA→HTG→AP), or (2) a secondary complication of AP (HTG→AP→DKA). Several previous studies have primarily followed the first research approach [22,23]. In DKA, insulin deficiency activates lipolysis in adipose tissue, leading to the release of free fatty acids that accelerate the formation of very low-density lipoproteins (VLDL) in the liver; additionally, reduced lipoprotein lipase activity in peripheral tissues decreases VLDL clearance from plasma, both resulting in hypertriglyceridemia, which can induce acute pancreatitis by exerting direct toxic effects on acinar cells and pancreatic capillaries. DKA patients manifest with disorders of glucose and lipid metabolism, thereby leading to hypertriglyceridemia-induced AP. In contrast, the second research pathway demonstrates that hypertriglyceridemia (HTG)-induced AP can cause transient insulin deficiency through pancreatic β -cell damage. At this point, due to the ineffective utilization of glucose, the liver engages in excessive lipolysis and fatty acid oxidation to supply energy. During this process, large amounts of ketone bodies—exceeding the body's metabolic capacity—are produced, leading to ketone body accumulation and subsequently inducing metabolic acidosis. This forms the pathological cascade represented as "HTG→AP→DKA" [13,24]. This mechanism is particularly prominent in our cohort, HTAP patients with poorly controlled diabetes mellitus. Emerging

evidence suggests that pancreatic exocrine parenchyma damage during AP may increase diabetes risk, leading to post-pancreatitis diabetes mellitus (PPDM) - a distinct entity first characterized in 2017 that has gained increasing recognition [25]. The exact pathogenesis of PPDM remains unclear, and various proposed mechanisms include loss of islet cell mass, autoimmunity induced by acute pancreatitis (AP), and alterations in the insulin incretin axis [26]. Multiple meta-analyses indicate that approximately 20% of AP patients develop diabetes within 5 years, with the prevalence rising to nearly 40% in long-term follow-up [27]. Patients with PPDM demonstrate significantly poorer glycemic control and higher all-cause mortality rates compared to those with conventional type 2 diabetes mellitus [28]. Notably, the frequency of HTAP recurrences shows a significant positive correlation with PPDM incidence, while repeated episodes are associated with progressively worsening glycemic control [29]. Among patients in the DKA group of our study, some also had a history of multiple recurrent episodes of HTAP; in addition, some case reports have already emerged. Regrettably, there are no objective and widely accepted diagnostic criteria for PPDM, and it mainly relies on detailed medical history for diagnosis. Therefore, we tentatively incorporate the new concept of PPDM into the second pathological pathway, thus forming the sequence of "HTG→AP→PPDM→DKA", though this sequence may be applicable only to a small subset of the population. These new findings provide opportunities to explain the complex mechanisms underlying the interactions between the aforementioned diseases, while the relevant hypotheses still require further research for verification.

Our study had some limitations. First, due to the nature of this single-center, retrospective study, it was difficult for us to avoid selection bias during patient selection. For instance, we excluded patients with missing HbA1c and blood glucose data. Additionally, we were unable to prospectively collect some important indicators, such as documentation of medication use (e.g., SGLT2 inhibitors, a recognized risk factor for euglycemic DKA [30], insulin adherence in patients with pre-existing diabetes), and the detailed timing of DKA onset in relation to AP presentation. Second, the small sample size limited the statistical power of post hoc tests and thus restricted result generalizability, due to the disease's actual low

incidence. Nevertheless, our sample size was relatively larger than previous studies, and we enhanced the credibility of the results through LASSO analysis and the bootstrap method in Logistic regression. Third, although AP severity is considered a predictive factor, it relies on final clinical diagnosis and lacks appropriate surrogates - e.g., Ranson and APACHE II scores, which could not be calculated in this study due to missing specific indicators, especially in some mild cases. Though we attempted substitution with MCTSI, the results were suboptimal. Fourth, PPDM may play an important role in the entire pathogenesis of DKA, but it was not included in our study due to the absence of recognized diagnostic criteria, which mainly relies on detailed medical history.

5. Conclusion

In summary, patients with HTAP and concurrent DKA exhibited greater disease severity and prolonged hospitalization compared to HTAP patients without DKA. Our findings suggest that severe acute pancreatitis, pre-existing T2DM and poor glycemic control may increase the risk of DKA in HTAP patients. Early recognition and aggressive management of these high-risk individuals could mitigate complications and improve clinical outcomes. However, future prospective, multicenter, large-sample studies are needed to validate our findings and further investigate the risk factors and prognosis of HTAP complicated by DKA.

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Table 1 Comparison of demographic and clinical characteristics of HTAP patients with and without DKA at admission.

Variables	DKA n=33	Non-DKA n=188	Z/x ²	p-value
Age (years)	35.5[29.0-39.0]	37.0[32.00-43.00]	-1.594	0.111
BMI (kg/m ²)	27.68[25.39-31.60]	27.73[25.49-30.86]	-0.068	0.946
Weight (kg)	80.00[70.00-92.75]	82.40[75.00-95.00]	-0.767	0.443
Sex(M/F)	25/8	157/31	1.156	0.282
TG(mmol/L)	23.57[14.19-34.28]	21.78[14.56-30.52]	-0.576	0.565
Ca+(mmol/L)	2.31[2.20-2.42]	2.31[2.21-2.39]	-0.254	0.800
HbA1c(%)	11.25[9.55-12.10]	7.20[5.90-9.88]	-6.471	<0.01
Blood glucose (mmol/L)	15.40[13.49-17.71]	9.12[6.60-14.01]	-6.082	<0.01
HDL(mmol/L)	1.00[0.0.65-1.56]	1.09[0.68-1.44]	-0.029	0.977
LDL (mmol/L)	1.42[0.84-2.28]	1.10[0.63-1.59]	-2.009	<0.05
WBC(×10 ⁹ /L)	12.56[9.51-15.92]	12.23[9.64-14.66]	-0.825	0.409
NEU(×10 ⁹ /L)	11.74[8.99-16.33]	10.25[7.95-12.56]	-2.080	<0.05
LYM(×10 ⁹ /L)	1.57[1.11-2.14]	1.54[1.18-2.03]	-0.308	0.758
CV (%)	12.40[11.90-13.10]	12.60[12.10-13.20]	-1.284	0.200
RDW (%)	40.10[37.40-41.98]	41.30[39.00-43.65]	-2.437	<0.05
CRP (mg/L)	72.94[12.21-152.54]	25.21[5.54-88.42]	-2.186	<0.05
PCT(μg/L)	0.14[0.08-0.42]	0.07[0.05-0.19]	-2.630	<0.01
AMY(U/L)	150.50[54.50-449.00]	169.00[89.00-378.75]	-0.836	0.403
LPS(U/L)	262.00[102.75-528.00]	290.00[118.00-502.00]	-0.168	0.886
ALT(U/L)	25.00[15.00-35.50]	27.00[19.00-41.00]	-1.642	0.100
AST(U/L)	22.00[14.75-30.25]	25.50[19.00-36.00]	-1.994	<0.05
ALP(U/L)	92.00[67.75-101.75]	80.00[67.00-97.75]	-1.267	0.205
GGT(U/L)	43.00[35.00-58.75]	54.50[35.00-86.00]	-1.746	0.081
BUN(mg/dL)	3.92[3.18-4.62]	4.46[3.52-5.24]	-1.758	0.079
Crea(μmol/L)	56.00[42.25-77.75]	62.00[50.25-75.00]	-1.185	0.236
UA(μmol/L)	377.00[315.00-509.00]	386.00[281.50-467.00]	-0.031	0.975
D-D(μmol/L)	0.14[0.06-0.56]	0.17[0.03-0.50]	-0.852	0.394
Cholesterol(mmol/L)	11.21[9.20-12.73]	9.11[6.71-12.17]	-3.200	<0.05
Apo-A1(g/L)	0.90[0.69-1.20]	0.98[0.76-1.20]	-1.271	0.204
Apo-B(g/L)	0.56[0.40-1.01]	0.54[0.39-0.84]	-1.511	0.131
ALB(g/L)	45.20[42.13-48.00]	44.10[41.70-46.78]	-1.528	0.127
K+(mmol/L)	3.90[3.50-4.31]	3.80[3.60-4.00]	-1.092	0.275
LDH(U/L)	221.00[173.75-289.75]	239.50[193.50-290.50]	-0.650	0.516
PLT(×10 ⁹ /L)	241.00[203.00-279.75]	237.00[194.00-273.00]	-0.458	0.647
INR	0.98[0.91-1.02]	0.96[0.91-1.02]	-0.481	0.631
MCTSI	6.00[4.00-8.00]	4.00[2.00-6.00]	-2.575	<0.05
T2DM (yes/no)	31/2	83/105	27.739	<0.01
AHT (yes/no)	16/17	75/113	0.852	0.356
AP severity(severe/no severe)	14/19	39/149	7.205	<0.01

ALB - Albumin; **ALP** - Alkaline Phosphatase; **ALT** - Alanine Aminotransferase; **AMY** - Amylase **Apo-A1** - Apolipoprotein A1; **Apo-B** - Apolipoprotein B; **AST** - Aspartate Aminotransferase; **BUN** - Blood Urea Nitrogen ;**Ca²⁺** - Calcium; **CRP** - C-Reactive Protein; **Crea** - Creatinine ;**CV** - Coefficient of Variation **D-D** - D-Dimer; **DM** - Diabetes Mellitus ;**GGT** - Gamma-Glutamyl Transferase;**HbA1c** - Hemoglobin A1c;**HDL** - High-Density Lipoprotein ;**HTN** - Hypertension; **INR** - International Normalized Ratio; **K⁺** - Potassium; **LDL** - Low-Density Lipoprotein; **LPS** - Lipase; **LYM** - Lymphocytes ;**MCTSI** - Modified CT Severity Index; **NEU** - Neutrophils; **NHDL** - Non-HDL;**PCT** - Procalcitonin;**RDW** - Red Cell Distribution Width; **TG** - Triglycerides; **UA** - Uric Acid; **WBC** - White Blood Cells; **LDH**- Lactate Dehydrogenase; PLT-Platelet Count; **T2DM** - type 2 diabetes mellitus; **AHT**-Arterial Hypertension.

Table 2. Multivariate analysis for factors associated with the development of DKA in HTAP patients

Variable	β	SE	Wals	OR	95% CI	P- value	P-value by Bootstrap
HbA1c	0.46	0.14	10.02	1.58	1.19-2.09	0.002	0.001
T2DM	1.96	0.83	5.63	7.11	1.41-35.91	0.018	0.004
AP severity	1.53	.53	8.42	4.60	1.64-12.88	0.004	0.003
Blood glucose	0.10	.06	3.17	1.11	0.99-1.24	0.074	0.109

HbA1c - Hemoglobin A1c; **T2DM**- type 2 diabetes mellitus.

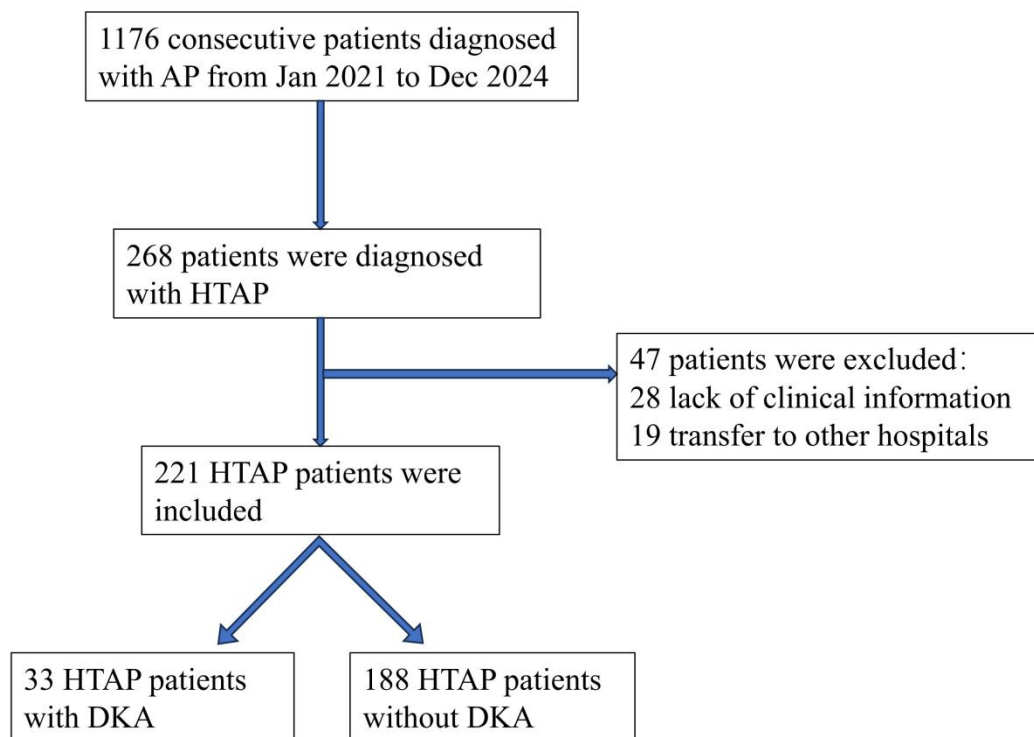


Figure 1. Flowchart of the process of inclusion of patients in the study.

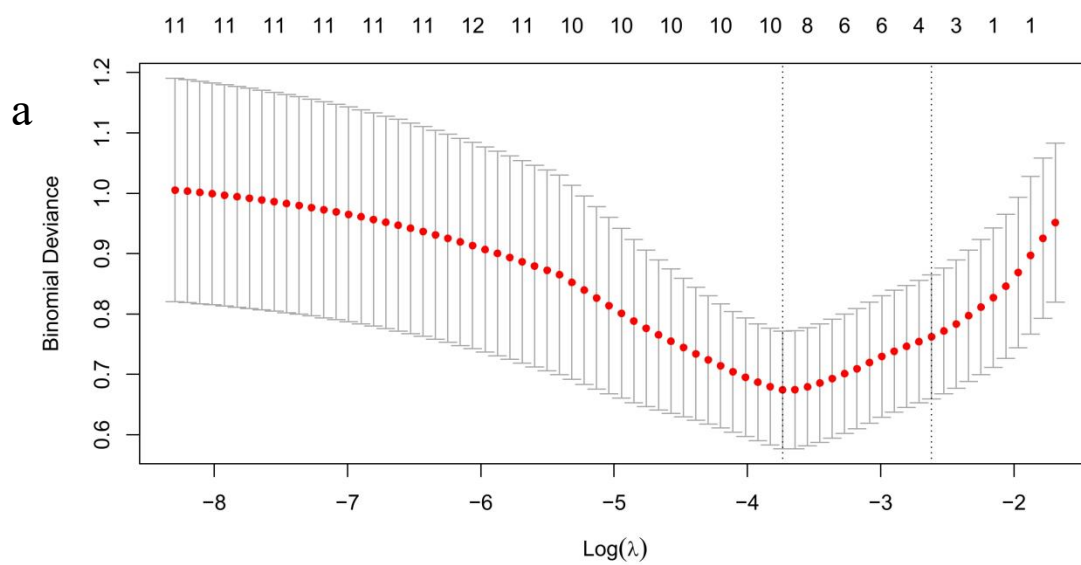


Figure 2a

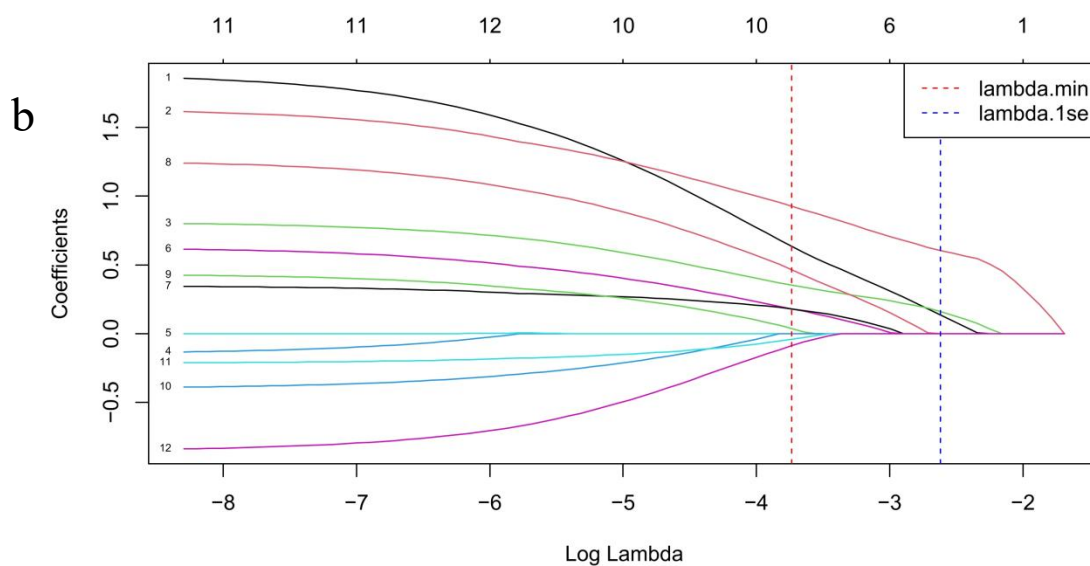


Figure 2b

Figure 2: Clinical feature selection using the LASSO regression analysis with tenfold cross-validation. (a) Selection of optimal parameters (lambda) from the LASSO model using 10-fold cross-validation and minimum criteria. The partial likelihood deviance (binomial deviance) curve was plotted versus log (lambda). Dotted vertical lines were drawn at the optimal values using the minimum criteria and the 1 standard error of the minimum criteria (1-SE criteria). (b) LASSO coefficient profiles of the 12 features. A vertical line was drawn at the value selected using 10-fold cross-validation, where the best lambda resulted in 9 features with nonzero coefficients.

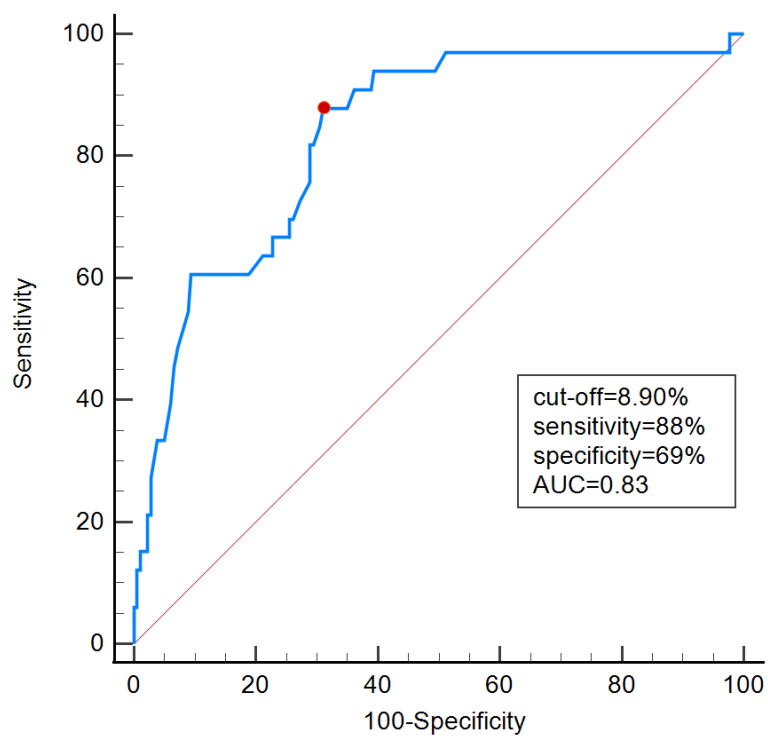


Figure 3. ROC curve analysis for HbA1c for predicting concomitant DKA in HTAP patients.