Characteristics of acute pancreatitis with diabetic ketoacidosis and analysis of factors related to the length of hospital stay

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Abstract

Obejective 11% of adults with diabetic ketoacidosis (DKA) also suffer from AP. The obejective of this research was to study the characteristics of AP with DKA, the factors related to the length of hospital stay, and to explore indicators for the severity of AP.

Methods A retrospective analysis of 173 AP with DKA cases treated in our hospital from July 2011 to December 2020 was performed. We analyzed the gender, age, systemic inflammatory response syndrome(SIRS), pleural effusion, blood urea nitrogen（BUN）, bedside index for the severity in acute pancreatitis（BISAP）score, white blood cell（WBC）, aspartate transaminase （AST）, lactate dehydrogenase （LDH）, blood glucose, Ranson score, partial pressure of carbon dioxide （PaCO 2 ）,triglyceride, modified CT severity index （MCTSI）, potential of hydrogen potential of hydrogen （PH）, amylase, glycated hemoglobin, C-reactive protein（CRP）, creatinine（Cr）, blood calcium, procalcitonin （PCT）, the length of stay.

Result Blood calcium, LDH, BUN, pleural effusion, MCTSI, Ranson score and BISAP score were related to the length of stay (P <0.05). WBC, AST, blood glucose, PaCO 2 , triglyceride, PH, glycated hemoglobin, CRP, Cr , PCT were not related to the length of stay (P> 0.05).

Conclusion The current Atlanta classification is not suitable for evaluating the severity of AP with DKA. Serum calcium, LDH, BUN, pleural effusion, and MCTSI are suitable for evaluating the length of stay and severity of AP with DKA.

1. Introduction

Acute pancreatitis (AP) is a common critical disease of the digestive system, and the morbidity is increasing year by year. Patients with diabetes mellitus (DM) have a higher risk of developing AP than ordinary people.[1 2] The literature reports that 11% of adults with diabetic ketoacidosis (DKA) also suffer from AP, and the Ranson score is not suitable for evaluating the severity of AP.[3] DM can lead to impaired renal function. Most patients with hyperglycemia will have an increased white blood cell count. DKA can also occur with increased breathing, tachycardia, hypotension, and mental changes, which can confuse the severity of AP. The use of the current AP scoring system and classification will inevitably affect the judgment of AP severity. This study used the length of hospital stay as the end event to evaluate the clinical use and value of the AP scoring system and classification.

1.1 General data

We conducted a retrospective analysis of clinical data of 173 patients with AP ,elevated Urine sugar and elevated urinary ketone diagnosed from 2011.7 to 2020.12.We analyzed factors including gender, age, systemic inflammatory response syndrome(SIRS), pleural effusion, blood urea nitrogen（BUN）, bedside index for the severity in acute pancreatitis（BISAP）score, white blood cell（WBC）, aspartate transaminase （AST）, lactate dehydrogenase（LDH）, blood glucose, Ranson score, partial pressure of carbon dioxide

（$PaCO_2$）,triglyceride, modified CT severity index （MCTSI）, potential of hydrogen potential of hydrogen （PH）, amylase, glycated hemoglobin, C-reactive protein（CRP）, creatinine（Cr）, blood calcium, procalcitonin （PCT）, length of hospital stay.

1.2 Diagnostic Criteria

The AP diagnostic criteria refers to the 2012 Atlanta International Pancreatitis Classification and Definitions(revised international edition), [4] which meets at least two of the following items: (1) persistent abdominal pain; (2) level of amylase or lipase is three times or more than the upper limit values; (3) enhanced CT shows AP signs such as enlarged pancreas, blurred edges, edema bands, air bubbles, etc. and / or imaging examinations such as MRI and ultrasound revealed pancreatitis signs.

DKA diagnostic criteria: [5] plasma glucose> 13.9 mmol / L (250 mg / d1), arterial blood pH <7.3, bicarbonate <18 mmol / L, and ketonuria. Symptoms with only ketosis and without acidosis is called diabetic ketosis.

1.3 Statistical methods

Statistical analysis was performed using SPSS 16.0 statistical software. If the measurement data conforms to the normal distribution, it is expressed in the form of mean ± standard deviation (x ± s). The correlation of measurement data is analyzed by Pearson correlation. If it does not conform to the homogeneity of variance, the nonparametric test of 2 independent samples is adopted.P <0.05 was considered statistically significant.

2. Results

2.1 Patient age average was (41.79 ± 12.28) years old and the age range is (12 to 80) years old. We had 113 males and 40 females patients on record. Among them, 69 cases of DM were found for the first time, 32 recurred cases, and 150 cases of increased triglyceride (8.40 ± 8.88) mmol / L. The length of hospital stay was an average of (11.46 ± 5.40) days. The number of cases of AP with DM from 2011 to 2020 was 8, 8, 20, 10, 22, 22, 30, 30, 23 respectively. The number of cases in the first, second, third, and fourth quarters were 49, 42, 34, and 49, with an average length of hospital stay (11.46 ± 5.40) days. SIRS were more than local complications of AP (P <0.05).

2.2 AP with DM age, blood amylase, blood calcium, LDH, pleural effusion, BUN, Ranson score, BISAP score, MCTSI were positively correlated with length of stay (P <0.05), SIRS, blood glucose, WBC, PH, $PaCO_2$, glycated hemoglobin, CRP, PCT, Cr, AST, and triglycerides were not related to length of stay, as shown in Table 1 below.

Table1 AP Correlation between biochemical parameters and length of hospital stay in AP with DKA complication

	Average	Counts	P-Value
SIRS	0.65±0.48	173	0.065
Ranson Score	1.22±0.86	173	0.000
Age	41.8±12.3	173	0.035
Blood Sugar	16.5±4.5	172	0.228
WBC	14.8±5.3	171	0.569
AST	37.9±168.7	172	0.379
LDH	284.7±175.6	172	0.000
Amylase	421±503	170	0.002
PH	7.34±0.10	151	0.168
$PaCO_2$	34.5±7.8	150	0.492
CRP	118.7±69.4	167	0.077
PCT	2.0±4.8	101	0.756
Blood Calcium	2.13±0.37	172	0.002
Glycated Hemoglobin	9.7±2.23	164	0.383
Triglyceride	8.4±8.9	173	0.503
MCTSI	2.6±1.2	170	0.000
BISAP	1.22±0.86	172	0.000
Pleural Effusion	0.4±0.5	166	0.000
BUN	5.16±3.66	151	0.009
Cr	64.4±31.0	171	0.068

P□0.05 is statistical significant

Discussion

It is reported in the literature that DKA is more common in younger patients (<65 years), while HHS is mostly seen in patients over 65 years of age. [6 7] This study found that AP patients with DKA were mainly young and middle-aged. Males accounted for 76.9%, which was higher than 65.3% reported by Simons-Linares CR et al. [8] The number of cases was increasing over the years, consistent with the increase in the incidence of DKA. According to the United States CDC Diabetes Surveillance System, from 2009 to 2014, DKA steadily increased at an average annual rate of 6.3%, and the hospital mortality rate decreased from 1.1% to 0.4% during the study period. [9] The disease commonly occurred in the first and fourth quarters of

the year. This suggest that the disease was more likely to occur in cold weather, because human activity is reduced in the cold season, and dietary calories are increased. The effect of season on glycemic control may vary by population and geographic location. The reasons may be as follows: (1)insulin resistance is increased in winter, plasma cortisol levels are increased in winter, and tissue sensitivity to glucocorticoids is increased in winter;[10] (2) the incidence of type 1 diabetes is increased in winter and / or spring.[11] Among these incidents, 69 patients with DKA were diagnosed for the first time. DKA often occurs in type 1 diabetes (T1DM). A 2002 survey from the United States showed that the incidence of DKA in T1DM patients was 8 per 100 person-years.[12] A survey in Guangdong Province, China showed that the incidence of DKA in T1DM patients reached 26.4 per 100 person-years.[13] Nearly 20% of T1DMs have experienced hyperglycemia and DKA. Therefore, blood glucose testing should be strengthened in young people to reduce the incidence of DKA with AP.Recurrent episodes of AP with DKA were present in 32 patients, DKA often occurred due to the causes of acute infection, inappropriate insulin reduction or sudden interruption of treatment, improper diet, gastrointestinal disease, stroke, myocardial infarction, trauma, surgery, pregnancy, childbirth, and mental stimulation. Therefore, people with known DM should strengthen blood glucose testing and control blood glucose. In this study, 150 cases were with triglyceride levels exceeded the normal level of 1.71mmol / L. Hypertriglyceridemic pancreatitis (HTGP) increased gradually, and they were younger and more severe, and they had surpassed alcoholic AP as the second largest etiology. [21] When serum triglycerides exceeds 1000mg / dL (11.3mmol / L), the risk of AP is about 5%, and when serum triglycerides exceeds 2000mg / dL (22.6mmol / L), the risk is 10%- 20%.[14] A prospective study included 400 cases of AP and found that HTGP patients were younger (44 vs. 52), mainly males (65% vs 35%), and a higher proportion of obesity (57% vs 34%).), Diabetes was also higher (38% vs 17%).[15] People with AP and DKA need to pay more attention to blood lipid levels. Nair S et al[3] considered that hypertriglyceridemia is temporary. Once the onset of DKA is corrected, hypertriglyceridemia will disappear, but the study included only a small number of cases, and further study is needed to observe the patient's lipid profile.

In AP caused by hypertriglyceridemia, the blood amylase and lipase can be normal. In this study, it was found that the increase in blood amylase was related to the length of hospital stay, suggesting that blood amylase can be used as one of the indicators for the length of stay. Previous study found that blood amylase has nothing to do with the severity of AP-only. In some patients with severe pancreatitis, the blood amylase does not increase, so the value of blood amylase as a judgement of hospital stay is limited. PCT and CRP are indicators to evaluate the severity of AP-only,but this study found that PCT and CRP were not related to the length of hospital stay.

Age is reported to be the only factor in lengthening DKA hospital stays in the literature. [16] This study found that age was related to length of hospital stay. SIRS and PH were not related to the length of hospital stay. PH decreases during DKA, heart rate and respiration increase, PaCO2 decreases, and WBC rises due to hyperosmotic state. The 2012 Atlanta International Consensus[4] regards local and systemic complications as the basis for AP classification. Systemic complications include SIRS, organ failure (OF), etc. OF is evaluated based on a modified Marshall score, including relayatory (PaO2 / FiO2), renal,

cardiovascular. Due to the influence of DKA, AP classification cannot be fully referred to the Atlanta International Consensus. Roberto et al[17] found that the mortality of AP with DKA was higher than that of AP-only. All patients included in this study were cured, because some patients had ketosis without ketoacidosis, there were fewer severe APs, misdiagnosis and mistreatment did not occurr, and we control patients'blood glucose in time. The current scoring systems for predicting the prognosis of AP include Ranson score, MCTSI, BISAP score, etc.[18-20] This study found that the length of hospital stay was related to MCTSI, Ranson score, and BISAP score, indicating that all the three can judge the prognosis and length of stay. However, the indicators of blood glucose, WBC, and AST in the Ranson score had nothing to do with the length of hospital stay, which indicates that the score is too high. It can be reduced to several indicators such as age, LDH, and blood calcium to easily and effectively evaluate the length of stay for this disease. The indicators such as BUN, pleural fluid, and age in the BISAP score were related to the length of stay. The mental state score in DKA cannot accurately reflect the actual situation of the patient. Therefore, the BISAP scoring is sometimes overly high. It is easier to use age, BUN, and pleural fluid to predict the length of stay effectively.

In summary, hyperlipidemia often occurs in patients with AP associated DKA. Diabetes screening should be strengthened in healthy people, blood glucose control should be strengthened in diabetic patients, and DKA and AP should be reduced. The severity classification of AP with DKA is mainly based on the MCTSI. The length of hospital stay is positively related to age, amylase, LDH, blood calcium, and pleural effusion. These indicators can be used to determine the length of hospital stay. Due to DKA interference, the AP needs to further improve its classification system for pancreatitis in Atlanta. Due to the small number of severe pancreatitis in this study, the clinical characteristics of DKA complicated by severe pancreatitis need to be further studied.

Declarations

Ethics approval and consent to participate: The experimental protocol was established, according to the ethical guidelines of the Helsinki Declaration and was approved by the Human Ethics Committee of Yiwu Tianxiang medical Oriental Hospital. Written informed consent was obtained from individual or guardian participants.

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References

1. Yuzheng X , Yingyue S , Hong D , et al. Risk of development of acute pancreatitis with pre-existing diabetes: a meta-analysis. European Journal of Gastroenterology & Hepatology, 2012, 24(9):1092.
2. Hisashi U , Masanori T , Ying L , et al. Increased Risk of Acute Pancreatitis in Patients with Type 2 Diabetes: An Observational Study Using a Japanese Hospital Database. PLoS ONE, 2012, 7(12):e53224-.
3. Nair S , Yadav D , Pitchumoni C S . Association of Diabetic Ketoacidosis and Acute Pancreatitis: Observations in 100 Consecutive Episodes of DKA. American Journal of Gastroenterology, 2000, 95(10):2795-2800.
4. Banks P A , Bollen T L , Dervenis C , et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut, 2013, 62(1):102-111.
5. Wolfsdorf J I , Glaser N , Agus M , et al. ISPAD Clinical Practice Consensus Guidelines 2018: Diabetic ketoacidosis and the hyperglycemic hyperosmolar state. Pediatric Diabetes, 2018.
6. Kitabchi AE, Umpierrez GE, Miles JM, Fisher JN. Hyperglycemic crises in adult patients with diabetes. Diabetes Care 2009; 32:1335.
7. Centers for Disease Control and Prevention,Diabetes Public Health Resource http://www.cdc.gov/diabetes/statistics/hospitalization_national.htm (Accessed on March 26, 2014).
8. C. Roberto Simons-Linares, et al. The triad of diabetes ketoacidosis, hypertriglyceridemia and acute pancreatitis. How does it affect mortality and morbidity?: A 10-year analysis of the National Inpatient Sample. Medicine, 2019.
9. Benoit S R , Zhang Y , Geiss L S , et al. Trends in Diabetic Ketoacidosis Hospitalizations and In-Hospital Mortality — United States, 2000–2014[J]. MMWR. Morbidity and mortality weekly report, 2018, 67(12):362-365.
10. Maguire G A , Edwards O M . Seasonal variation in glycated haemoglobin in diabetics. Annals of Clinical Biochemistry, 2001, 38(1):59-60.
11. Gorham E D , Barrett-Connor E , Highfill-Mcroy R M , et al. Incidence of insulin-requiring diabetes in the US military. Diabetologia, 2009, 52(10):2087-2091.
12. Rewers A , Chase H P , Mackenzie T , et al. Predictors of acute complications in children with type 1 diabetes. JAMA The Journal of the American Medical Association, 2002, 287(19):2511-2518.
13. YAN Jin-hua, YANG Dai-zhi,DEN Hong-rong,et al.Incidence and related risk factors of diabetic ketoacidosis in Guangdong type 1 diabetics.National medical journal of china, 2013, 93(12):897-901.
14. Scherer J , Singh V P , Pitchumoni C S , et al. Issues in hypertriglyceridemic pancreatitis: an update. Journal of clinical gastroenterology, 2014, 48(3):195.
15. Nawaz H, Koutroumpakis E, Easler J, et al. Elevated serum triglycerides are independently associated with persistent organ failure in acute pancreatitis. Am J Gastroenterol 2015; 110:1497.
16. Idampitiya C , Sithole J , Idris I . Age is the only independent predictor for the length of hospital stay in patients admitted to a UK district general hospital with diabetic ketoacidosis. European Journal of

Internal Medicine, 2006, 17(8):1.

17. C, Roberto, Simons-Linares, et al. The triad of diabetes ketoacidosis, hypertriglyceridemia and acute pancreatitis. How does it affect mortality and morbidity?: A 10-year analysis of the National Inpatient Sample. Medicine, 2019.
18. Zhao K, Adam SZ, Keswani RN, et al. Acute pancreatitis:revised Atlanta classification and the role of cross-sectional imaging. Am J Roentgenol, 2015, 205 (1): W32-W41.
19. Ranson J H , Rifkind K M , Roses D F , et al. Objective early identification of severe acute pancreatitis. American Journal of Gastroenterology, 1974, 61(6):443.
20. Wu B U , Johannes R S , Sun X , et al. The early prediction of mortality in acute pancreatitis: a large population-based study. Gut, 2008, 57(12):1698-1703.
21. Carr R A , Rejowski B J , Cote G A , et al. Systematic review of hypertriglyceridemia-induced acute pancreatitis: A more virulent etiology?. Pancreatology, 2016:S1424390316000508.