Int J Clin Exp Med 2019;12(11):13005-13011
www.ijcem.com /ISSN:1940-5901/IJCEM0100658

Original Article

Prognostic value of venous blood gas analysis in patients with diabetic ketoacidosis

Na Zhao[1], Liang Ma[2], Sen Bai[1], Lifeng Gao[3], Hui Zhao[2]

Departments of [1]Veteran Carder, [2]Imaging, [3]First Department of Pediatrics, Ji'nan Jiyang District People's Hospital, Ji'nan, Shandong Province, China

Received August 7, 2019; Accepted October 8, 2019; Epub November 15, 2019; Published November 30, 2019

Abstract: Objective: To investigate the application value of venous blood gas analysis in the diagnosis and treatment of patients with diabetic ketoacidosis (DKA). Methods: Eighty-six patients with diabetic ketoacidosis who underwent routine emergency treatment during the period of illness were enrolled in the study. During a 25-day follow up, 68 patients survived and 18 died. According to the follow-up results, the patients were grouped, retrospectively analyzed for pre-treatment arterial blood gas, pre- and post-treatment venous blood gas using receiver operating characteristic curve. Besides, acute physiology and chronic health evaluation II (APACHE II) score was used to evaluate the prognosis of DKA. Results: The overall correlation coefficients of pH, PO_2, PCO_2, HCO_3^- and BE values in arterial and venous blood gas analysis were 0.561, 0.367, 0.782, 0.749, and 0.674, respectively (all $P<0.05$). The APACHE II score of the survival group was significantly lower than that of the death group ($t=6.321$, $P=0.004$). The area under the curve of the PO_2 and APACHE II scores were 0.915 and 1.000, respectively, with significant differences ($\chi^2=4.395$, $P=0.036$). There was significant correlation between APACHE II score and PO_2, PCO_2 and pH, and the correlation coefficients were 0.548, 0.572 and -0.441, respectively (all $P<0.05$). Conclusion: The venous blood gas analysis can replace the arterial blood gas analysis in early evaluation of prognosis in patients with DKA. The PO_2 and PCO_2 were significantly correlated with APACHE II score. So, the two easily analyzed indices, PO_2 and PCO_2, are accurate indices for the evaluation of the therapeutic effect of DKA and are conducive to clinical promotion.

Keywords: Venous blood gas analysis, diabetic ketoacidosis, acute physiology and chronic health evaluation II, prognostic value

Introduction

Diabetic ketoacidosis (DKA) is a kind of hyperglycemia caused by metabolic disorders of sugar, protein and fat because of severe insulin deficiency, infection or inflammation [1]. As a common acute complication of diabetes, DKA mainly threats life due to damage and failure of brain, kidney and other organs [2]. The global incidence of DKA is 13%-80%, with a clinical mortality of about 20% [3].

Blood gas analysis, as an important method to understand the acid-base balance state and pulmonary gas exchange function of patients, is significant for the diagnosis and evaluation of the therapeutic effect of DKA [4]. Arterial blood gas (ABG) analysis is the major tool for the diagnosis and treatment of acid-base imbalance [5]. However, the invasiveness of arterial puncture and its possible hazards (such as arterial spasm) have disadvantages such as large amount of suffering, the formation of thrombosis and aneurysm, or infection in patients [6]. In recent years, venous blood gas (VBG) analysis in patients with DKA has been studied and showed equally accurate results, but with simpler procedures and less suffering [7]. This study was designed to investigate the accuracy of VBG analysis for the prediction of prognosis in patients with DKA.

Materials and methods

Baseline data

A total of 86 patients with DKA admitted to Ji'nan Jiyang District People's Hospital from January 2018 to January 2019 were included as subjects, all of which met the clinical diag-

nostic criteria for DKA developed by the Chinese Diabetes Society in 2013 [8]. The patients were followed up for 25 days, and then included in the survival group (68 cases) and the death group (18 cases) according to different prognosis. In the survival group, there were 41 males and 27 females, aged 47-72 years, with a mean age of 56.32±8.51 years. In the death group, there were 10 males and 8 females, aged 48-75 years, with a mean age of 56.89±9.15 years. This study was approved by the Ethics Committee of Ji'nan Jiyang District People's Hospital, and informed consent was obtained from all the patients prior to the enrollment.

Patients were eligible if they met the diagnostic criteria for DKA, developed by the Chinese Diabetes Society in 2013 (clinical manifestations: nausea and vomiting, polyuria, and dehydration; blood glucose >16 mmol/L, blood pH<7.3, and CO_2 binding capacity <22 mmol/L; positive urine acetone bodies) [8]; had acute physiology and chronic health evaluation II (APACHE II) score ≥8 points [9]; were willing to participate in this study and signed informed consent.

Patients were excluded if they had heart, lung, kidney disease; had acidosis caused by alcoholism or hunger; were pregnant or in lactation; or had mental disorders.

Methods

All patients were collected for medical history after admission, closely and continuously monitored for vital signs and disease condition. Fluid infusion, acid-base balance, and water-electrolyte balance were performed by giving sodium bicarbonate, liquid potassium, and isotonic sodium chloride. Besides, conventional treatments such as intravenous insulin were carried out for reducing blood glucose and ketone bodies. The treatment period was ≥2 days.

Examination and outcome measures

Before treatment, 1 mL of radial artery blood and 1 mL of elbow venous blood were collected from patients at rest for examination using a disposable syringe moistened uniformly with heparin sodium. The arterial and VBG indices were analyzed using a RAPIDLab 248 blood gas analyzer (Siemens AG, Germany), and electrolyte concentrations of K^+, Na^+, Cl^-, and AG were measured using a PL1000A electrolyte analyzer (Beijing Prelong, China). After treatment, the VBG indices were reexamined.

APACHE II score

The APACHE II score was determined by self-made scale, consisting of acute physiologic score, age score, and chronic physiologic score. Higher score indicated more serious condition [9].

Statistical analyses

Data were processed using SPSS 21.0 statistical software. Count data were presented as number of cases and percentage (n, %), and compared between groups using the Mann-Whitney U test, chi-square test or Fisher's exact test. Measurement data were presented as mean ± standard deviation and compared between groups using t-test. The correlation analyses between VBG indices and ABG indices, APACHE II score were performed with the use of Pearson's correlation coefficient. The area under the curve (AUC) was calculated using the receiver operating characteristic curve. The blood gas indices and APACHE II score were analyzed for the predication of the prognosis of DKA. P<0.05 was considered statistically significant.

Results

Comparison of general data

The causes of onset, fingertip blood glucose, urine sugar, urinary ketone body, and ABG before treatment were compared between the two groups, while the differences were not statistically significant (all P>0.05). The electrolyte concentrations at baseline between the two groups were also compared. The levels K^+, Cl^-, and AG were slightly higher in the survival group than those in the death group, while the Na^+ had the opposite results, but the differences between the two groups were also not significant (all P>0.05). See **Tables 1** and **2**.

Comparison of VBG analysis

The overall correlation coefficients of pH, PO_2, PCO_2, HCO_3^- and BE values in ABG analysis and VBG analysis were 0.561, 0.367, 0.782, 0.749, and 0.674, respectively (all P<0.05). The results

Table 1. Causes of onset (n, %)

Cause of onset	Survival group (n=68)	Death group (n=18)	χ^2	*P* value
Infection or inflammation	23 (33.82)	6 (33.33)	0.002	0.969
Upper respiratory infection	13 (19.12)	3 (16.67)	0.057	0.812
Skin (including foot) infection	4 (5.88)	1 (5.56)		1.000
Gastrointestinal infections	4 (5.88)	1 (5.56)		1.000
Others (lung, urinary, etc.)	2 (2.94)	1 (5.56)	0.289	0.591
Stop or unregulated treatment	7 (10.29)	3 (16.67)	0.563	0.453
Irregular diet, drinking, or sweet drinks	7 (10.29)	3 (16.67)	0.563	0.453
Fatigue	4 (5.88)	1 (5.56)		1.000
Others	2 (2.94)	1 (5.56)	0.289	0.591
No obvious cause	25 (36.76)	4 (22.22)	1.347	0.246

Table 2. Comparison of baseline data

Item	Survival group (n=68)	Death group (n=18)	t/z value	*P* value
Fingertip blood glucose (mmol/L)	23.91±6.58	23.72±6.35	0.110	0.457
Urine sugar			1.806	0.071
1^+	16 (23.53)	1 (5.56)		
2^+	21 (30.88)	5 (27.78)		
3^+	19 (27.94)	7 (38.89)		
4^+	12 (17.65)	5 (27.78)		
Urine acetone body			1.168	0.243
1^+	19 (27.94)	3 (16.67)		
2^+	18 (26.47)	4 (22.22)		
3^+	17 (25.00)	6 (33.33)		
4^+	14 (20.59)	5 (27.78)		
Arterial blood gas analysis				
pH	7.20±0.14	7.21±0.12	0.277	0.391
HCO_3^-	9.42±2.64	9.81±3.75	0.508	0.307
BE	-17.37±6.51	-17.26±7.47	0.062	0.525
Electrolyte concentration				
K^+	4.02±0.46	3.89±0.35	1.115	0.134
Na^+	138.37±2.51	139.42±2.64	1.561	0.061
Cl^-	101.26±3.47	99.81±3.75	1.550	0.062
AG	16.36±3.92	14.73±3.58	1.596	0.057

of VBG analysis of the two groups before and after treatment are shown in **Table 3**. Before treatment, the pH and PO_2 values of the survival group were slightly higher than those of the death group, while the PCO_2, HCO_3^- and BE of the survival group were slightly lower than those of the death group, without significant differences between the two groups (all P>0.05). After treatment, the pH of the survival group was significantly higher than that of the death group, while the PO_2, PCO_2, HCO_3^- and BE of the survival group were significantly lower than those of the death group (all P<0.05). There were significant differences in VBG indices between before and after treatment in both groups (all P<0.05), except for the difference in PO_2 in the survival group.

Comparison of APACHE II score

The APACHE II scores of the two groups are shown in **Table 4**. The APACHE II score of the survival group was significantly lower than that of the death group (t=9.250, P=0.000).

Table 3. Venous blood gas analysis before and after treatment

Group	Survival group		Death group	
	Before treatment	After treatment	Before treatment	After treatment
pH	7.05±0.11	7.35±0.02*	7.04±0.09	7.32±0.03*,#
PO_2 (mmHg)	57.12±8.17	60.12±6.78	56.46±7.68	66.46±6.18*,#
PCO_2 (mmHg)	40.18±3.47	45.31±9.85*	41.02±3.75	52.09±9.25*,#
HCO_3^- (mmol/L)	15.12±3.05	16.46±1.13*	15.19±3.24	19.11±1.45*,#
BE (mmol/L)	17.91±8.11	1.79±0.82*	18.12±7.89	2.23±0.84*,#

Note: *indicates statistically significant difference (P<0.05) between before and after treatment in the same group; #indicates statistically significant difference (P<0.05) between the survival group and the death group at the same time point.

Table 4. Comparison of APACHE II scores

Group	N	APACHE II score (point)
Survival group	68	17.44±4.21
Death group	18	29.79±7.45
t		9.250
P		0.000

Note: APACHE: acute physiology and chronic health evaluation.

Table 5. AUC of blood gas analysis indices and APACHE II score

Index	AUC	SE	95% CI
pH	0.873	0.0459	0.784-0.935
PO_2	0.915	0.0405	0.835-0.964
PCO_2	0.854	0.0557	0.762-0.921
HCO_3^-	0.597	0.0785	0.486-0.701
BE	0.511	0.0964	0.401-0.620
APACHE II	1.000	0.0000	0.958-1.000

Note: ACU: area under the curve; APACHE: acute physiology and chronic health evaluation; SE: standard error; CI: confidential interval.

Receiver operating characteristic curve

The AUC of PO_2 and APACHE II score were 0.915 and 1.000, respectively, with statistically significant difference (χ^2=4.395, P=0.036). The differences in AUC between the APACHE II score and the blood gas analysis indices were statistically significant (all P<0.05). The AUC of PO_2 was larger than other blood gas indices. The difference in AUC between PO_2 and PCO_2 was not significant (χ^2=2.913, P=0.088), while the differences between PO_2 and HCO_3^-, BE were statistically significant (both P<0.05). There was significant correlation between APACHE II score and PO_2, PCO_2, pH, and the correlation coefficients were 0.548, 0.572 and -0.441, respectively (all P<0.01). See **Table 5** and **Figure 1**.

Discussion

In recent years, the prevalence of diabetes has increased rapidly with the improvement of living standards, so the risk of its complications has increased accordingly [10]. DKA is a common acute complication in clinical diabetic patients, mainly characterized by elevated blood glucose, increased blood ketone bodies and metabolic acidosis. DKA will cause other complications and even lead to death without timely treatment [11, 12]. In addition, the severity of DKA is closely related to hospitalization time, nursing costs, intensive care requirements, intravenous or non-venous needs, and mortality [13]. Therefore, early diagnosis and effective treatment are important for the prognosis of patients with DKA [14].

Blood gas analysis is a commonly used diagnostic tool to evaluate the partial pressure and acid-base content in blood, so as to explain the pathological mechanisms of respiratory, circulatory and metabolic disorders, monitor the severity and progression of cardiopulmonary diseases, and assess the response of patients from certain therapeutic interventions [15]. Blood gas analysis can be performed by blood taken from anywhere in the circulatory system (arteries, veins, or capillaries) [16]. ABG analysis is the best way to assess the severity of acute or chronic disease, primary or secondary disease, as well as metabolic or respiratory disorders [5]. A major method for preliminary assessment of the severity of DKA and the treatment efficacy is using ABG analysis to measure the pH and bicarbonate [7]. However, there is growing evidence showing that VBG analysis can be used as an alternative to ABG analysis [6]. Kelly et al. reported that the weighted mean difference between arterial and venous pH values in DKA patients was 0.02 pH units (95% range: -0.009 to +0.021 pH units), and the weighted mean difference between arterial and venous bicarbonates was -1.88 mEq/L, suggesting that the arterial and venous pH values are consistent and clinically inter-

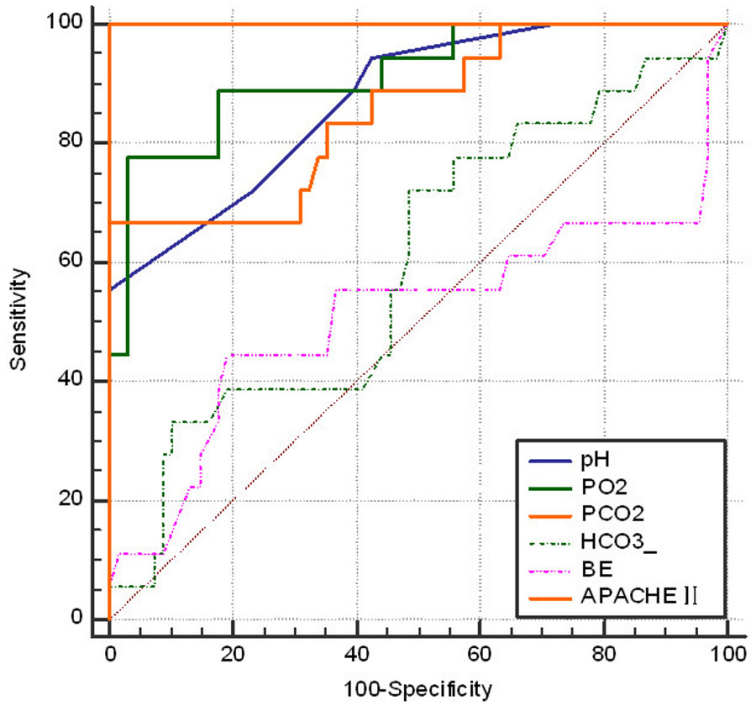

Figure 1. ROC curves of blood gas analysis indices and APACHE II score. ROC: receiver operating characteristic; APACHE: acute physiology and chronic health evaluation.

changeable in DKA patients with stable hemodynamics and without respiratory failure [15, 16]. Hale et al. compared the measurements of pH and blood gas indices in the arteries and non-arterial capillary blood vessels collected from patients with DKA, and found high correlation in pH, PCO_2 and bicarbonate. The pH value of the capillaries was slightly lower, while the PCO_2 and bicarbonate of the capillaries were slightly higher than those in the arteries, without significant difference [17]. In this study, the overall correlation coefficients of pH, PO_2, PCO_2, HCO_3^- and BE values in ABG analysis and VBG analysis were 0.561, 0.367, 0.782, 0.749, and 0.674, respectively, which again proved the promising correlation between VBG and ABG analyses [18]. The pH value obtained by VBG is not only accurate, but also easy to obtain, and it brings the patients less suffering [19]. Furthermore, the turnaround time of VBG is approximately 15 minutes, which is much faster than the 1-hour turnaround time in serum chemical analysis. In this way, the clinicians can make faster treatment decisions, so VBG is worthy of clinical promotion. In this study, the pH value was higher in the survival group than that in the death group, and other indices were all lower in the survival group than those in the death group, which is consistent with the findings of Lee et al., who believed that low pH and high serum potassium levels at admission were independent predictors of favorable prognosis of DKA [20]. The electrolyte concentrations of blood are of great significance for the diagnosis of DKA. The results of Menchine et al. showed that the correlation coefficients of VBG with serum chemical sodium, chloride, bicarbonate and anion gap were 0.90, 0.73, 0.94 and 0.81, respectively. Besides, VBG had excellent sensitivity (97.8%) and specificity (100%) for the diagnosis of DKA in patients with hyperglycemia [19]. In addition, von Oettingen et al. believed that HCO_3^->15 mmol/L was associated with a venous pH≥7.30, with 76% sensitivity and 85% specificity for predicting DKA [21]. Nyenwe derived arterial pH =6.97+0.0163*HCO_3^-, which predicated that when the serum venous bicarbonate concentration is less than 20.6 mEq/L, the arterial pH is less than 7.3, with a sensitivity of over 95%, and accuracy of 92% [22]. Therefore, in areas with insufficient medical conditions for VBG, electrolyte parameters can be used alone to diagnose DKA [21].

APACHE II score is calculated based on 12 physiological criteria, age, and previous status, and is closely related to hospitalization and 1-month mortality in critically ill patients [9]. Aminiahidashti et al. reported Simplified Acute Physiologic Score (SAPS) II and APACHE II scores in 82 critically ill patients in the emergency department, and the scores were significantly higher in the patients who died (48%) than those in survived patients. The AUC of SAPS II and APACHE II for predicting mortality were 0.75 (95% CI: 0.64-0.86) and 0.72 (95% CI: 0.60-0.83), respectively [23]. In this study, the APACHE II score was significantly higher in the death group than that in the survival group, indicating that the APACHE II score can be used

as a prognostic indicator for patients with DKA. Moreover, the AUC of the PO_2 and APACHE II scores was the largest, indicating that these two indicators are the most accurate and can be used in evaluating the prognosis of DKA [24].

However, there are some limitations in this study. The acceptable normal range of ABG values may vary in different laboratories and different age groups. ABG cannot be replaced by VBG in diseases such as neonatal epilepsy, shock, congestive heart failure and congenital heart disease [25]. Therefore, further researches about application range of VBG are needed.

In conclusion, the VBG analysis can replace the ABG analysis in early evaluation of the prognosis of patients with DKA. The PO_2 and PCO_2 were significantly correlated with APACHE II scores. So, the two indices, PO_2 and PCO_2, which can be easily analyzed, are accurate for the evaluation of therapeutic effect of DKA, and are worthy of clinical promotion.

Disclosure of conflict of interest

None.

Address correspondence to: Na Zhao, Department of Veteran Carder, Ji'nan Jiyang District People's Hospital, No. 17 Xinyuan Street, Jiyang District, Ji'nan 251400, Shandong Province, China. Tel: +86-18678871933; E-mail: zhaona03s@163.com

References

[1] Voss TS, Vendelbo MH, Kampmann U, Pedersen SB, Nielsen TS, Johannsen M, Svart MV, Jessen N and Moller N. Substrate metabolism, hormone and cytokine levels and adipose tissue signalling in individuals with type 1 diabetes after insulin withdrawal and subsequent insulin therapy to model the initiating steps of ketoacidosis. Diabetologia 2019; 62: 494-503.

[2] Desai R, Singh S, Syed MH, Dave H, Hasnain M, Zahid D, Haider M, Jilani SMA, Mirza MA, Kiran N and Aziz A. Temporal trends in the prevalence of diabetes decompensation (diabetic ketoacidosis and hyperosmolar hyperglycemic state) among adult patients hospitalized with diabetes mellitus: a nationwide analysis stratified by age, gender, and race. Cureus 2019; 11: e4353.

[3] Gaffney A, Christopher A, Katz A, Chateau D, McDougall C, Bor D, Himmelstein D, Woolhandler S and McCormick D. The incidence of diabetic ketoacidosis during "emerging adulthood" in the USA and Canada: a population-based study. J Gen Intern Med 2019; 34: 1244-1250.

[4] Martin CM and Priestap F. Agreement between venous and arterial blood gas analysis of acid-base status in critical care and ward patients: a retrospective cohort study. Can J Anaesth 2017; 64: 1138-1143.

[5] McKeever TM, Hearson G, Housley G, Reynolds C, Kinnear W, Harrison TW, Kelly AM and Shaw DE. Using venous blood gas analysis in the assessment of COPD exacerbations: a prospective cohort study. Thorax 2016; 71: 210-215.

[6] Esmaeilivand M, Khatony A, Moradi G, Najafi F and Abdi A. Agreement and correlation between arterial and central venous blood gas following coronary artery bypass graft surgery. J Clin Diagn Res 2017; 11: OC43-OC46.

[7] Kelly AM. Review article: can venous blood gas analysis replace arterial in emergency medical care. Emerg Med Australas 2010; 22: 493-498.

[8] Chinese Diabetes Society. Guidelines of diagnosis and therapy of hyperglycemia crisis in China. Chin J Diabetes Mellitus 2013; 5: 449-461.

[9] Safari S, Rahmani F, Soleimanpour H, Ebrahimi Bakhtavar H and Mehdizadeh Esfanjani R. Can APACHE II score predict diabetic ketoacidosis in hyperglycemic patients presenting to emergency department? Anesth Pain Med 2014; 4: e21365.

[10] Ndebele NFM and Naidoo M. The management of diabetic ketoacidosis at a rural regional hospital in KwaZulu-Natal. Afr J Prim Health Care Fam Med 2018; 10: e1-e6.

[11] Mao W, Yip CW and Chen W. Complications of diabetes in China: health system and economic implications. BMC Public Health 2019; 19: 269.

[12] Desai D, Mehta D, Mathias P, Menon G and Schubart UK. Health care utilization and burden of diabetic ketoacidosis in the U.S. over the past decade: a nationwide analysis. Diabetes Care 2018; 41: 1631-1638.

[13] George JT, Mishra AK and Iyadurai R. Correlation between the outcomes and severity of diabetic ketoacidosis: a retrospective pilot study. J Family Med Prim Care 2018; 7: 787-790.

[14] Thewjitcharoen Y, Plianpan P, Chotjirat A, Nakasatien S, Chotwanvirat P, Wanothayaroj E, Krittiyawong S and Himathongkam T. Clinical characteristics and outcomes of care in adult patients with diabetic ketoacidosis: a retrospective study from a tertiary diabetes center in Thailand. J Clin Transl Endocrinol 2019; 16: 100188.

[15] Kelly AM. The case for venous rather than arterial blood gases in diabetic ketoacidosis. Emerg Med Australas 2006; 18: 64-67.
[16] Patel MP, Ahmed A, Gunapalan T and Hesselbacher SE. Use of sodium bicarbonate and blood gas monitoring in diabetic ketoacidosis: a review. World J Diabetes 2018; 9: 199-205.
[17] Hale PJ and Nattrass M. A comparison of arterial and non-arterialized capillary blood gases in diabetic ketoacidosis. Diabet Med 1988; 5: 76-78.
[18] Ma OJ, Rush MD, Godfrey MM and Gaddis G. Arterial blood gas results rarely influence emergency physician management of patients with suspected diabetic ketoacidosis. Acad Emerg Med 2003; 10: 836-841.
[19] Menchine M, Probst MA, Agy C, Bach D and Arora S. Diagnostic accuracy of venous blood gas electrolytes for identifying diabetic ketoacidosis in the emergency department. Acad Emerg Med 2011; 18: 1105-1108.
[20] Lee MH, Calder GL, Santamaria JD and MacIsaac RJ. Diabetic ketoacidosis in adult patients: an audit of factors influencing time to normalisation of metabolic parameters. Intern Med J 2018; 48: 529-534.
[21] von Oettingen JE, Rhodes ET and Wolfsdorf JI. Resolution of ketoacidosis in children with new onset diabetes: evaluation of various definitions. Diabetes Res Clin Pract 2018; 135: 76-84.
[22] Nyenwe EA, Wan JY and Kitabchi AE. Venous serum bicarbonate concentration predicts arterial pH in adults with diabetic ketoacidosis. Endocr Pract 2014; 20: 201-206.
[23] Aminiahidashti H, Bozorgi F, Montazer SH, Baboli M and Firouzian A. Comparison of APACHE II and SAPS II scoring systems in Prediction of Critically Ill patients' outcome. Emerg (Tehran) 2017; 5: e4.
[24] Huang J, Xuan D, Li X, Ma L, Zhou Y and Zou H. The value of APACHE II in predicting mortality after paraquat poisoning in Chinese and Korean population: a systematic review and meta-analysis. Medicine (Baltimore) 2017; 96: e6838.
[25] Bilan N, Behbahan AG and Khosroshahi AJ. Validity of venous blood gas analysis for diagnosis of acid-base imbalance in children admitted to pediatric intensive care unit. World J Pediatr 2008; 4: 114-117.