Arterial vs Venous Blood Gas Analysis in Diabetic Ketoacidosis A Cross Sectional Study

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Abstract: Background and Objectives**:** Diabetic Ketoacidosis (DKA) is an endocrinal emergency responsible for significant amount of admissions in Medical Emergency Ward (EW) for which Arterial blood gas analysis (ABGA) is a cornerstone in diagnosis and management. The objective was to study, compare and determine degree of agreement between values of ABGA and Venous blood gas analysis (VBGA) (pH, HCO_3^-, pCO_2) in DKA patients before commencement of treatment and whether VBGA can replace ABGA in evaluation of these patients. Methods: A cross-sectional study was conducted in which a total of 40 patients, above the age of 18 years, both males and females, presenting with DKA were enrolled. Patients' samples for ABGA and VBGA were taken and the strength of association between arterial and venous pH, HCO_3^-, pCO_2 values was assessed with Pearson Correlation Coefficient (r). Results: Strong linear correlation was found between Arterial and Venous pH, HCO_3^- and pCO_2 values. The p value (< 0.0001) for all the three was statistically significant with >95% degree of agreement. Conclusion: Based on the strong correlation, VBGA can be used as an alternative to ABGA in DKA patients in Emergency Ward to evaluate as well as monitor blood pH, HCO_3^- and pCO_2 levels [Pathak J Natl J Integr Res Med, 2019; 10(4):52-58]

Key Words: Arterial Blood Gas Analysis, Diabetic Ketoacidosis, Venous Blood Gas Analysis.

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Introduction: Diabetic Ketoacidosis (DKA) is a metabolic derangement consisting of high blood glucose concentration, measurable ketone bodies in blood and/or urine, and metabolic acidosis. It mainly occurs in patients with type 1 Diabetes Mellitus (DM), but it is not uncommon in patients with type 2 DM[1].

DKA is an endocrinal emergency, responsible for significant amount of admissions in Medical Emergency Ward (EW). It is the most common serious and life-threatening acute complication of DM. The mortality rate is currently estimated at 2% to 10% for patients hospitalized with DKA. Due to its increasing incidence and economic impact related to the treatment and associated morbidity, effective management and prevention is the key. Elements of management include making the appropriate diagnosis using current laboratory tools and clinical criteria and coordinating fluid resuscitation, insulin therapy, and electrolyte replacement through feedback obtained from timely patient monitoring and knowledge of resolution criteria.

DKA is defined as an increase in the serum concentration of ketones greater than 5 mEq/L, a blood glucose level greater than 250 mg/dl (although it is usually much higher), and a blood (usually arterial) pH less than 7.3. Ketonemia and ketonuria are characteristic, as is a serum bicarbonate level of 18 mEq/L or less (less than 5 mEq/L is indicative of severe DKA). These biochemical changes are frequently associated with increased anion gap, increased serum osmolarity and increased serum uric acid[2-4]. Arterial blood gas analysis (ABGA) is indicated for identification of respiratory, metabolic, and mixed acid-base disorders, with or without physiologic compensation, by means of pH, pCO_2 level, pO_2 level, and HCO_3^- level. Determination of Arterial blood gas (ABG) values is currently considered essential for evaluation of patients with suspected DKA.

Sampling of arterial blood is a painful, sometimes technically difficult procedure that must be done in addition to the sampling of venous blood for testing electrolytes, ketones, and other parameters. Arterial blood gas analysis (ABGA) sampling may also be complicated with local haemorrhage/ hematoma, arterial occlusion, air/thrombus embolism, infection at puncture site, needle stick injury to health care personnel, etc[5-6].

Several authors have recommended the use of venous pH in place of arterial pH in the evaluation of DKA. The correlation between arterial and venous pH measurements is well established. However, this relationship has not been established in DKA. If venous pH, HCO_3^- and pCO_2 values were found to be highly correlated and show a high level of agreement with arterial pH, HCO_3^- and pCO_2 values in patients who present with DKA, then it might be possible to

eliminate arterial blood sampling in the initial diagnosis and evaluation of DKA[7-16].

The purpose of this study is to observe whether venous blood gas analysis (VBGA) can produce comparable results as Arterial blood gas analysis (ABGA) as this would be an easier method with lesser complications to diagnose and manage DKA.

Material and Methods: In this cross-sectional study conducted from February to October 2017, a total of 40 patients (both males and females) above the age of 18 years presenting with DKA and admitted in Emergency Ward (EW) of SSG Hospital, Baroda were enrolled. The inclusion criteria included patients who were confirmed cases of DM (Type 1/Type 2) as well as newly detected DM patients. Exclusion criteria included patients below 18 years of age and those who did not give informed consent.

A standardized proforma was used to record clinical history and perform a detailed clinical examination. Informed consent was taken from every participant. Patients were diagnosed to have DKA on the basis of detailed history, clinical symptoms/signs; and a bedside Random blood sugar (RBS) test was done with a glucometer. If it was >250 mg/dl, patients' samples for (Urine) ketones, ABGA, and VBGA were taken. A sample of arterial blood (0.5 to 1.0 mL) for ABGA was obtained from the radial artery of the patient. A sample of venous blood (0.5 to 1.0 mL) for VBGA was obtained from peripheral vein at the time of venipuncture for other laboratory reports. Both samples were obtained with strict antiseptic precautions. The two blood samples were obtained as temporally close to each other as possible and before the initiation of treatment, and were immediately sent to the laboratory in a strict sterile manner. The arterial and venous blood gas determinations were performed with Arterial blood gas analyzer with ID-LSCHABJMC/HITECH/ABG- E-3, Model- Combiline, Sr. no.CL0495, manufactured by M/S Eschweiler GmbH & Co., Germany. Urinary ketones were tested by using Multiple reagent strip and graded as (+), (++), and (+++) by color code method.

Demographic and laboratory data were recorded on a database form and then they were entered into a computer using Microsoft Excel Windows version 8.0 for statistical analysis. The strength of association (linear correlation) between arterial and venous pH, arterial and venous HCO_3^-, and arterial and venous pCO_2 results were assessed with Pearson Correlation Coefficient (r). The Coefficient of Determination (r^2) was used to measure the proportion of the variance in arterial levels that could be accounted for by the venous levels using a linear model. The degree of agreement between the arterial and venous pH measurements, arterial and venous HCO_3^- values, and the arterial pCO_2 and venous pCO_2 values was evaluated on Bland and Altman graph in which the difference between the paired determinations was plotted against the mean of any two determinations, as described by Bland and Altman. This type of plot is bounded by limits of agreement, defined as the mean of the arteriovenous differences ±2 Standard Deviation (SD).

Result: A total of 40 patients of DKA participated in the study. The demographic data of participants is shown in Table 1.

Table 1. Age and Gender wise distribution

Age (years)	Male	Female	Total
≤20	1	1	2
21-30	8	3	11
31-40	3	5	8
41-50	6	2	8
51-60	8	1	9
61-70	2	0	2
>70	0	0	0
Total	28	12	40

The known as well as newly detected cases are summarized in Table 2.

Table 2. History of DM

	Newly detected DM	Known case of DM	Total
Type 1 DM	9	16	25
Type 2 DM	0	15	15
Total	9	31	40

In the study, most common symptom was Nausea/Vomiting in 32 (80%) patients; followed by abdominal pain in 17 (42.5%), breathlessness in 13 (32.5%) and fever in 17 (42.5%) patients. Also, 12(30%) patients were found to have Mild DKA, 18 (45%) patients with Moderate DKA, and 10 (25%) patients with Severe DKA.

The aim of present study was to compare Venous Blood Gas (VBG) and Arterial Blood Gas (ABG) values in DKA patients. The results are shown in Figures 1, 2, 3 and the descriptive statistics of the study are summarized in Table 3.

Table 3. Descriptive statistics of present study

Variable	Mean	SD	Range
RBS (mg/dl)	423.7	107.5611	256-600
Arterial pH	7.0902	0.241613	6.38-7.3
Venous pH	7.2	0.178799	6.65-7.42
Arterial HCO_3^- (mmol/L)	7.915	5.10658	1.8-18
Venous HCO_3^- (mmol/L)	9.2275	5.62534	2.1-21.5
Arterial pCO_2(mmol/L)	19.95	7.46145	9.7-39.5
Venous pCO_2(mmol/L)	23.95	7.44848	9.9-40.8

Figure 1. pH range in arterial and venous blood

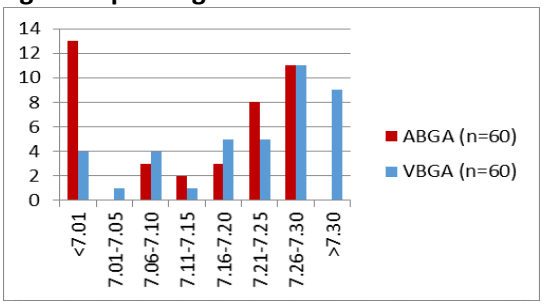


Figure 2. HCO_3^- range (mmol/L) in arterial and venous blood

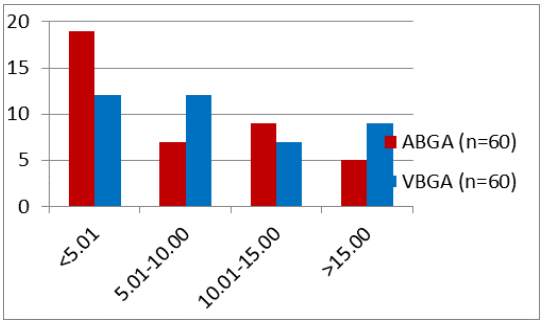
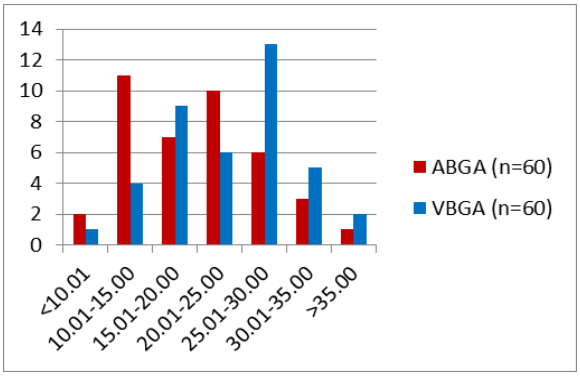


Figure 3. pCO_2 range (mmol/L) in arterial and venous blood



Strong linear correlation was found between Arterial and Venous pH, HCO_3^- and pCO_2 values. The p value for all the three were statistically significant with >95% degree of agreement. This suggests that Venous blood gas analysis (VBGA) can be used as an alternative to Arterial blood gas analysis (ABGA) in patients presenting with DKA in Emergency ward to evaluate as well as monitor the blood pH, HCO_3^- and pCO_2 levels.

Discussion: Arterial blood gases (ABGs) are commonly used for estimating the acid-base status, oxygenation and carbon dioxide concentration of unwell patients including DKA. However, arterial blood can be difficult to obtain due to weak pulses or patient movement. Due to thicker, muscular and innervated walls, arteries are also more painful to puncture than veins. As such, a venous blood gas analysis (VBGA) can be done. In the current study we have compared the values of both the analyses to determine whether VBGA can replace ABGA in the initial evaluation of DKA.

The findings of the study showed that maximum number of DKA patients belonged to a younger age group with majority being males. It was found that DKA was more common in Type 1 than Type 2 DM. All the newly detected cases were mainly of type 1 DM and most of them were already diagnosed cases of DM.

These findings are quite similar to the study done by Christopher A. Newton[17], in which incidence of Type 1 DM and Type 2 DM were 78.27% and 21.73% respectively. He found 19.9% patients with newly detected DM, and all of them having Type 1 DM. According to a study by Kitabchi in 2009, 66% of DKA patients were considered to have type 1 diabetes and 34% to have type 2 diabetes. Two-thirds of DKA patients were considered to have type 1 diabetes and 34% to have type 2 diabetes; 50% were females[18]. A study by Seth in 2015 showed that in six (10%) patients' Diabetic status (Type 1) was detected only when they presented with DKA complication[19]. Hence the results of the studies by Christopher A. Newton, Kitabchi and Seth were all consistent with the results of the present study.

The present study showed that the most common symptoms in patients presenting with DKA were nausea/vomiting followed by abdominal pain, breathlessness and fever. This

was similar to the study done by Christopher A. Newton, who found 81.4% patients having nausea, 78% having vomiting, 54.3% having breathlessness and 51.2% having abdominal pain[17]. These findings were consistent with a study by Kitabchi in 2009 in which nausea, vomiting and diffuse abdominal pain are frequent in patients with DKA (>50%)[18]. In a study by Westerberg, polyuria with polydipsia was the most common presenting symptom and was found in 98 percent of persons in one study of childhood type 1 diabetes. Other common symptoms included weight loss (81 percent), fatigue (62 percent), dyspnoea (57 percent), vomiting (46 percent), preceding febrile illness (40 percent), abdominal pain (32 percent), and polyphagia (23 percent)[20]. Thus, the results of the studies by Christopher A. Newton, Kitabchi and Seth were all consistent with the results of the present study while the results differed from those of the study by Westerberg.

In the present study, mean RBS was 423.7 with SD of 107.56 (Range 256-600). The mean Arterial pH was 7.090 with SD of 0.24 (Range 6.38-7.3) and the mean Venous pH was 7.2 with SD of 0.17 (Range 6.65-7.42). The mean difference between arterial and venous pH values was 0.11. Mean Arterial HCO_3^- (mmol/L) was 7.915 with SD of 5.106 (Range- 1.8-18) and mean Venous HCO_3^- (mmol/L) was 9.227 with SD of 5.625 (Range- 2.1-21.5). The mean difference between arterial and venous HCO_3^- values was 0.519. Mean of Arterial pCO_2 (mmol/L) was 19.95 with SD of 7.46 (Range-9.7-39.5) and mean of Venous pCO_2 was 23.95 with SD of 7.44 (Range- 9.9-40.8). The mean difference between arterial and venous CO2 Values was 4.

In 1996, Mark A Brandenburg and Daniel J Dire[21] did the study of comparison of Arterial and Venous Blood Gas Values in the Initial Emergency Department Evaluation of Patients with Diabetic Ketoacidosis. In their study, mean RBS was 609.9 with SD of 288 (Range 250-1464). The mean Arterial pH was 7.20 with SD of 0.14 (Range 6.78-7.39), the mean Venous pH was 7.170 with SD of 0.13 (Range 6.99-7.38).

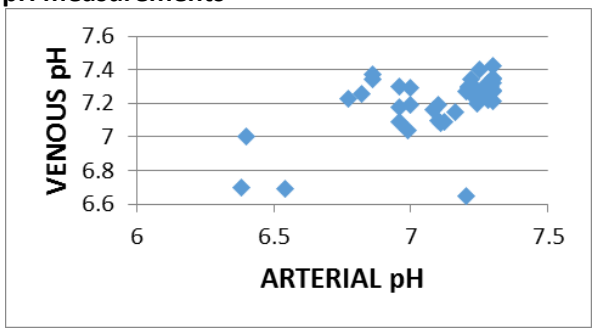
The mean difference between arterial and venous pH values was 0.03. Mean Arterial HCO_3^- (mmol/L) was 11.0 with SD of 6.0 (Range- 2-23), the mean Venous HCO_3^- (mmol/L) was 12.8 with SD of 5.5 (Range- 3-24). The mean difference between arterial and venous $pHCO_3^-$ values was 1.80. Mean of serum CO2 (mmol/L) was 11.8 with SD of 5.0 (Range- 2-24).

In a study by Seth, mean blood glucose at admission was 535.6 mg/dl in Type 1 and 380.07 mg/dl in Type 2 DM patients[19]. Mean serum potassium (4.55mEq/l), arterial pH (7.23) & bicarbonate level (12.46 mmol/l) were calculated. In our study severe acidosis with arterial pH <7.0 was found mainly in Type 1 Diabetic patients with DKA. According to a study by Ugramurthy[22] pH of capillary blood was reduced by a mean value of 0.04 with correlation of 0.709 and t-value of 6.5. The difference being not statistically significant.

A regression plot of arterial and venous pH measurements was made which suggested that the Coefficient of correlation (r) was 0.5654 with a p value of <0.0001which is statistically significant (Figure 4).

These values were similar to study done by Mark A Brandenburg and Daniel J Dire, which suggested that the Coefficient of correlation(r) was 0.9689 with a p value of <0.0001 which is statistically significant[21]. This shows a strong linear correlation between Arterial and Venous pH values.

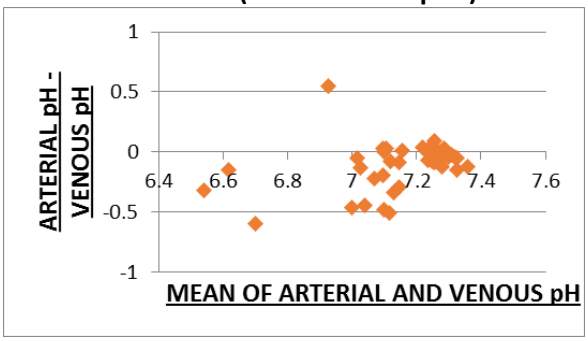
Figure 4. Regression plot of arterial and venous pH measurements



Differences between the arterial and venous pH measurements were plotted on the vertical axis against the corresponding means on the horizontal axis (Bland Altman plot). This showed that the Degree of agreement between arterial and venous pH was >95 % (Figure 5).

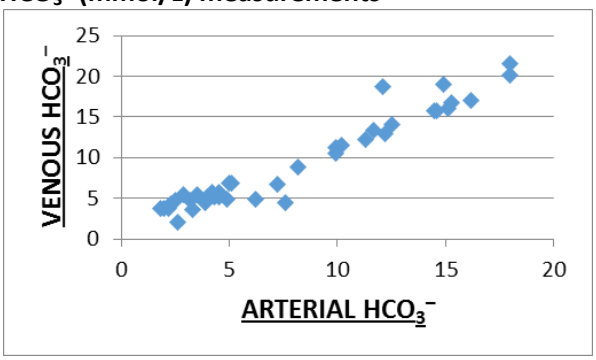
This value was similar with study done by Mark A Brandenburg and Daniel J Dire, who also had Degree of agreement >95 %[21]. This suggests that venous pH is almost equivalent to Arterial pH; and venous pH can be used in place of Arterial pH in initial evaluation of DKA patient.

Figure 5. Differences between arterial and venous pH measurements on the vertical axis are plotted against the corresponding means on the horizontal axis. (Bland Altman plot)



A regression plot of arterial and venous HCO_3^- (mmol/L) measurements showed that the Coefficient of correlation(r) was 0.9669 with p value of <0.0001 which was statistically significant (Figure 6).

Figure 6. Regression plot of arterial and venous HCO_3^- (mmol/L) measurements



These values were similar to study done by Mark A Brandenburg and Daniel J Dire[21], which suggested that the Coefficient of correlation (r) was 0.9543 with a p value of <0.0001 which was statistically significant.

This showed a strong linear correlation between Arterial and Venous HCO_3^- values suggesting that Venous HCO_3^- can replace Arterial HCO_3^-. The differences between arterial and venous HCO_3^- measurements (mmol/L) on the vertical axis were plotted against the corresponding means on the horizontal axis. (Bland Altman plot) showing a Degree of agreement >95 % (Figure 7). This value was similar to study done by Mark A Brandenburg and Daniel J Dire[21], who also had Degree of agreement >95 %. This suggests that Venous HCO_3^- is almost equivalent to Arterial HCO_3^-; and Venous HCO_3^- can be used in place of Arterial HCO_3^- in initial evaluation of DKA patient.

Regression plot of arterial and venous pCO_2 (mmol/L) measurements showed that the Coefficient of correlation r between the two was 0.9639 with p value <.0001 which is statistically significant (Figure 8). In a study by Ugramurthy[22] capillary pCO_2 was raised by a mean value of 3 with correlation of 0.91 and t-value of 16.18, indicating the deviation in opposite direction. The difference being not statistically significant. This showed a strong linear correlation between Arterial and venous pCO_2 values suggesting that venous pCO_2 can replace Arterial pCO_2.

Figure 7. Differences between arterial and venous HCO_3^- measurements (mmol/L) on the vertical axis are plotted against the corresponding means on the horizontal axis. (Bland Altman plot)

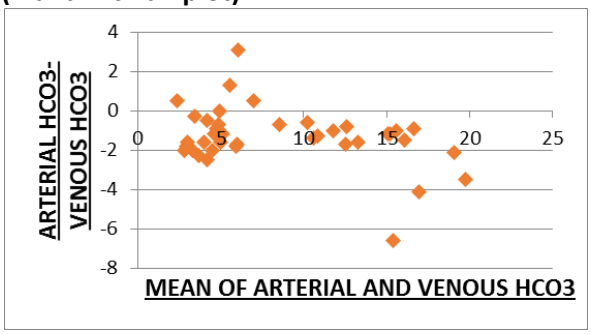


Figure 8. Regression plot of arterial and venous pCO_2 (mmol/L) measurements

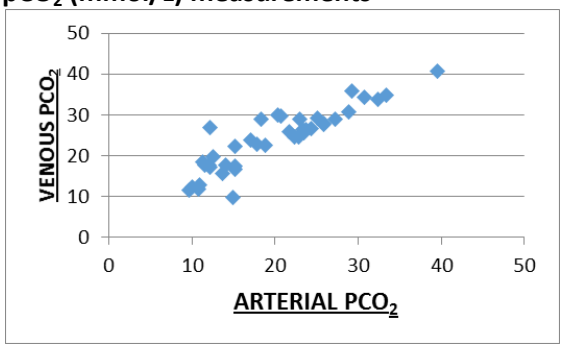
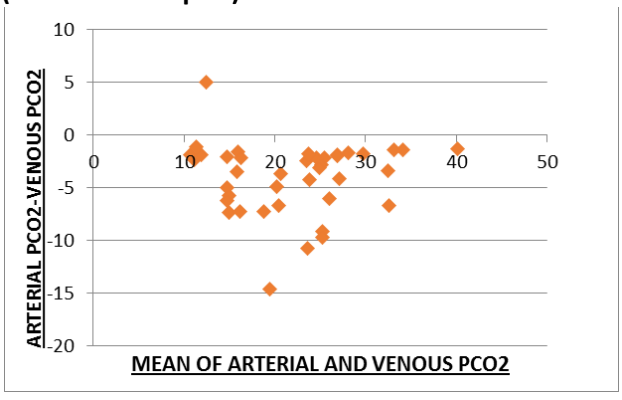


Figure 9. Differences between arterial and venous pCO_2 measurements (mmol/L) on the vertical axis are plotted against the corresponding means on the horizontal axis. (Bland Altman plot)



Differences between arterial and venous pCO_2 measurements (mmol/L) on the vertical axis were plotted against the corresponding means on the horizontal axis which showed a Degree of agreement >95 % (Figure 9).

Arterial and central venous blood gas values in a study by Treger were as follows[23]

Parameter		pH	pCO_2 (mm Hg)	HCO_3^- (mmol/L)
ABG	Mean	7.370	38.4	22.40
	SD	0.138	12.4	7.60
VBG	Mean	7.340	42.3	22.80
	SD	0.134	12.6	7.80
A-V Difference	Mean	0.027	3.8	0.80
	SD	0.027	4.3	1.58

This suggests that venous pCO_2 is equivalent to Arterial pCO_2; and venous pCO_2 can be used in place of Arterial pCO_2 in evaluation of DKA patient.

Strong linear correlation was found between Arterial and Venous pH, HCO_3^- and pCO_2 values. Our study was based on patients of DKA. Apart from DKA, there are also studies showing significant correlation between peripheral venous and arterial blood gas measurements in patients admitted to Intensive care unit by Treger et al[23], patients with uremic acidosis by Gokel et al[24], patients with COPD by Lim et al[25] and those presenting to the emergency ward by A-M Kelly[26] where the results have shown that venous blood gas can replace arterial blood gas.

A study by Kelly in Venous pH estimation shows a high degree of correlation and agreement with the arterial value, with acceptably narrow 95% limits of agreement. Venous pH estimation is an acceptable substitute for arterial measurement and may reduce risks of complications both for patients and health care workers[26].

Similarly, a study by Maltesha showed that venous blood gas analysis for pH, bicarbonate and pCO_2 may be a reliable substitute for ABG analysis in the initial evaluation of an adult patient population presenting to the ED[27].

Therefore, Venous blood gas analysis (VBGA) can be used as an alternative to Arterial blood gas analysis (ABGA) in patients presenting with DKA in Emergency ward to evaluate as well as monitor the blood pH, HCO_3^- and pCO_2 levels.

A limitation that we encountered was that we were not able to recruit more subjects as some did not give consent to participate. Therefore, studies with larger sample size are needed for extrapolation of data and greater reproducibility of results.

Conclusion: Venous blood gas analysis (VBGA) can be used as an alternative to Arterial blood gas analysis (ABGA) in patients presenting with DKA in Emergency ward to evaluate as well as monitor the blood pH, HCO_3^- and PCO_2 levels.

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