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Comparison of Blood Gas and Acid–Base Measurement in Arterial and Venous Blood Samples in Patients with Diabetic Ketoacidosis

Sandeep K. Immadisetty and Aparna P. Patange*

Department of General Medicine, Krishna Institute of Medical Sciences (Deemed to be University), Karad, Maharashtra, India - 415110.
*Corresponding Author E-mail: kimssubmission1@gmail.com

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Diabetic ketoacidosis (DKA) is one of the most severe complications of diabetes mellitus (DM). Arterial blood gas analysis (ABGA) has been used as a conclusive diagnostic test for DKA. However, ABGA sampling is technically challenging, painful and may cause multiple complications. Venous blood gas analysis (VBGA) is a minimally invasive alternative for ABGA; however, the correlation between ABGA and VBGA has been controversial. Thus, the correlation between arterial and venous pH, partial pressure of CO2 (PCO2), and bicarbonate (HCO3) was studied. To determine whether VBGA can replace ABGA in the evaluation of patients presenting with DKA. The present observational study was carried out in 76 patients with DKA. Two samples for ABGA and VBGA were obtained from each patient as close to each other as possible and were immediately sent to the laboratory. Data analysis was done using Pearson's correlation coefficient (R) and Bland and Altman plots. The Bland and Altman plots and Pearson's correlation coefficient depicted excellent agreement between arterial and venous pH (R = 0.69) and acceptably good agreement between arterial and venous PCO2 (R = 0.93) and HCO3 (R = 0.82). Thus, VBGA can be used in the initial diagnosis and evaluation of DKA, allowing the utilisation of a minimally invasive, safer option to ABGA.

Keywords: Blood Gas Analysis; Diabetic Ketoacidosis; Diagnostic Tests; Hydrogen-Ion Concentration.

Diabetes mellitus (DM) is a group of common metabolic disorders characterized by hyperglycaemia. It is due to a defect in insulin action, insulin secretion or both. A host of genetic and environmental factors are responsible for this. Diabetes as well as the complications arising from it are major causes of death in many countries (Trachtenbarg, 2005).

Diabetic Ketoacidosis (DKA) is one of the most severe complications of DM characterized by hyperglycaemia, ketonemia, ketonuria, and metabolic acidosis (Trachtenbarg, 2005; Jameson *et al.,* 2018). The annual incidence in the western countries has been reported as 4.6 cases per 100,000 of patients with DM and 0.14 cases per 100,000 of the general population (Ganie *et al.,* 2012). Although inpatient mortality rates in western countries are low (< 1%), 30% of hospitalised DKA cases result in inpatient death in India (Farsani *et al.,* 2017). This metric proves the severity of this complication in India.

DKA is biochemically characterised by hyperglycaemia (blood glucose > 250 mg/dL), a blood pH of < 7.30, and a bicarbonate (HCO_3) level

of d" 18 mmol/L and can be categorized as mild (pH 7.25–7.30, HCO_3 15–18 mmol/L), moderate (pH 7–7.24, HCO_3 < 10 mmol/L) or severe (pH of < 7, HCO_3 < 10 mmol/L) (Trachtenbarg *et al.,* 2005; Cashen and Petersen, 2019). Arterial blood gas analysis (ABGA), which measures the blood pH, partial pressure of CO_2 (pCO_2), and bicarbonate (HCO_3) levels, is an essential diagnostic test in patients with suspected DKA as metabolic acidosis is a prominent feature of DKA (Kitabchi and Wall, 1995; Gokel *et al.,* 2000).

However, arterial blood sampling is a technically challenging and painful procedure associated with risks such as haemorrhage, pain, artery damage or thrombosis, infection, aneurysm formation, and even loss of limb function. Additionally, it increases the risk of needlestick injury to the healthcare personnel (Roberts *et al.* 2017; Mortensen, 1967). Therefore, many studies have tried to search for an alternative to ABGA and have compared arterial and venous blood gas in patients with DKA in an attempt to eliminate ABGA in the initial diagnosis and evaluation of DKA (Gokel *et al.,* 2000; Brandenburg and Dire, 1998; Kelly, 2006) Venous blood gas analysis (VBGA) is a minimally invasive procedure that bypasses all the complications of ABGA. Although the correlation between arterial and venous blood parameters (especially pH) is well established, several studies have conflicting opinions on the same (Kelly, 2006; Brashear *et al.,* 1979).

Therefore, this study was designed to determine whether VBGA could replace ABGA as the initial diagnostic measure in patients with DKA by correlating the values.

MATERIAL AND METHODS

Study design

The present cross-sectional, observational, comparative study was conducted on 76 patients above 18 years of age with DKA admitted to the medical emergency ward of a tertiary care centre in Karad, Maharashtra from November 2017 to May 2019 after institutional ethics committee clearance was obtained. Farsani *et al.,* (2017) conducted a systematic review on the incidence and prevalence of DKA, and reported an overall prevalence of 50–100 events per 1000 adult patients of DM. Hence, the error of the study was set at 5% and the power of the study was set at 95%. Using the formula for cross-sectional studies,

N=4pq/d2

the sample size came to 76 patients. Sample allocation was done using convenient sampling technique. Patients > 18 years with random blood sugar > 250 mg/dl, urinary ketone bodies, HCO_3 level < 18 mmol/L, and pH < 7.35 with known or newly detected DM (Type 1/Type 2) were included in the study. Patients not fulfilling the abovementioned criteria were excluded from the study. Data were recorded in the study proforma of consenting individuals.

Data collection

A pre-tested validated proforma was developed to collect data for the research purpose. A detailed case history of the patient was taken including chief complaint, history of present illness, family and medical history; a thorough clinical examination was performed; and the necessary investigations (blood and urine tests) were done.

A sample of arterial blood (0.5–1.0 mL) for ABGA was obtained from the radial artery of the patient using a 2.5-ml syringe (Dispovan, India) (Lwanga and Lemeshow, 1991) whereas a sample of venous blood (0.5–1.0mL) for VBGA was obtained from a peripheral vein at the time of venepuncture for other laboratory reports. The two blood gas samples were obtained as temporally close to each other as possible before the initiation of treatment and were immediately sent to the laboratory.

Statistical Analysis

Data were analysed using the statistical software R version 3.6.3 and MS Excel. Categorical variables such as age group, type of DM, severity of DKA, and clinical symptoms were represented by frequency tables and continuous variables were represented by mean ± SD form. The strength of association between arterial and venous pH, PCO2, and HCO_3 was measured using Pearson's correlation coefficient (R). A P-value less than or equal to 0.05 was considered statistical significance. The degree of agreement between the arterial and venous measurements were evaluated on Bland and Altman plots.

RESULTS

Table 1 presents the demographic variation and characteristics of the patients with DKA. Of the total 76 patients, 53 (69.74%) were males and 23 (30.26%) were females, with a mean age of 55.99 ± 16.19 years. Out of 76 patients, 9 (11.84%) had type 1 DM and 67 (88.16%) had type 2 DM. Also, 59 (77.63%) patients were known cases of DM and 17 (22.37%) were newly diagnosed cases of Diabetes Mellitus on admission.

Out of 76 patients, 35 (46.05%) patients had mild DKA and 9 (11.84%) patients had severe DKA, whereas 15 (19.74%) patients had mild hyperglycaemia (RBS 250-350 mg/dl) and 26 (34.21%) patients had severe hyperglycaemia (RBS >450 mg/dl). The mean RBS was 415.55 ± 79.37 mg/dl.

Table 1. Demographic Variation and Characteristics of Patients with Diabetic Ketoacidosis

Distribution of patients based on Age and Gender			
Age Group	Number of Patients		
	Male	Female	Total
<20	1 (1.32%)	1 (1.32%)	2 (2.63%)
21-30	3 (3.95%)	2 (2.63%)	5 (6.58%)
31-40	4 (5.26%)	3 (3.95%)	7 (9.21%)
41-50	11 (14.47%)	2 (2.63%)	13 (17.11%)
51-60	12 (15.79%)	6 (23.68%)	18 (23.68%)
>60	22 (28.95%)	9 (40.79%)	31 (40.79%)
Total	53 (69.74%)	23 (30.26%)	76 (100%)

Distribution of patients based on History of Diabetes Mellitus			
Type of DM	Number of Patients		
	Known case of DM	Newly diagnosed DM	Total
Type1	5 (6.58%)	4 (5.26%)	9 (11.84%)
Type2	54 (71.05%)	13 (17.11%)	67 (88.16%)
Total	59 (77.63%)	17 (22.37%)	76 (100%)

Distribution of patients based on clinical symptoms	
Clinical symptoms	Number of Patients
Abdominal pain	35 (46.05%)
Breathlessness/Dyspnea	19 (25%)
Nausea/Vomiting	34 (44.74%)

Distribution of patients based on Severity of DKA and Random Blood Sugar		
	Sub-Category	Number of Patients
Severity of Diabetic Ketoacidosis	Mild (pH 7.25-7.35 and HCO_3 15-18)	35 (46.05%)
	Moderate (pH 7.00-7.25 and HCO_3 10-15)	32 (42.11%)
	Severe (pH <7.00 and HCO_3 <10)	9 (11.84%)
Random Blood Sugar	250-350 mg/dl	15 (19.74%)
	351-450 mg/dl	35 (46.05%)
	>450 mg/dl	26 (34.21%)

Table 2 exhibits the pH range, PCO_2 range, and HCO_3 range in arterial and venous blood. Most of the patients had a pH range between 7.00–7.25 in both arterial and venous blood (i.e. 48.68% and 46.05% respectively). Also, the HCO_3 range was > 15 in both arterial and venous blood (i.e. 56.58% and 64.47%, respectively).

Figure 1 depicts the Bland-Altman plots for arterial and venous pH, PCO_2, and HCO_3. Figure 1a illustrates that majority of the points lie within the interval and are close to the line representing mean difference. Hence, there was excellent agreement between Arterial pH and venous pH. Figure 1b illustrates that majority of the points lie within the interval but are scattered. Hence, there was acceptably good agreement between Arterial PCO_2 and Venous PCO_2. Figure 1c illustrates that, majority of the points lie within the interval but are scattered. Hence, there was acceptably good agreement between Arterial HCO_3 and Venous HCO_3.

Pearson's Correlation test proves that there was significantly high positive correlation between arterial parameters and venous parameters (Table 3). The scatter plots in Figure 2 depict the same.

Table 4 gives the summary of the simple linear regression models. The regression analysis demonstrated that arterial pH increased by 0.48 as venous pH increased by a unit, and venous pH explained 69% of variation in arterial pH.

The arterial PCO_2 increased by 0.91 as venous PCO_2 increased by a unit, and venous PCO_2 explained 93% of variation in arterial PCO_2.

The arterial HCO_3 increases by 0.83 as venous HCO_3 increases by a unit. Venous HCO_3 explains 82% of variation in Arterial HCO_3.

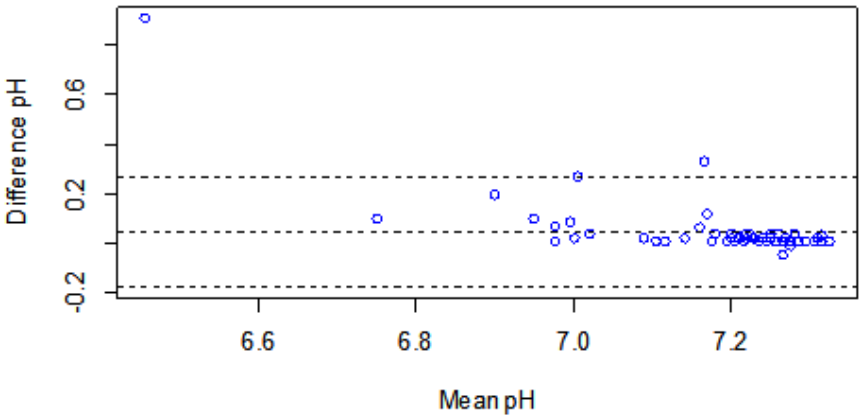
DISCUSSION

ABGA is often used as a confirmative test for DKA. However, due to the several associated complications with this test, VBGA is being investigated as an alternative diagnostic test for DKA. Thus, this study attempts to correlate the ABGA and VBGA findings in 76 patients with DKA.

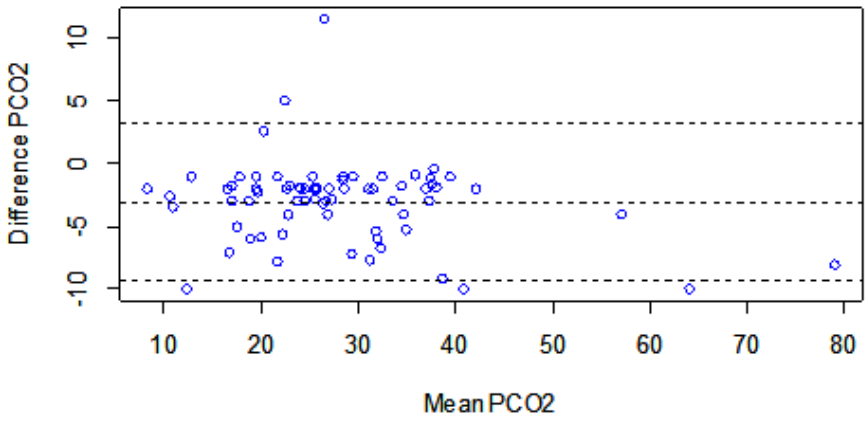
The mean age of patients in our study was 56 years with 41% being above 60 years. This finding was concurrent with a study by Lee et al. who reported a peak in the incidence of DKA in patients in their fifties. This may be probably because patients in their fifties are usually long-standing diabetics, increasing the probability of absolute insulin deficiency and thus DKA. However, he also reported a peak in DKA incidence in the twenties which is contrary to the findings of this study (Lee *et al.,* 1987). The present study reports a marked male predilection for DKA (69.74% male). This finding was concurrent with a study by Elleman *et al.,* (1984) whereas it was contrary to the findings of (Lee *et al.,* 1987)

Table 2. pH range, PCO_2 range and HCO_3 range in Arterial and Venous Blood

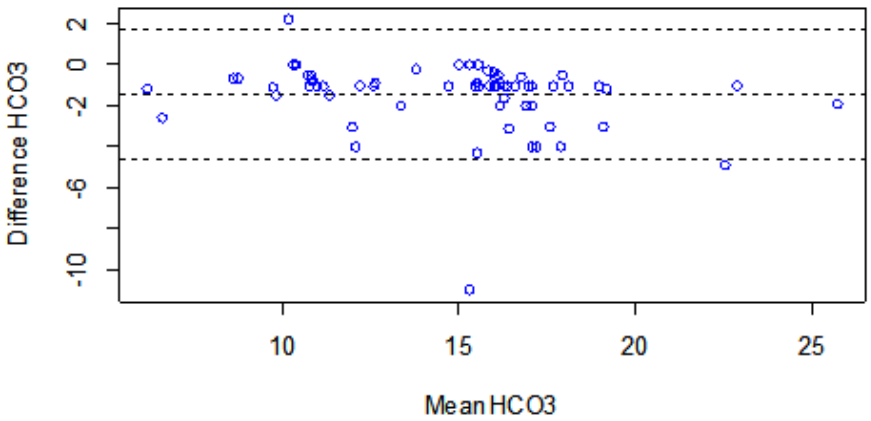
	Sub-Category	Number of Patients	
		Arterial	Venous
pH	<7.00	5 (6.58%)	11 (14.47%)
	7.00-7.25	37 (48.68%)	35 (46.05%)
	7.25-7.35	34 (44.74%)	30 (39.47%)
PCO_2	<10.00	4 (5.26%)	1 (1.32%)
	10.01-15.00	4 (5.26%)	3 (3.95%)
	15.01-20.00	14 (18.42%)	11 (14.47%)
	20.01-25.00	19 (25%)	14 (18.42%)
	25.01-30.00	13 (17.11%)	21 (27.631%)
	30.01-35.00	9 (11.84%)	8 (10.53%)
	> 35.00	13 (17.11%)	18 (23.68%)
HCO_3	10.01-15.00	25 (32.89%)	22 (28.95%)
	5.01-10.00	8 (10.53%)	5 (6.58%)
	> 15.00	43 (56.58%)	49 (64.47%)



1 (a)

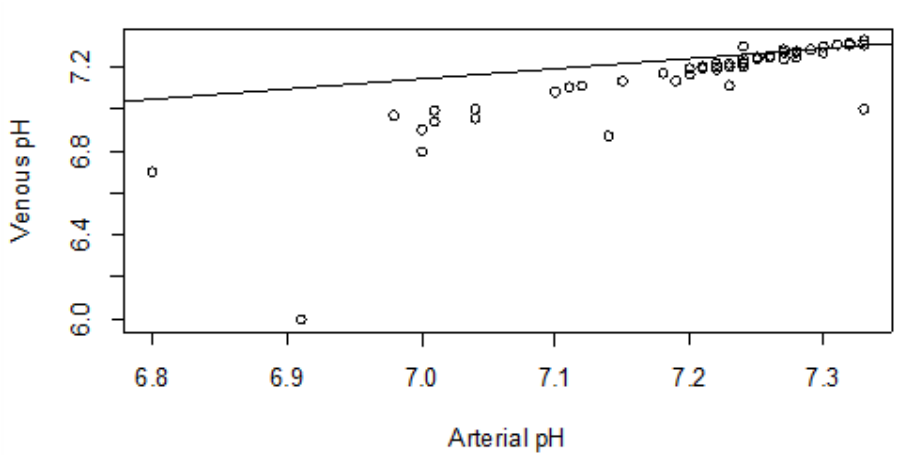


1 (b)

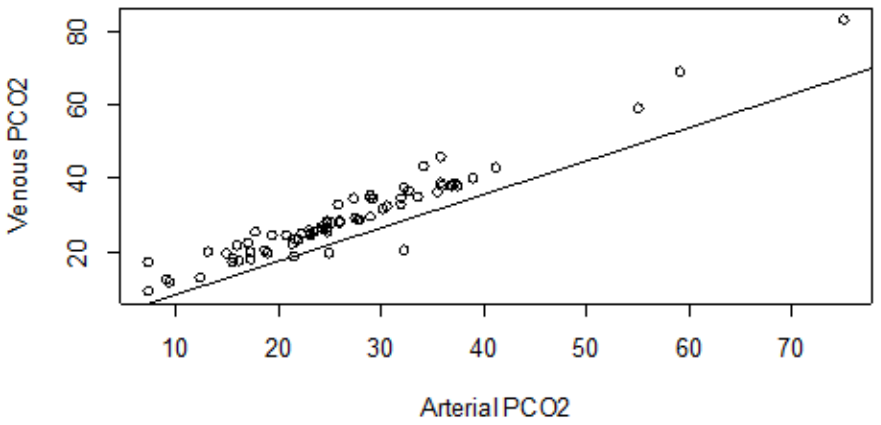


1 (c)

Fig. 1. a. Bland-Altman plot of arterial and venous pH showing the 95% limits of agreement. b. Bland-Altman plot of arterial and venous PCO_2 showing the 95% limits of agreement c. Bland-Altman plot of arterial and venous HCO_3 showing the 95% limits of agreement



1 (a)



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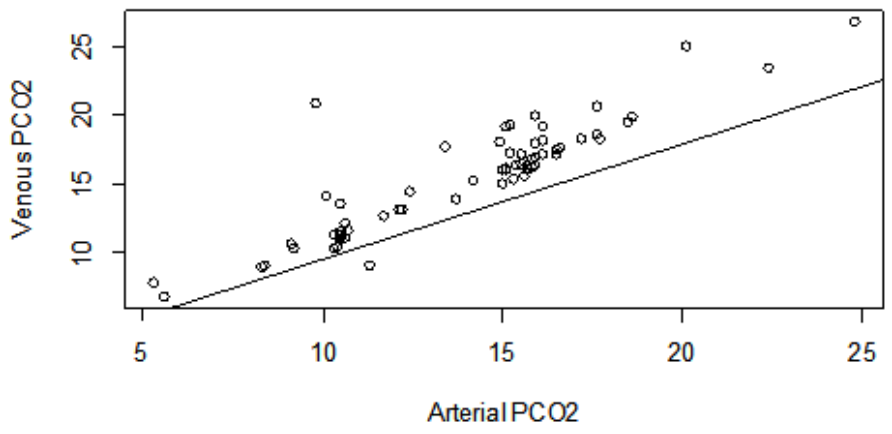

1 (c)

Fig. 2. a. Scatter plot of arterial and venous pH. b. Scatter plot of arterial and venous PCO_2. c. Scatter plot of arterial and venous HCO_3

Table 3. Correlation of arterial and venous pH, PCO_2, and HCO_3

Parameters	Correlation	p-value
pH	0.83	< 0.001*
PCO_2	0.96	< 0.001*
HCO_3	0.91	<0.001*

who reported that DKA is more common among females.

DKA mainly occurs in patients with type 1 DM because these patients present with a complete lack of insulin that inhibits gluconeogenesis and glycogenolysis. However, in insulin resistant states (Type 2 DM), the body remains sensitive to the anti-lipolytic effects of insulin. Thus, patients with type 2 DM are rarely affected (Barski *et al.,* 2013; Puttanna *et al.,* 2014)). However, this finding has been challenged in larger number of patients with type 2 DM presenting with DKA. This was aptly seen in a study by Balasubramanian et al, (1999) who reported that 39% of the patients with DKA in their study had Type 2 DM (Balasubramanyam *et al.,* 1999). A remarkable finding in our study was that a majority of the patients presenting with DKA (88%) had type 2 DM. In our study, 22.4% of patients presenting with DKA were newly diagnosed as DM. This finding was mirrored in studies by Elleman *et al.,* (1984). The majority of the patients presented with mild to moderate DKA, whereas 12% presented with severe DKA.

Table 4. Summary of Simple linear regression models

Response	Predictor	Estimate	p-value	Coefficient of Determination (R^2)
Arterial pH	Intercept	3.78	< 0.001*	0.69
	Venous pH	0.48	< 0.001*	
Arterial PCO_2	Intercept	-0.33	0.726	0.93
	Venous PCO_2	0.91	< 0.001*	
Arterial HCO_3	Intercept	1.21	0.0943	0.82
	Venous HCO_3	0.83	< 0.001*	

In the present study, there was excellent agreement between Arterial pH and venous pH, and acceptably good agreement between arterial and venous PCO_2 and HCO_3. This finding was concurrent with Kelly (2006) in the author's review on the validity of VBGA in DKA. However, some studies such as the one by Brashear *et al.,* (1979) have not shown good correlation. The reasons for the contrasting findings may be the differing sample size, geographic location, the method used for sample collection, and the experience level and expertise of the pathologist. ABGA is considered essential in patients with suspected DKA. VBGA is an alternative method of estimating pH and blood gas values. It has several advantages over ABGA such as the lower rate and severity of complications, quicker and easier to perform than ABGA, and it is safe in hemodynamically unstable patients (Singh *et al.,* 2013).

If arterial and venous pH, pCO2, and HCO3 values show high correlation and a high level of agreement in patients presenting with DKA, ABGA can be eliminated for VBGA in the conclusive diagnosis of DKA. Although we found excellent correlation and a high level of agreement in values of arterial and venous pH only, the agreement was lesser between PCO_2 and HCO_3. However, as the correlation between PCO_2 and HCO_3 was in a good range, this study recommends VBGA in the initial diagnosis and evaluation of DKA. This study has certain limitations such as the small sample size and the single centre design of the study. Additionally, the cross-sectional design of the study with no follow-ups may also be considered a limitation. Thus, a prospective, multicentric study with a larger sample size would further strengthen the correlation between arterial and venous blood gas parameters. Furthermore, a comparative prospective study between two groups with DKA, one diagnosed with VBGA and the other with ABGA would further underline the advantages of VBGA.

CONCLUSION

Although studies have stated that DKA mainly occurs in patients with type 1 DM, this study presented with a majority of patients with DKA as suffering from type 2 DM. Excellent correlation and a high level of agreement was found between values of arterial and venous pH, whereas good agreement was found between arterial and venous PCO_2 and HCO_3. This suggests that a minimally invasive method such as VBGA with no or minimal complications can be used as an alternative to ABGA in the diagnosis of DKA, thus reducing the chances of morbidity while diagnosing DKA.

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