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Original Article

Biochemistry Section

Analysis of Arterial Blood Gas Report in Chronic Kidney Diseases – Comparison between Bedside and Multistep Systematic Method

ISHITA GHATAK[1], VAISHALI DHAT[2], MONA A TILAK[3], INDRANATH ROY[4]

ABSTRACT

Introduction: Acid Base Disorders (ABDs) are commonly encountered in critically ill Chronic Kidney Disease (CKD) patients. Timely and correct analysis of Arterial Blood Gases (ABG) is critical for the diagnosis, treatment and prediction of outcome of the patients.

Aim: The aim was to explore type and prevalence of ABDs in 31 critically ill CKD patients from a tertiary care hospital in Maharashtra, to compare two methods of analysis- bedside and systematic approaches and to clinically correlate the nature of ABDs in these patients.

Materials and Methods: The initial ABG reports of 31 consecutive CKD patients were analysed by two methods. Medica Easy stat analyser was the equipment for analysis with Principle of potentiometry and ion selective electrode for pH and pCO_2 and amperometry for pO_2. Serum albumin was also measured by Bromocresol green dye binding method using liquixx albumin kit in Erba XL 300 autoanalyser.

Statistical Analysis: Chi-square test was used for statistical analysis using Epi Info version 3.5.4 and SPSS 14.0 softwares.

Results: The systematic method showed a significantly higher prevalence of mixed disorders (50%) compared to bedside method (12.9%). Most prevalent disorder by bedside method was metabolic acidosis in 15 cases (48.39%). By the systematic method, 3 reports were invalid. As a single category, most prevalent type was both simple respiratory alkalosis and mixed metabolic acidosis with respiratory alkalosis- 6 of 31 cases in each type (19.36% each). As a whole, metabolic acidosis (including both High Anion Gap Metabolic Acidosis or HAGMA and Non Anion Gap Metabolic Acidosis or NAGMA with 4 in each type) was most prevalent- 8 of 31(25.8%).

Conclusion: Systematic approach was more effective in diagnosing mixed acid base disorders. By systematic method the findings of analysis in most cases could be correlated with the clinical condition and provisional diagnosis. Thus interpretation of ABDs by using stepwise approach could be useful to the clinicians in early diagnosis and management of the patients.

Keywords: Acid base disorders, Metabolic acidosis, Mixed acid base disorders

INTRODUCTION

Hydrogen bond is one of the forces that build higher structures and three dimensional conformations of proteins. A change in pH causes gain or loss of proton(s) by proteins and alters charge distribution on them and hence, changes molecular conformation, structure and function [1]. Therefore, strict regulation of pH and acid base homeostasis are crucial for normal cell, tissue and organ performance [2,3].

Chronic Kidney Disease (CKD) is a worldwide public health problem, with adverse outcomes of kidney failure, Cardiovascular Disease (CVD) and premature death. CKD is an increasing entity as per demographic trend due to increasing number of diabetic patients, growing size of elderly population (increased average life span), increased and improved techniques for detection of renal insufficiency and better access to health care facility [4]. CKD eventually leads to an advanced and terminal stage of Chronic Kidney Failure (CKF). CKF presents with plenty of metabolic changes caused by kidney impairment and by the dialysis itself (renal replacement therapy – essential in advanced stages of CKD).

Acid Base Disorders (ABDs) are very commonly encountered in critically ill CKD population. Their diagnosis is made from stepwise interpretation of reports of Arterial Blood Gas (ABG) analysis. The disorder may be single or primary disorder or may be a mixed acid base disorder.

This study analyzed initial ABG reports of 31 critically ill CKD patients. Two approaches (bedside approach and systematic multistep approach) were used for interpretation of reports. The aim was to explore the nature and prevalence of ABD in CKD patients, correlation of laboratory diagnosis with the clinical picture and comparison between findings of two approaches.

The bedside method provided an easy and rapid interpretation of dominant ABD without considering the rules of compensation and anion gap. The hidden co-existent primary ABD was often unrevealed by this method. Systematic multistep method analysed the ABG report in a stepwise comprehensive manner with consideration of anion gap, categorization of acidosis into elevated and normal anion gap type and exclusion of mixed disorder by evaluating the compensatory response, i.e., whether expected or not according to rules of compensation. Some other variables, i.e., corrected anion gap for hypo albuminaemia, delta ratio were also considered. This method provided complete diagnosis of acid base disorders in those patients that correlated with clinical picture.

MATERIALS AND METHODS

This was a prospective study which was conducted in a tertiary care, private teaching hospital in Pimpri, Pune on approval and clearance from the institutional ethical and research committee. The study was conducted from June 2014 to September 2014.

Study Population

Inclusion Criteria: Thirty one consecutive critically ill adult CKD patients representing semi-urban population Maharashtra were included. Most of the patients belonged to stage 3,4 and 5 After obtaining clearance from hospital ethical committee and written informed consent from patients or their family was obtained.

Stages of CKD were defined by an international consensus according to GFR (Glomerular filtration rate) and signs of renal damage [5].

Stage 1: GFR ≥ 90 ml / min (per 1.73m^2 body surface area) and presence of signs of renal failure Stage 2: GFR = 60- 89 ml/ min with signs of renal damage.

Stage 3: GFR = 30- 59 ml/ min

Stage 4 = GFR = 15-29 ml/min

Stage 5 = GFR< 15 ml /min (this stage is incompatible with life without renal replacement therapy) [4,6].

Exclusion Criteria: Patients in paediatric age group, pregnant females, patients in stage1-2 of CKD without any acid base disturbances were excluded from the study group.

A 2 ml of arterial blood was collected by a heparin flushed syringe and sent (in ice pack) to central clinical laboratory immediately for analysis. A 2 ml of blood was collected in plain sterile bulb for estimation of serum albumin.

Analyser of Arterial Blood Gases: Medica Easy Stat Analyser was used for analysis.

Principle of Analysis: Principle was potentiometry and pH sensitive glass electrode for pH and Severinghaus CO_2 electrode for pCO_2 and amperometry and Clark oxygen electrode for pO_2 [7].

Above 3 parameters were measured by machine whereas bicarbonate (HCO_3-), BEb, (base excess of blood), percent SO_2c (percent saturation of available Hb at normal P50), etc were calculated by machine.

Estimation of Serum Albumin: Serum albumin of each patient was measured (on same day of the analysis of arterial blood) by BCG (bromo-cresol green) dye binding [8], end point method using Liquixx albumin kit on Erba XL 300 fully automatic analyser.

Methods of Analysis of the Reports: The initial ABG reports of those 31 patients were analysed by two methods: 1) bedside approach; and 2) multistep systematic approach.

Bedside approach [9]: Each report's pH, pCO_2, bicarbonate and BEb were noted. The observed pH indicated whether or not the primary Acid Base Disorder (ABD) was compensated (by comparison with the normal range of pH: 7.35-7.45). Direction of change of pH from mean denoted the primary disorder.

If pH and pCO_2 moved opposite and bicarbonate and pCO_2 moved in same direction, the result was primary respiratory disorder with compensatory metabolic response.

If pH, pCO_2 and bicarbonate moved in same direction, result was primary metabolic disorder with compensatory respiratory response.

If pCO_2 and bicarbonate moved opposite with pH at mean, within range or abnormal, the disorder was mixed. The direction of pH shift from mean indicated the stronger component.

Multistep systematic approach: First the approach tested the consistency of analytical report that was produced as printouts by analyser.

The Henderson- Hasselbach's equation tested the validity of analysis as follows [10].

Concentration of H+ ions = 24 × pCO_2 / HCO_3-

The respective pH against calculated (H^+) was obtained from a table of pH and corresponding (H^+). This was the expected pH which should agree with observed pH estimated by pH electrode of analyser. If they agree the report of analysis is valid. But if they do not, the report is not valid, hence not reliable for interpretation and diagnosis.

Following validation, the valid reports were analysed stepwise for interpretation following Steps were used [Table/Fig-1].

Steps	Interpretation
Step 1: pH was acidemic or alkalemic?	1: Note pH < 7.4 : acidemic >7.4: alkalemic
Step 2: Was it respiratory or metabolic disorder?	If pH moved opposite to pCO_2, the disorder was respiratory If pH and pCO_2 moved same, the disorder was metabolic Or the trend of change in bicarbonate when explained the change in pH, the disorder was metabolic
Step 3: When it was a respiratory disorder, was it acute or chronic or acute on chronic?	3: If Δ [H^+] / ΔpCO_2 was < 0.3: chronic If was < 0.3- 0.8: acute on chronic If > 0.8: acute
Step 4: For metabolic acidosis, anion gap (AG) Was calculated	AG = [Na^+] – [HCO_3-] – [Cl-] [1,11] Normal AG = 8 ± 3 meq/ L [1] If normal, result was normal AG metabolic acidosis (NAGMA) If increased, result was high anion gap metabolic acidosis (HAGMA)
Step 5: Report was looked for hidden additional component	5: Ratio of increment in AG (Δ AG) to decrease in bicarbonate (Δ HCO_3-) i.e. Δ ratio was noted If Δ ratio 0.8- 2 – pure HAGMA IF < 0.8 - mixed HAGMA and NAGMA IF > 2 - mixed HAGMA and metabolic alkalosis
Step 6: AG was corrected for hypoalbuminemia	6: For each 1 gram /dl fall in albumin from mean value of 4 gram/dl, AG drop was 2.5 meq/ L.1Corrected AG revealed hidden HAGMA in critically ill patients with hypoalbuminemia
Step 7: Compensation was evaluated by rules of compensation	7: Metabolic Acidosis: Expected PCO_2 = [1.5× HCO_3-] + 8 ± 2 [10] If expecteted value agree with observed value, Result was simple metabolic acidosis pCO_2> expected value : concomitant respiratory acidosis pCO_2< expected value : concomitant respiratory alkalosis Metabolic Alkalosis: Expected pCO_2 = [0.7 × HCO_3-] + 21± 2 If expected pCO_2> expected value : concomitant respiratory acidosis If pCO_2< expected value : concomitant respiratory alkalosis Respiratory acidosis: Acute: Expected bicarbonate: 24 + 1× [pCO_2- 40] / 10 Chronic : Expected bicarbonate: 24+ 3.5× [pCO_2- 40] / 10 Alkalosis: Acute: Expected bicarbonate: 24-2× [40- pCO_2] /10 Chronic : Expected bicarbonate: 24- 5× [40- pCO_2]/ 10 Observed bicarbonate when did not agree with expected bicarbonate, that implied a mixeddisorder.

[Table/Fig-1]: Multistep comprehensive analysis of acid base disorders.

STATISTICAL ANALYSIS

Microsoft office excel was used to compile data for statistical analysis. Chi square test was used as the statistical test and analysis of data were done with two soft wares, namely, Epi Info version 3.5.4 and SPSS 14.0.

RESULTS

The statistical analysis of result showed the systematic method was significantly more effective to diagnose mixed acid base disorders, as the incidence of the same increased from 12.9% by 1st approach to 50% by 2nd approach.

The significant increase in incidence of mixed disorders by the systematic method was explained by its multistep comprehensive

Acid base disorders	No. of patients N (%)
Metabolic acidosis	15 (48.39%)*
Respiratory alkalosis	9 (29.03%)
Metabolic alkalosis	3 (9.68%)
Mixed metabolic & respiratory (dual) acidoses	2 (6.45%)
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Total number of patients: 31(100%)	

[Table/Fig-2]: Distribution / Prevalence of acid base disorders in CKD patients applying bedside approach of analysis.

Acid base disorders	No. of patients N (%)
Respiratory alkalosis	6(21.43%)*
Simple NAGMA	4(14.29%)
Simple HAGMA	4(14.9%)
Mixed metabolic acidosis with respiratory alkalosis	6(19.36%)*
Mixed metabolic and respiratory alkaloses	4(21.43%)
Mixed metabolic and respiratory dual acidoses	2(7.14%)
Mixed NAGMA, HAGMA and respiratory acidosis- triple acidoses	2(6.45%)
Invalid results (out of total 31cases)	3
Total number of patients: 28(100%)	

[Table/Fig-3]: Distribution /prevalence of acid base disorders in CKD patients by the multistep systematic method.

Method of interpretation	Simple acid base disorder n(%)	Mixed acid base disorders n(%)
Bedside method	27(87.1%)	4(12.9%)
Systematic multistep method	14(50%)	14(50%) *

[Table/Fig-4]: Comparison of distribution of simple and mixed acid base disorders as obtained by 2 different methods.
*Chi-sq value: 9.55, df: 1, p: 0.0019, i.e. statistically highly significant

approach. It evaluated anion gap, degree of compensation (whether appropriate in a simple disorder or not indicating mixed disorder), corrected anion gap for hypoalbuminaemia, delta ratio, etc. Hidden primary co-existent disorder became unmasked in this approach.

DISCUSSION

CKD is a condition characterized by progressive decline of renal function due to progressive loss of nephrons (functional units of kidney) as a result of some primary underlying disease process. Clinical and laboratory complications become more pronounced as disease progresses to stage 3 and 4. These complications include acid base disorders, retention and accumulation of substances (like urea, creatinine, electrolytes, water, etc), deficiency of required factors in body and metabolic dysregulation - all leading to metabolic complications. ABDs reflect the primary disorder and themselves lead to potentially life- threatening complications.

The ABD may be of simple (single) or primary type with a secondary compensatory response or may be of mixed type- occurrence of two or more independently existing primary ABDs in the same patient [12]. The laboratory diagnosis should always be correlated with clinical details. The cause of individual acidemia or alkalaemia should be explored in each cases. That unmasks the complete diagnosis, complications, co-morbidities and also guides management.

In this study, out of 31patients of CKD, by bedside approach of interpretation of ABGs, 27 (87.1%) had simple (single) disorders. Only 4 (12.9%) had mixed disorders. Most prevalent type was metabolic acidosis (15 of 31, i.e., 48.39%), followed by respiratory alkalosis (9 of 31, i.e., 29.03%) [Table/Fig-2].

By this method, differentiation of metabolic acidosis (whether HAGMA or NAGMA) was not possible. The reasons were that the bedside method did not consider the rules of compensation, anion gap, AG adjusted for hypoalbuminaemia and delta ratio.

By systematic method 3 reports were found to be invalid, hence were not considered for further interpretation. Of the rest, 14 (50% of total 28) were simple disorders and remaining 14 (same 50%) were mixed. Hence the systematic method could effectively diagnose the type of ABD and higher incidence of mixed disorders [Table/Fig-3,4].

In a similar study by Bhasin et al., [3] approaches were used on same data obtained from patients of ICU in a tertiary care hospital- namely, single step bedside method, 1 quick look method for mixed disorder and the multistep systematic method [13]. A 560 blood samples were first analysed by the bedside approach. Out of those appearing as single disorder in the bedside approach, 62% were proved to be mixed type by the systematic method. The latter method was able to detect significantly higher incidence of mixed disorders.

In another study by Song ZF et al., arterial blood gas data (from critically ill patients at emergency room) were analysed using 2 different approaches [14]. First method included pH, pCO_2, HCO_3- and rules of compensation. Second method added AG and potential bicarbonate (bicarbonate and Δ AG) - same as the systematic method in the present study. On applying the second method, incidence of metabolic acidosis (both simple and as a part of mixed disorders) increased from 538 to 678. The number of triple ABDs increased from 12 to 71 cases. Hence the second method was more effective.

In the present study, including both HAGMA and NAGMA, as a whole metabolic acidosis was most prevalent, i.e. 8 out of 31 (4 were HAGMA and 4 were NAGMA), i.e. 25.8% of the population. Several authors, Das B, Dubose TD, Oosthuizen NM, etc, described metabolic acidosis to be a very common occurrence in chronic renal failure and uremia [3,15,16]. The severity of acidosis is more with lower GFR [4]. Normal anion gap metabolic acidosis may occur in stage 4 or even at times at stage 5. Earlier in the course impaired bicarbonate reabsorption, reduced secretion of titratable acids and reduced excretion of ammonia- all lead to NAGMA. In more advanced stage, accumulation of organic and inorganic acid anions leads to elevated AG acidosis-also called uremic acidosis.

In the present study, all 4 patients with NAGMA, were in earlier (milder) stages of CKD - non dialysis dependent. The acidosis could be explained by role of CKD itself in them. In those 4 patients with HAGMA, 2 were with uremia due to sepsis and obstructive uropathy and 1 was having ESRD with maintenance haemodialysis. So laboratory diagnosis supported clinical picture.

As a single category of ABD, most prevalent ABD in the study group were both simple respiratory alkalosis and mixed metabolic acidosis with respiratory alkalosis (each were found in 6 patients, i.e., 19.36%). Respiratory alkalosis was mostly acute on chronic type. For example, one patient's report showed pH = 7.421, pCO_2 = 27 mm Hg and pO2= 74mmHg (mild hypoxia) [9]. Bicarbonate = 17. 6 meq/L. On considering bedside approach it was compensated respiratory alkalosis with metabolic compensation.

But using systematic approach it was as follows:
pH> 7.4, hence it was alkalosis,

pCO_2 :< 40 mm Hg and bicarbonate < 24 meq/L,

So change of pCO_2 explained change of pH and pH moved opposite to pCO_2. So the disorder was respiratory alkalosis.

Here (H^+) was = 24× 27 /17.6 = 36.8 nanomole /L [10].

So $\Delta (H^+)/ \Delta pCO_2$ = 3.2/ 6.4 = 0.5.

Hence, it was an acute on chronic respiratory alkalosis. The patient had acute on CKD, urosepsis, obstructive uropathy with fever and chill, severe anaemia with jaundice, alcoholic liver disease and diabetes mellitus type 2 with known diabetic nephropathy. Severe anaemia, liver disease with superimposed fever and sepsis explained the acute on chronic respiratory alkalosis.

Chronic respiratory alkalosis is described as the commonest ABD in critically ill population [15]. The cause of respiratory alkalosis is hyperventilation due to diverse underlying pathology. Here, in the subgroup of CKD population, it was attributed to presence of severe anaemia, hypoxaemia, volume overload and milder form of pulmonary oedema, pneumonia, sepsis, fever, etc in those patients. These are established causes of respiratory alkalosis [3,15,17]. Hence the analytical findings could be correlated clinically.

Equally prevalent disorder was mixed metabolic acidosis and respiratory alkalosis- that is observed frequently in critically ill patients [17,18]. Causes of this mixed disorder are septic shock, renal failure with sepsis and/ or congestive cardiac failure (pulmonary oedema) and salicylate toxicity [12,16]. Pulmonary oedema may itself develop this mixed disorder [17,19]. In this study group, the occurrence of this ABD in those 6 patients were due to volume overload and pulmonary oedema, sepsis, septicemic shock and also fever, severe anaemia- each complicating chronic renal failure – in each cases supporting the known causes and clinical diagnosis.

Another 4 patients (12.9%) had mixed metabolic and respiratory alkalosis. The causes of these dual mixed disorders are said to be congestive cardiac failure and vomiting, diuretics and pneumonia, diuretics and hepatic failure, etc [12,16]. These patients also had pulmonary oedema, pneumonitis, sepsis, fever, co-existent alcoholic liver disease, episodes of vomiting, etc and some were on diuretics as well.

Mixed metabolic and respiratory acidosis were observed in 2 patients only (6.45%). Both had re-exacerbation of COPD with pneumonia, hypoxia and worsening of renal insufficiency. However the causes of this mixed acidosis are cardiopulmonary arrest, CVA and renal failure, respiratory failure with anoxia [12,16]. Grogan H and Hopkins PM described severe form of pulmonary oedema and COPD with hypoxia as causes of this particular ABD [17]. Hence findings could be correlated with clinical condition.

Two patients had occurrence of mixed triple acidosis- occurrence of HAGMA, NAGMA and respiratory acidosis together. However little is known about triple acid base disorders. It is shown as a type of mixed disorder consisting of a respiratory disorder (acidosis or alkalosis) with co existing mixed metabolic acidosis and metabolic alkalosis [12,16]. Causes are said to be renal failure, vomiting and congestive heart failure, Chronic Obstructive Pulmonary Disease (COPD) with severe hypoxia and volume depletion or renal failure with vomiting or sepsis and hypokalaemia [16]. In this study, one of those 2 patients, had MI with cardiogenic shock, congestive cardiac failure, pulmonary oedema and accompanying CKD with interstitial nephritis. The conditions are however known causes of HAGMA, respiratory acidosis and NAGMA, respectively. Another person had intracranial haemorrage (may cause respiratory acidosis), shock (a known cause of HAGMA) with end stage renal failure (tubule-interstitial disease) on maintenance haemodialysis. The occurrence of mixed NAGMA and HAGMA is a feature of early uremic acidosis, and early renal failure of interstitial nephritis [12,17]. Here the reason was most likely hyperkalaemia superimposed in advanced tubule-interstitial disease and simultaneous use of ACE inhibitors –those explained mixed HAGMA and NAGMA. Both these patient became unconscious and unresponsive with circulatory failure on the second day of admission (day after the intial ABG) and succumbed within next 24 hours. In both, the acid base status could be related with the complicated clinical picture.

In a nutshell, systematic approach revealed a high incidence of mixed acid base disorders in critically ill CKD patients. In most of the cases the laboratory findings of ABD by systematic approach could be correlated with clinical conditions and provisional diagnosis. Among all mixed disorders most were dual ABD, only 2 cases had triple ABD – which were soon followed by death. Overall the diagnosis of acid base disorder by ABG analysis was useful for understanding the underlying disease process, co-morbidities and complications. Hence, the diagnosis helps the clinician in patient management.

However the sample size was very small to observe prevalence of different acid base disorders in chronic kidney failure- including single, mixed dual and triple ABDs. Also, only critically ill patients with mostly stages 4 and 5 were included in the study. For observation of types and incidence of different ABD in critically ill CKD population, a much larger sample size, equal number of study subjects in each stages of CKD and exclusion of other confounding major comorbidities are required.

CONCLUSION

This cross-sectional study showed a high prevalence of mixed type ABDs (using systematic approach) in critically ill CKD patients admitted in ICU of a tertiary care teaching hospital in Pimpri (admitted during the period of June 2014 - September 2014). Commonest acid base disorder was both simple respiratory alkalosis and mixed metabolic acidosis with respiratory alkalosis. Using the systematic approach the incidence of mixed disorder was considerably increased as compared with the bedside approach. The diagnosis by the systematic approach correlated with the clinical condition of the patients. Hence systematic multistep approach was highly efficient to explore the nature of acid base status in those patients and helped in understanding the clinical diagnosis, pathology and complications and in overall management.

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REFERENCES

[1] Rose BD, Post TW. Clinical Physiology of Acid Base and Electrolyte Disorders. 5th ed. Boston: Mc Graw-Hill; 2001. Chapter 17. Introduction to simple and mixed acid base disorders; 535-48.
[2] Androgue HJ, Madias NE. Management of life threatning acid base disorders. first of two parts. *N Engl J Med*. 1998;338(1):26-32.
[3] Das B. Acid base disorders. *Indian J Anaesth*. 2003;47(5):373-79.
[4] Cibulka R, Racek J. Metabolic disorders in patients with chronic kidney failure. *Physiol Res*. 2007;56:695-705.
[5] Levey AS, Eckardt KU, Tsukamoto Y, Levin A, Coresh J, Rossert J, et al. Definition and classification of chronic kidney disease: a position statement from kidney disease: improving global outcomes (KDIGO). *Kideney Int*. 2005;67:2089-100.
[6] Skorecki K, Green J, Brenner BM. Chronic Renal Failure. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's Principle of Internal Medicine.16th Ed. McGraw Hill. New York. 2005;(2)261:1653-56.
[7] D' Oranzio P, Meyerhoff ME. Electrochemistry and Chemical Sensors. Burtis CA, Ashwood ER, Bruns DE. Tietz Textbook of Clinical Chemistry and Molecular Diagnostic. 5th Ed. Elsevier. Philadelphia 2014; 11: 259 – 67.
[8] Hartin GL. Amino Acids, Peptides and Proteins. Burtis CA, Ashwood ER, Bruns DE.Tietz Textbook of Clinical Chemistry and Molecular Diagnostics. 5th edi. Elsevier. Philadelphia 2004;529.
[9] Singh V, Khatana S, Gupta P. Blood gas analysis for bedside diagnosis. *Natl J Maxillofac Surg*. 2013;4(2):136-41.
[10] Sood P, Paul G, Puri S. Interpretation of arterial blood gas. *Indian J Crit Care Med*. 2010;14(2):57-64.
[11] Sacks GS. The ABC's of acid base balance. *J Pediatr Pharmacol Ther*. 2004;9:235-42.
[12] Vladimir F, Jabor A,Kazda A, Figge J. Diagnosis of metabolic acid–base disturbances in critically ill patients. *Am J Resp Crit Care Med*. 2000;162:2246–51.
[13] Bhasin A, Singal RK. Analytical calculation and acid base analysis for detection of mixed disorders in critical care medicine. *JIACM*. 2012;13(3):180-84.
[14] Song ZF, Gu WH, Li HJ, Ge XL. The incidence and types of acid base imbalance for critically ill patients in emergency. *Hong Kong Journal of Emergency Medicine*. 2012;19(1):13-17.
[15] Dubose TD. Acidosis and Alkalosis. Kasper DL, Fauci AS, Longo DL, Braunwald E, Hauser SL, Jameson JL. Harrison's principles of internal medicine. 16th ed. mcgraw hill. *New York*. 2005;(1)42:263-70.

[16] Oosthuizen NM. Approach to acid-base disorders- a clinical chemistry perspective. *CME.* 2012;30(7):230-33.
[17] Grogan H, Hopkins PM. Heat stroke: implications for critical care and anaesthesia. *British Journal of Anaesthesia*. 2002;88(5):700-07.
[18] Morris CG, Low J. Metabolic acidosis in the critically ill: Part 1. Classification and pathophysiology. *Anaesthesia*. 2008;63(3):294-30.
[19] Masip J, Paez J, Merino M, Parejo S, Vecilla F, Reira C, et al. Risk factors for intubation as a guide for noninvasive ventilation in patients with severe acute cardiogenic pulmonary edema. *Intensive Care Medicine*. 2003;29(11):1921-28.

PARTICULARS OF CONTRIBUTORS:
1. Resident, Department of Biochemistry, Dr D Y Patil Medical College, Pimpri, Pune, Maharashtra, India.
2. Professor, Department of Biochemistry, Dr D Y Patil Medical College, Pune, Maharashtra, India.
3. Professor and Head, Department of Biochemistry, Dr D Y Patil Medical College, Pune, Maharashtra, India.
4. Medical Officer in Charge-Government Blood Bank, Chandannagar SD Hospital, Government of West Bengal, India.

NAME, ADDRESS, E-MAIL ID OF THE CORRESPONDING AUTHOR:
Dr. Ishita Ghatak,
Resident, Department of Biochemistry, Dr D Y Patil Medical College,
Pimpri, Pune-411018, Maharashtra, India.
E-mail: Ishitaghatak80@gmail.com

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