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Original Research Article

PATTERN OF ARTERIAL BLOOD GAS ABNORMALITIES AND UTILITY OF ANION GAP AND PH LEVEL AT THE TIME OF ADMISSION IN PATIENTS WITH SEPSIS IN PREDICTING MORTALITY

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Abstract
Background: To assess the utility of anion gap and pH value at the time of admission in outcome of patients with sepsis and to delineate the pattern of ABG abnormalities of patient admitted in intensive care unit with sepsis. **Materials and Methods:** This Observational prospective study conducted in the Department of General Medicine, Pushpagiri Institute of Medical Sciences and Research Center, Tiruvalla. Patients admitted with sepsis during the period of One and a half years from ethical committee clearance are included for the study. Sample size was calculated as 49 patients with confidence level (1-α/2) of 99%. **Results:** Total 49 patients included in the study.18.4% belonged to less than 50 years of age, 12.2% belonged to 51-60 years, 28.6% belonged to the61-70 years, 26.5% was in 71-80 year age group and 14.3% belongs to the category of more than 80years.The mean age of the study population was 65.9 ± 14.2. Males were 61.2% and females were 38.8% of the total population. Maximum number of cases reported was in the age group of 61 to 70 years followed by 71 to 80 years of age. And the mortality was more in age group >65years. Receiver operating characteristic curve was drawn for pH levels and anion gap at the time of admission in patients with sepsis and outcome was observed. Which was statistically significant? We have also observed the pattern of blood gas abnormalities in patients with sepsis and the predominant abnormality observed is high anion gap metabolic acidosis with lactic acidosis. **Conclusions:** This study illustrated that the Utility of pH and Anion gap at the time of admission in sepsis is a good marker in predicting mortality. Statistically significant associations were proven with Anion gap and pH level at the time of admission in sepsis in predicting outcome. The predominant blood gas abnormality observed in sepsis patients were high anion gap metabolic acidosis (HAGMA) with lactic acidosis.

INTRODUCTION

The word sepsis is the original Greek word for the "decomposition of animal or vegetable organic matter in the presence of bacteria." Sepsis is a derivative of the verb form sepo, which means "I rot". This word "sepsis" was first used in the medical context in the poems of Homer over 2700 years ago. The word "sepsis" has thus persisted for 2,700 years with more or less unchanged meaning.[1] Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern, accounting for more than $20 billion (5.2%) of total US hospital costs in 2011.[2]

A 1991 consensus conference developed initial definitions that focused on the then-prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection.[3]

A 2001 task force, recognizing limitations with these definitions, expanded the list of diagnostic criteria but did not offer alternatives because of the lack of supporting evidence. In effect, the definitions of sepsis, septic shock, and organ dysfunction have remained largely unchanged for more than 2 decades.[5,4]

Sepsis, a syndrome of physiologic, pathologic, and biochemical abnormalities induced by infection, is a major public health concern, accounting for more than $20 billion (5.2%) of total US hospital costs in

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2011. The reported incidence of sepsis is increasing, likely reflecting aging populations with more co morbidities, greater recognition, and, in some countries, reimbursement-favorable coding. Although the true incidence is unknown, conservative estimates indicate that sepsis is a leading cause of mortality and critical illness worldwide. Furthermore, there is increasing awareness that patients who survive sepsis often have long-term physical, psychological, and cognitive disabilities with significant health care and social implications. A 1991 consensus conference developed initial definitions that focused on the then-prevailing view that sepsis resulted from a host's systemic inflammatory response syndrome (SIRS) to infection.

Sepsis complicated by organ dysfunction was termed severe sepsis, which could progress to septic shock, defined as "sepsis-induced hypotension persisting despite adequate fluid resuscitation." A 2001 task force, recognizing limitations with these definitions, expanded the list of diagnostic criteria but did not offer alternatives because of the lack of supporting evidence. In effect, the definitions of sepsis, septic shock, and organ dysfunction have remained largely unchanged for more than 2 decades.[5]

MATERIALS AND METHODS

This Observational prospective study conducted in the Department of General Medicine, Pushpagiri Institute of Medical Sciences and Research Center, Tiruvalla. Patients admitted with sepsis during the period of One and a half years from ethical committee clearance are included for the study. Sample size was calculated as 49 patients with confidence level (1-α/2) of 99%. Absolute allowable error 15% (d) and proportion of lactic acidosis as 21% from previous study done by Kartik Ganesh et al, 20166.

Inclusion Criteria
Patients diagnosed to have Sepsis are included.

Exclusion Criteria
- Patients unwilling to participate.
- Patients with established CKD.
- Patients with established lymphoproliferative diseases and other malignancies.
- Patient admitted with poisoning known to produce acidosis.

Methods of Data Collection
- Patient admitted with sepsis are selected.
- Obtained ABG at the time of admission from radial or femoral artery and analyze with ABL 800 BASIC blood gas analyzer in MICU I.
- ABG obtained was analyzed in a stepwise pattern to arrive at the acid base status. They were having various abnormalities like metabolic acidosis, metabolic alkalosis, respiratory alkalosis, respiratory acidosis and mixed acid base disorders.

RESULTS

The study sample varied from 35 years to 92 years and maximum number of cases reported was in the age group of 61 to 70 years followed by 71 to 80 years of age as shown.

Table 1: Percentage distribution of the sample according to age

Age	Count	Percent
<=50	9	18.4
51 - 60	6	12.2
61 - 70	14	28.6
71 - 80	13	26.5
>80	7	14.3
Mean ± SD	65.9 ± 14.2	

Male cases reported were nearly 61.2% and 38.8% of the cases were female, indicating a male predominance. Gender and Age wise distribution of samples in relation to sepsis are tabulated.

**Table 2: Distribution of age and sex of patients with sepsis**

Age	Male		Female		Total	
	Count	Percent	Count	Percent	Count	Percent
<=50	7	23.3	2	10.5	9	18.4
51 - 60	3	10.0	3	15.8	6	12.2
61 - 70	7	23.3	7	36.8	14	28.6
71 - 80	10	33.3	3	15.8	13	26.5
>80	3	10.0	4	21.1	7	14.3
Total	30	100.0	19	100.0	49	100.0

Pattern of Blood Gas Abnormalities

Types of Blood Gas abnormalities observed in patients are shown. The predominant abnormality observed is Metabolic acidosis with lactic acidosis seen 21 patients (42.9%), and 20 of them were having high anion gap.

Table 3: Percentage distribution of the sample according to pattern of blood gas abnormality

Pattern of blood gas abnormality	Count	Percent
Metabolic acidosis	17	34.7
Metabolic alkalosis	2	4.1
Respiratory acidosis	1	2.0
Respiratory alkalosis	3	6.1
Mixed acidosis	1	2.0
Metabolic acidosis/lactic acidosis	21	42.9
Metabolic acidosis+alkalosis	1	2.0
Respiratory acidosis/lactic acidosis	1	2.0
Mixed acidosis/lactic acidosis	1	2.0
Metabolic acidosis+alkalosis/lactic acidosis	1	2.0
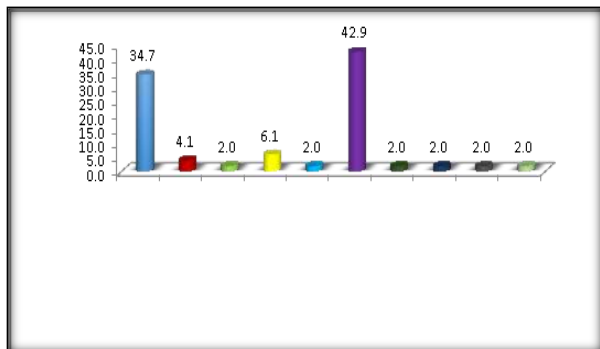
Percentage distribution of the sample according to pattern of blood gas abnormality

Association of anion gap and pattern of blood gas abnormalities. Out of 49 patients 20 had HAGMA+Lactic acidosis.

Table 4: Association of Pattern of blood gas abnormality with Anion gap

Pattern of blood gas abnormality	<12		>12		χ^2	p
	Count	Percent	Count	Percent		
Metabolic acidosis	8	47.1	9	52.9	4.91*	0.027
Metabolic acidosis/lactic acidosis	3	14.3	20	85.7		

*: - Significant at 0.05 level

Outcome of Patients

Out of 49 patients admitted with sepsis, 12 patients died and 37 patients survived. Constituting 24.5% and 75.5% of the sample respectively

Table 5: Percentage distribution of the sample according to outcome

Outcome	Count	Percent
Alive	37	75.5
Expired	12	24.5

Comparison of selected quantitative variables based on outcome

Different Quantitative variables observed at the time of admission and their relationship with outcome is shown.

Table 6: Descriptive statistics for quantitative variables based on outcome

	Alive				Expired			
	Mean ± SD	Median (IQR)	Min	Max	Mean ± SD	Median (IQR)	Min	Max
pH	7.3 ± 0.1	7.33 (7.32-7.34)	6.9	7.5	7.1 ± 0.2	7.02 (6.9 -7.26)	6.9	7.3
PCO2	37 ± 8.4	36.2 (34-40)	18.6	72.1	37.1 ± 11	34 (28.75-46.75)	21.0	56.0
Lactate 1	2.1 ± 2.2	1.2 (1-2.5)	0.7	12.9	5.3 ± 4.2	4.25 (2.95 -7.2)	0.8	17.0
AG1	12.8 ± 3.7	13 (10-14.5)	7.0	26.6	16.6 ± 3	17.45 (14.25-18.75)	11.0	21.0
HCO3-1	20.1 ± 3.7	21 (19-21.5)	6.2	28.0	18.4 ± 3.4	18.5 (14.98-20.75)	14.0	25.0
SOFA	4.4 ± 2.6	4 (3-6)	1.0	13.0	8.3 ± 2.9	9 (7.25-10)	2.0	13.0

Utility of anion gap and pH value at the time of admission in outcome of patients with sepsis

Outcome of patients were observed and compared with pH at the time of admission.

Table 7: Comparison of pH at admission based on outcome

pH	Alive		Expired		Z#	p
	Count	Percent	Count	Percent		
Acidemia	31	72.1	12	27.9		
Normal	1	100.0	0	0.0		
Alkalemia	5	100.0	0	0.0	1.47	0.141

Comparison of pH at admission based on outcome

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Receiver operating characteristic curve (ROC) was drawn for pH levels at the time of admission in patients with sepsis and outcome was observed. Area under the curve is showing a value of 0.911(91%), which means there is an excellent association in predicting mortality Shown.
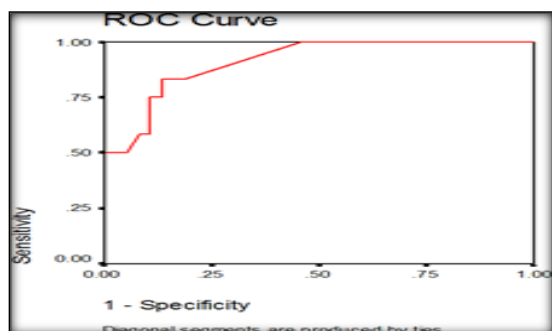
Area under the curve = 0.911 (0.826 – 0.996), p<0.01, Best cut off = 7.28

ROC curve for pH at admission in predicting mortality
Below table and figure showing overall accuracy (sensitivity + specificity) of 85.7% in predicting mortality based on pH at the time of admission.

Table 8: Diagnostic accuracy of pH at admission in detection mortality among patients with sepsis

pH	Outcome		
	Expired	Alive	Total
<=7.28	10	5	15
>7.28	2	32	34
Total	12	37	49

Sensitivity	83.3
Specificity	86.5
False Negative	16.7
False positive	13.5
Positive Predictive value	66.7
Negative Predictive value	94.1
Positive Likelihood ratio	6.2
Negative Likelihood ratio	0.2
Accuracy	85.7
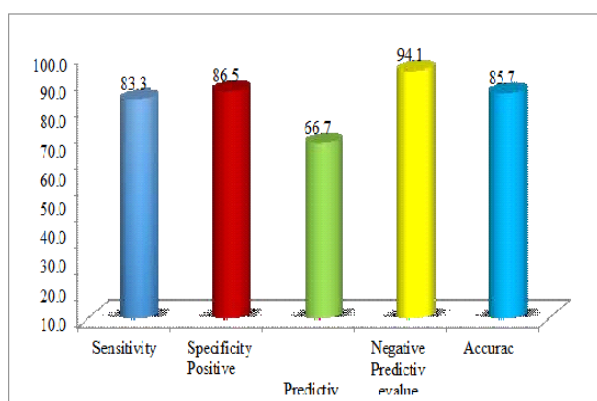
Diagnostic accuracy of pH at admission in detection mortality among patients with sepsis.

Below table showing Anion gap at admission on outcome and the Mean value of AG in expired patients is 16.6 and the P value is 0.003, which is statistically significant.

Table 9: Comparison of anion gap at admission based on outcome

Outcome	Mean	SD	N	t	p
Alive	12.8	3.7	37		
Expired	16.6	3.0	12	3.19**	0.003

**: - Significant at 0.01 level
Receiver operating characteristic curve (ROC) was drawn for anion gap at the time of admission in patients with sepsis and outcome was observed. Area under the curve is showing a value of 0.819(81.9%). Which means there is Good association in predicting mortality?
Below showing anion gap at the time of admission has overall accuracy (sensitivity+specificity) of 83.7% in predicting mortality in patients with sepsis

Table 10: Diagnostic accuracy of anion gap at admission in detection mortality among patients with sepsis

Anion Gap	Outcome		
	Expired	Alive	Total
≥16.65	8	4	12
<16.65	4	33	37
Total	12	37	49

Sensitivity	66.7
Specificity	89.2
False Negative	33.3
False positive	10.8
Positive Predictive value	66.7

Negative Predictive value	89.2
Positive Likelihood ratio	6.2
Negative Likelihood ratio	0.4
Accuracy	83.7
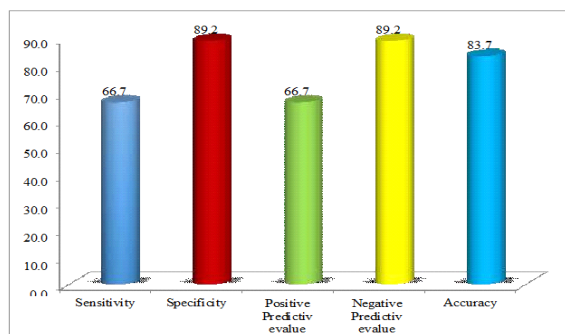
Diagnostic accuracy of anion gap at admission in detection mortality among patients with sepsis

Table 11: Comparison of SOFA score based on outcome

Outcome	Mean	SD	N	t	p
Alive	4.4	2.6	37		
Expired	8.3	2.9	12	4.53	p<0.01

DISCUSSION

This is a prospective observational follow up study over a period of 18 months conducted in Pushpagiri institute of medical sciences, Tiruvalla, Kerala. In this study, the patients admitted with Sepsis are included as per inclusion and exclusion criteria. Their final outcome is compared with pH level and anion gap at the time of admission and their association is studied. We have also looked into the pattern of blood gas abnormalities in those patients and our observation is discussed here. The diagnostic accuracy of SOFA score in predicting mortality of the patient is also analyzed.

This study is mainly to validate the utility of pH level and anion gap at the time of admission in patient with sepsis as predictor of outcome, and also to delineate the pattern of blood gas abnormalities in patients with sepsis.

Among the studied population of 49 patients, 18.4% belonged to less than 50 years of age, 12.2% belonged to 51-60 years, 28.6% belonged to 61-70 years, 26.5% was in 71-80 year age group and 14.3% belongs to the category of more than 80 years. The mean age of the study population was 65.9 ± 14.2. Males were 61.2% and females were 38.8% of the total population. Maximum number of cases reported was in the age group of 61 to 70 years followed by 71 to 80 years of age. And the mortality was more in age group >65years. In 2006 Martin GS et al conducted a study and observed that there are high mortality rates of around 50% in elderly patients with severe sepsis and septic shock. The mortality due to severe sepsis in elderly patients is 1.3-1.5 times higher than that in younger cohort.[7] Another study conducted by Vosylius S et al also observed that hospital mortality was increased with age.[8]

Outcome of the patients were observed. Which showed Out of 49 patients admitted with sepsis, 12 patients died and 37 patients survived? Constituting 24.5% and 75.5% of the sample respectively. Receiver operating characteristic curve was drawn for pH levels at the time of admission in patients with sepsis and outcome was observed. Area under the curve showed a value of 0.911(91%).Which means there is an excellent association in predicting mortality. And overall diagnostic accuracy (sensitivity+specificity) of 85.7% in predicting mortality was found.

Receiver operating characteristic curve was drawn for anion gap at the time of admission in patients with sepsis and outcome was observed. Area under the curve showed a value of 0.819(81.9%), which means anion gap at the time of admission in patients with sepsis have a Good association in predicting mortality. We have also studied the pattern of blood gas abnormalities in patients with sepsis. The predominant abnormalities were metabolic acidosis with lactic acidosis (42.9%), in that 20(41%) patients showed high anion gap. 37% patients showed metabolic acidosis with normal anion gap, other blood gas abnormalities observed were respiratory acidosis (6%), metabolic alkalosis (4.1%) metabolic acidosis/alkalosis (2.6%), respiratory alkalosis (2%), Respiratory acidosis with lactic acidosis (2%) and mixed acidosis (2%) are given.

We have also looked into the outcome based on SOFA score. Mean value of SOFA score in Alive cases were 4.4 and in Expired cases were 8.3 with a p value of <0.01 which was also statistically significant.

This study has conclusively established the role of anion gap and pH level at the time of admission in sepsis as a surrogate for predicting mortality. This study could have far reaching implications on the prediction of outcome of patients with sepsis with simple, yet dependable tools, thereby paving way for the avoidance unnecessary investigations and early aggressive management, particularly with reference to the rural scale of population where dependability on clinical tools becomes the yardstick for diagnosis.

CONCLUSION

The following are the conclusions from this study:

1. This study illustrated that, the Utility of pH and Anion gap at the time of admission in sepsis is a good marker in predicting mortality.
2. Statistically significant associations were proven with Anion gap and pH level at the time of admission in sepsis in predicting outcome.

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3. The predominant blood gas abnormality observed in sepsis patients were high anion gap metabolic acidosis (HAGMA) with lactic acidosis.

REFERENCES

1. Geroulanos S, Douka ET. Historical perspective of the word "sepsis." Intensive Care Med. 2006;32(12):2077–2077.
2. Rather AR, Kasana B. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JMS Ski. 2015;18(2):162–4.
3. Seymour CW, Liu VX, Iwashyna TJ, Brunkhorst FM, Rea TD, Scherag A, et al. Assessment of Clinical Criteria for Sepsis. JAMA. 2016;315(8):762.
4. Bone RC, Balk RA, Cerra FB, Dellinger RP, Fein AM, Knaus WA, et al. Definitions for Sepsis and Organ Failure and Guidelines for the Use of Innovative Therapies in Sepsis. Chest. 1992;101(6):1644–55.
5. Singer M, Deutschman CS, Seymour CW, Shankar-Hari M, Annane D, Bauer M, et al. The Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3). JAMA. 2016;315(8):801.
6. Ganesh K, Sharma R, Varghese J, Pillai MGK. A profile of metabolic acidosis in patients with sepsis in an Intensive Care Unit setting. Int J Crit Illn Inj Sci. 2016;6(4):178–81.
7. Martin GS, Mannino DM, Moss M. The effect of age on the development and outcome of adult sepsis*. Crit Care Med. 2006;34(1):15–21.
8. Vosylius S. Determinants of outcome in elderly patients admitted to the intensive care unit. Age Ageing. 2005;34(2):157–62.

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