A Study on Poor Prognosis Predictability of Serum Anion Gap in Medical ICU Patients

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ABSTRACT

Introduction: Anion gap (AG) has always been a matter of study, especially in relation to predicting mortality among critically ill patients. However, corrected anion gap and measuring lactate levels are being promoted as better predictors of outcome of the patient but in a limited setting hospital, tests to measure lactate and other markers might not be available. This study was carried out to evaluate the outcome predictability of routinely available anion gap, measured at the time of admission, among critically ill patients.

Material and Methods: The study was carried out in a hospital located in rural area among patients admitted to medical ICU, irrespective of the underlying illness, and anion gap was measured at the time of admission and the outcome noted. The normal range was taken to be 3-11 mEq/L (as per newer recommendations).

Results: Of the included 94 patients, 40% (38) died. Among the deceased patients, 76% (29) had high anion gaps (both positive and negative), while 0% mortality was noted among patients with anion gap within normal range.

Conclusion: Increased levels as well as more negative values were associated with higher mortality irrespective of the underlying etiology and hence serum anion gap can be used as a predictor of poor outcome especially in resource limited settings.

Keywords: Anion Gap, Resource, Mortality

INTRODUCTION

With the growing advances in critical illness management, there is a growing need of methods of predicting mortality. While some methods like pulmonary artery wedge pressure are invasive methods and carry their own risks, there are biomarkers that are non-invasive and are found to be associated with predicting mortality. One such marker is serum anion-gap (AG) and it has traditionally been associated with predicting outcomes.[1-5] It is simple to perform and available almost in every critical care unit. It is measured by subtracting concentrations of measured serum anions from that of measured serum cations.[1,6] In daily practice, the included anions are bicarbonate and chloride whereas the included cation is sodium ion (sometimes potassium ion).

In this study, we measured serum anion gaps of patients admitted in medical ICU and looked for any association between higher (positive or negative) anion gap and poor outcome. We included critically ill patients irrespective of the cause of admission in ICU, treatment was given as per protocols and outcome was noted.

MATERIAL AND METHODS

The study was performed in a hospital in a rural area in Indore district of Madhya Pradesh on patients admitted in medical ICU. In total, 94 patients were included, irrespective of age, gender, ethnicity or duration or symptoms of underlying illness. Ethical clearance obtained from form ethical committee of Institute The youngest patient was 17 years old and the oldest was 88 years old. Anion gap was measured in every patient at the time of admission and the outcome was logged. Method for the measurement of the anion gap consisted of ion-electrode technology. The reference range was taken to be 3-11 mEq/L.

RESULTS

Out of total 94 patients studied, 40% (38) patients died. 76% (29) of the deceased patients had anion gaps in the positive or negative extremes (difference of more than 20 mEq/L on the positive side or 10mEq/L on the negative side). None of the patients with normal anion gap died. Anion gaps were divided into 6 categories: < -20, -20 to -10, -10 to 0, 0-10, 10-20 and >20 (all values are in mEq/L) (table-1). In our study, maximum number of patients (68%) had anion gap in the range of -10 mEq/L to 20 mEq/L. (Graph 1)

We observed a steep rise in mortality when anion gap values approached positive and negative extremes. Patients with anion gaps in extremes of positive had mortality rates approaching 100% while those with anion gaps lower than -10 mEq/L had 100% mortality. (Graph 2)

None of the patients having anion gap within normal range had outcome as mortality. All (3) patients with anion gaps less than -20 mEq/L and 16 out of 17 patients with anion gaps more than 20 mEq/L died. (Graph 3)

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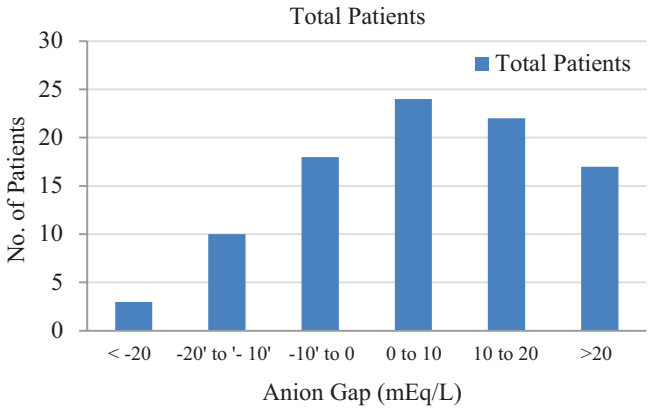
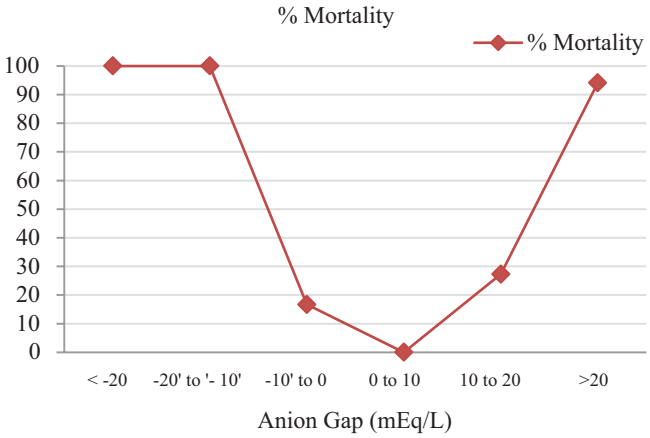
Anion Gap (mEq/L)	Total Patients	No. of Deaths	% Mortality
< -20	3	3	100
-20 to -10	10	10	100
-10 to 0	18	3	16.67
0 to 10	24	0	0
10 to 20	22	6	27.27
>20	17	16	94.12

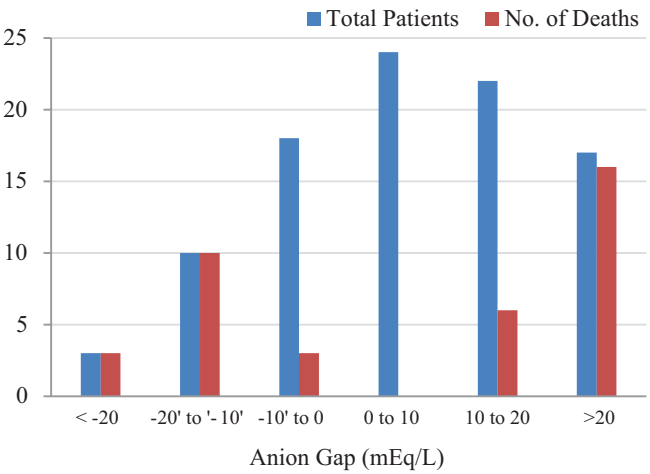
Table-1: Observed Anion gaps and corresponding number of patients and mortality.



Graph-1: Showing distribution of patients across various ranges of anion gap



Graph-2: Extremes of values showing steep rise in mortality



Graph-3: Graph showing proportional mortality among patients.

DISCUSSION

We studied utility of increased serum anion gap measured at the time of admission as a predictor of poor outcome in patients admitted to medical intensive care unit.

An elevation of AG signifies the presence of metabolic acidosis caused by overproduction of organic acids via lactate accumulation, ketoacid production, toxin/drugs, and uremia. An elevated AG usually reflects an imbalance between acid generation in hypoperfused tissues and the ability of the kidneys to excrete these acids. Thus, the presence of an elevated AG may indicate subtle hemodynamic abnormalities leading to tissue hypoperfusion but not overt shock.

The SAG is defined as the following equation:

SAG (initial) = serum sodium [mEq/L] − (serum chloride [mEq/L] + serum total bicarbonate [mEq/L]).

Farwell and colleagues analysed the data from the National Health and Nutrition Examination Survey (NHANES).[7] They proposed that increased SAG is associated with blood pressure, insulin resistance, and inflammation in the healthy general population. Moreover, SAG is an independent risk factor for mortality in acute myocardial infarction, critical illness, and an otherwise healthy elderly population.

Leskovan et al proposed that elevated anion gap i.e value >16 suggest the need for higher level of care and should mandate heightened index of clinical concern.

A low serum anion gap is a relatively uncommon occurrence, most frequently the result of laboratory error or severe hypoalbuminemia. Besides hypoalbuminemia, polyclonal gammopathy and monoclonal gammopathy with excessive accumulation of cationic IgG are the most common clinical disorders associated with a low serum anion gap.

A study by Brenner[8] showed that an elevated AG was associated with increased severity of illness including increased likelihood of hospital and ICU admission.

The current study was carried out in a limited resource setting to study the association of higher AG with poor outcome and we found that routinely available serum AG can be used a predictor of outcome irrespective of the underlying illness.

Serum anion gap is easily measured using serum electrolytes and available in most of the critical care setups. Other more specific biomarkers/tests are available and being studied for predicting outcome but they are not routinely available or are not cost effective.

This study had a limitation that serum albumin and serum lactate corrected values for serum anion gap were not available. Nevertheless, routinely available serum AG was still found to be a useful tool in critical care unit.

CONCLUSION

Anion gap is not a specific test[6] but is a good independent predictor for possible outcome among critically ill patients especially in limited resource setting. Both positive and negative extreme values were found to be associated with higher mortality rates but the more negative values were especially associated with higher (100%) mortality. Our study is consistent with previous studies carried out at various

scales and anion gap was found to be a useful biochemical tool to predict outcome at the time of admission in critical care unit.

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