Role of Anion Gap as a Prognostic Indicator in Acute Coronary Syndrome (ACS)

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Abstract

Background: Cardiovascular diseases are the leading cause of mortality in India and acute coronary syndrome (ACS) is one of its anomalies, affecting mainly the coronary arterial blood supply and further the functioning of heart muscle. Its subtypes are Non-ST elevation myocardial infarction (NSTEMI), unstable angina, and ST-elevation myocardial infarction (STEMI). There are various diagnostic tools available to detect ACS like; electrocardiography (ECG), Cardiac stress test, Coronary CT angiography, Coronary angiogram and cardiac biomarkers. Yet, tools for assessment of prognosis are scanty and new prognostic tools are always welcomed, one such is anion gap, which can be detected by assessment of certain ions present in the serum, urine or plasma, etc. In this study we will assess the role of anion gap, in the assessment of prognosis in ACS.

Objective:

1. To estimate anion gap (AG) in cases of acute coronary syndrome (ACS) at the time of diagnosis;
2. To evaluate association of anion gap (AG) with the prognosis of acute coronary syndrome (ACS)

Methodology: The study will be conducted in the Department of Medicine of a Rural Tertiary Care Hospital. Estimation of anion gap (AG) in cases of acute coronary syndrome (ACS) will be evaluated at the time of admission and after five days of treatment. Anion gap will be calculated or measured as difference between measured cations (Na+ + K+) and the measured anions (Cl- + HCO3-) in serum. Any complications during the management will be noted (Heart failure arrhythmias, Hypotension, Reinfarction, Death) will be correlated with anion gap (AG). Chi square test will be applied to evaluate statistical difference between among anion group quartile groups.

Results: The study will play a key role in identifying and assessing various other prognostic tools like anion gap, in assessing the severity of disease to some extent in patients with acute coronary syndrome.

Conclusion: High value of serum anion gap levels is associated with poorer prognosis of the disease outcome in patients with acute coronary syndrome.

Keywords: *Acute coronary syndrome, anion gap, cardiovascular disease, prognostic tool.*

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Introduction

India is the second most populated country of the world with a high mortality rate caused due to various medical conditions and diseases, especially cardiovascular diseases (CVDs) becoming the leading cause of mortality in India.[1] In 2017, CVD caused an estimated 17.8 million deaths worldwide.[2] Coronary

artery disease(CAD) is the most common type of heart disease caused due to reduction in oxygen and blood supply to the heart muscle due to build up of plaque in the arteries of the heart i.e. the coronary arteries. Epidemiologic studies have shown that there are at present over 30 million cases of CAD in the country.[3] Furthermore, acute coronary syndrome(ACS) is a subtype of CAD. Itis a group of diseases in which blood supply to any of the coronary arteries is decreased partially/completely which causes the heart muscle either to function improperly or its death. The following are the subtypes of ACS are:- Non-ST elevation myocardial infarction (NSTEMI), unstable angina, and ST-elevation myocardial infarction (STEMI) .There are various tools for diagnosing these conditions like- ECG, Cardiac stress test, Coronary CT angiography, Coronary angiogram, Blood Tests, etc.

Presently used prognostic tools for acute coronary syndrome are various biochemical markers like estimation of cardiac troponin, natriuretic peptides, growth-differentiation factor-15, etc. These are some of the mose efficient prognostic biochemical markers.

New prognostic tools in CAD patients are always welcomed. The serum anion gap (AG) is a mathematically derived parameter that has been used for more than 50 years.[4] Till now AG has been used as a prognostic indicator in studies related to advanced kidney disease,[4] hypertension,[5] insulin resistance[6] & cardiac deaths.[7] It is yet unknown whether AG can alter the course of prognosis of ACS. Therefore dearth of medical evidence relating to association of AG & ACS. So, this study will evaluate AG & its prognostic implication in case of ACS.

Aim: To assess the anion gap as a prognostic indicator or tool in patients with acute coronary disease.

Objective:

1. To estimate anion gap (AG) in cases of acute coronary syndrome (ACS) at the time of diagnosis
2. To evaluate association of anion gap (AG) with the prognosis of acute coronary syndrome (ACS)

Methodology

Study Design: Cross sectional study

Study Population: Will be carried out in 50 consecutive patients

Study period: Two-Months

Study setting: This cross-sectional study will be conducted in the Department of Medicine of a Rural Tertiary Care Hospital. Consecutive patients or subjects with diagnosis of acute coronary syndrome (Ischemic chest pain, ECG changes, and Cardiac biomarkers) admitted in the intensive care unit (ICU) of a tertiary care hospital. The study will begin after clearance from institutional ethical committee. Detailed history of Rural or Urban backgrounds, Physical activity levels, Addiction (smoking, alcohol intake), Family history of Blood Pressure and Diabetes will be recorded and Clinical Examination will be done.

Estimation of anion gap (AG) in cases of acute coronary syndrome (ACS) at the site of diagnosis:- Anion gap will be evaluated at the time of admission and after five days of treatment. Assessment of severity of coronary artery disease (CAD) will be done on the basis of severity of coronary artery stenosis (in coronary angiography), Killip's classification and cardiac function grades based on left ventricular ejection fraction (LVEF). Grades of cardiac function compromised normal (defined ≥50%), preserved (40%-49%), and reduced (<40%) LVEF.[8] Significant coronary artery stenosis was defined as ≥ 75% narrowing of the diameter of at least one major epicardial vessel.[9]

Evaluation of association of anion gap (AG) with the prognosis of acute coronary syndrome: Any complications during the management will be noted (Heart failure arrhythmias, Hypotension, Reinfarction, Death) will be correlated with anion gap (AG).

Calculation of Anion gap (AG)**:** Anion gap is calculated or measured as difference b/w measured cations (Na+ + K+) and the measured anions (Cl- + HCO3-) in serum.

Formula: The formula used will be

ANION GAP= (Na+ + K+) – (Cl- + HCO3-)

The concentrations will be expressed in the following units i.e. of milliequivalents/litre (mEq/L) or in millimoles/litre (mmol/L).

Selection Criteria:

Inclusion Criteria: Adults ≥ 18 years admitted to intensive care unit (ICU) with diagnosis of acute coronary syndrome

Exclusion Criteria:

1. Heart failure due to other causes
2. Acute coronary syndrome with cardiogenic shock
3. Any infection at the time of presentation
4. Subjects not giving consent
5. Other causes of high anion gap levels like advanced kidney disease, metabolic acidosis, etc

Implications: It is a rural tertiary hospital-based study carried out through assessment of anion gap levels in patients of acute coronary syndrome. High anion gap levels will be observed in patients with worsening cardiac functions. We can interpret prognosis of individual patients based on their anion gap levels along with its severity to some extent; allowing to give better treatment & management based on individual prognostic values; allowing better life value.

Methodology in PICOT format:

P (Population): 50 consecutive patients attending Medicine OPD and ICU of Rural Tertiary Care Hospital in the backdrop of Central India.

I (Intervention): Assessment and understanding of anion gap as a useful prognostic indicator in a group of cardiovascular diseases i.e. acute coronary syndrome.

C (Comparison): Not applicable.

O (Outcome): Knowledge of a prognostic indicator i.e. anion gap to assess and predict severity level of the disease in individual patients

T (Time): Study will be conducted over a duration of 2 months

Measurements: Anion gap is calculated or measured as difference b/w measured cations (Na+ + K+) and the measured anions (Cl- + HCO3-) in serum.

The formula used will be: ANION GAP = (Na+ + K+) – (Cl- + HCO3-)

Quantitative Variables: Serum albumin land phosphate levels and unmeasured ions

Statistical Method: Chi square test will be applied to evaluate statistical difference between among anion group quartile groups. Ordinal logistic regressions will be used to evaluate between anion gap and severity of acute coronary syndrome. P values of <0.05 will be considered statistical insignificant. Software used in analysis will be SPSS 25.0 version.

Results

The study will play a key role in studying the association of serum anion gap in prognosis of acute coronary diseases along with determining its severity to some extent.. It will be observed that in patients who are severely affected, high values of serum anion gap will be obtained. This is similar to high values of anion gap observed in patients with metabolic acidosis and kidney failure. This will enable us to understand a unique yet somewhat efficient prognostic tool for study i.e. anion gap.

Discussion

Cardiovascular diseases are one of the leading causes of death in our country. Acute coronary syndrome is one of the heart anomalies. Though there are many diagnostic tools for detection of the disease but prognostic tools are being developed every day. One such tool is anion gap which can be assessed to determine and give prognosis based on individual patients, thus providing somewhat efficacy in treatment and management options.

In a study done by Yang, Shi-Wei, et al. in the year 2017, it concluded that higher levels on anion gaps were associated with worsening cardiac functions and cardiovascular diseases [10], similar to the results expected results in this study.

A study by Taylor, Eric N., John P. Forman, and Wildon R. Farwell in 2007 and another study by Abramowitz, Matthew K., Thomas H. Hostetter, and Michal L. Melamed in 2012 on determinants like hypertension[11] and cardiorespiratory fitness[12] respectively;these determinants were associated with cardiovascular diseases which lead to increase values of anion gap levels.

Another study by Ahn, Shin Young, et al. in 2014 showed that higher levels of serum anion gap were associated with an increased risk of cardiac deaths or mortality.[7] This indicates a poorer prognosis if the serum anion gap levels are found to be high.

Similarly, higher value of serum anion gaps are obtained in diseases like metabolic acidosis and kidney disease. A study done by Cheng, Bihuan, et al. in 2020 showed that high levels of anion gap were associated with poor prognosis in patients with acute kidney

injury[13]. Few studies on related aspects of this issue are available[14-18].

The results will be concluded and determined from this study, and will help to indicate the role of anion gap as a prognostic indicator in acute coronary syndrome.

Ethical Clearance: Taken from institutional ethics committee.

Source of Funding: Self.

Conflict of Interest: Nil.

References

1. Prabhakaran D, Jeemon P, Roy A. Cardiovascular diseases in India: current epidemiology and future directions. Circulation. 2016 Apr 19;133(16):1605-20.
2. Mensah GA, Roth GA, Fuster V. The Global Burden of Cardiovascular Diseases and Risk Factors: 2020 and Beyond.
3. Krishnan MN. Coronary heart disease and risk factors in India–On the brink of an epidemic?. Indian heart journal. 2012 Jul;64(4):364.
4. Kraut JA, Madias NE. Serum anion gap: its uses and limitations in clinical medicine. Clinical Journal of the American Society of Nephrology. 2007 Jan 1;2(1):162-74.
5. Taylor EN, Forman JP, Farwell WR. Serum anion gap and blood pressure in the national health and nutrition examination survey. Hypertension. 2007 Aug 1;50(2):320-4.
6. Farwell WR, Taylor EN. Serum bicarbonate, anion gap and insulin resistance in the National Health and Nutrition Examination Survey. Diabetic medicine. 2008 Jul;25(7):798-804.
7. .Ahn SY, Ryu J, Baek SH, Han JW, Lee JH, Ahn S, Kim KI, Chin HJ, Na KY, Chae DW, Kim KW. Serum anion gap is predictive of mortality in an elderly population. Experimental gerontology. 2014 Feb 1;50:122-7.
8. Ponikowski P, Voors AA, Anker SD, Bueno H, Cleland JG, Coats AJ, Falk V, González-Juanatey JR, Harjola VP, Jankowska EA, Jessup M. 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure: The Task Force for the diagnosis and treatment of acute and chronic heart failure of the European Society of Cardiology (ESC). Developed with the special contribution of the Heart Failure Association (HFA) of the ESC. European journal of heart failure. 2016 Aug;18(8):891-975.
9. .Kim M, Park JH, Lee JH, Sun BJ, Jin SA, Kim JH, Choi S, Jeong JO, Seong IW. Comparison of long-term clinical outcomes of percutaneous coronary intervention in vasospastic angina patients associated with significant coronary artery stenosis. International journal of cardiology. 2016 Sep 1;218:75-8.
10. Yang SW, Zhou YJ, Zhao YX, Liu YY, Tian XF, Wang ZJ, Jia DA, Han HY, Hu B, Shen H, Gao F. The serum anion gap is associated with disease severity and all-cause mortality in coronary artery disease. Journal of geriatric cardiology: JGC. 2017 Jun;14(6):392.
11. Taylor EN, Forman JP, Farwell WR. Serum anion gap and blood pressure in the national health and nutrition examination survey. Hypertension. 2007 Aug 1;50(2):320-4.
12. Abramowitz MK, Hostetter TH, Melamed ML. Lower serum bicarbonate and a higher anion gap are associated with lower cardiorespiratory fitness in young adults. Kidney international. 2012 May 2;81(10):1033-42.
13. Cheng B, Li D, Gong Y, Ying B, Wang B. Serum Anion Gap Predicts All-Cause Mortality in Critically Ill Patients with Acute Kidney Injury: Analysis of the MIMIC-III Database. Disease markers. 2020 Jan 21;2020.
14. Chiwhane, A., and Pradeep. "Study of Rhythm Disturbances in Acute Myocardial Infarction." Journal of Association of Physicians of India 66, no. January (2018): 54–58.
15. Jyoti, J., V. Nitin, B. Shashank, and D. Pradeep. "Gamma Glutamyl Transferase Levels in Patients with Acute Coronary Syndrome: A Cross-Sectional Study." Journal of Temporalular Disease Research 8, no. 4 (2017): 121–25. https://doi.org/10.5530/jcdr.2017.4.28.
16. Choudhari, M.S., M.I. Sonkusale, and R.A. Deshpande. "Sudden Cardiac Arrest on 5 Th Day after Coronary Artery Bypass Graft Surgery: Diagnostic Dilemma." Annals of Cardiac Anaesthesia 21, no. 3 (2018): 341–42. https://doi.org/10.4103/aca.ACA-214-17.

17. Khatib, M.N., R. Kirubakaran, S. Gaidhane, A.H. Shankar, and Z. Quazi Syed. "Yoga for Improving Functional Capacity, Quality of Life and Cardiovascular Outcomes in People with Heart Failure." Cochrane Database of Systematic Reviews 2017, no. 7 (2017). https://doi.org/10.1002/14651858.CD012015.pub2.
18. Bhinder, H.H.P.S., and T.K. Kamble. "The Study of Carotid Intima-Media Thickness in Prediabetes and Its Correlation with Cardiovascular Risk Factors." Journal of Datta Meghe Institute of Medical Sciences University 13, no. 2 (2018): 79–82. https://doi.org/10.4103/jdmimsu.jdmimsu_58_18.