

**Relation of Serum Ionized Calcium Levels with Acid Base Disturbances in Critically ill Patients****R. Revathi<sup>1</sup>, Balaji Rajagopalan<sup>2</sup>**<sup>1</sup>MSc, Ph.D., Assistant Professor of Biochemistry, Shri Sathya Sai Medical College and Research institute, Sri Balaji Vidyapeeth Deemed to be University, Guduvancherry-Thiruporur Main Road, Ammapettai, Chengalpet<sup>2</sup>M.D, Professor & HOD of Biochemistry, Shri Sathya Sai Medical College and Research Institute, Sri Balaji Vidyapeeth Deemed to be University

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**Abstract:**

Ionized calcium levels play an important role for identification of disturbances in calcium homeostasis. This is due to the fact that deviation in Serum protein levels and blood pH will alter the Serum total calcium levels. In critically ill patients alteration in protein levels and changes in Blood pH are commonly observed. Ionized calcium concentrations vary inversely with pH. The current research study aims to investigate the ionized calcium levels in various acid base disturbances in critically ill patients. 190 arterial blood sample data's were utilized. The consistency of the report was verified using Modified Henderson Equation. ABG parameters like pH, pCO<sub>2</sub>, HCO<sub>3</sub>, Standard base excess and ionized calcium levels are noted and the predicted Ionized Calcium (at pH 7.4) was calculated. Arterial blood gas analysis revealed 20 normal cases, 8 respiratory acidosis, 50 respiratory alkalosis, 35 metabolic acidosis, 30 metabolic alkalosis and 47 mixed disorder cases. Acid base disorders are divided into 4 groups based on the ionized calcium levels namely  $\leq 1$  mg/dl,  $>1.0 \leq 2.5$  mg/dl,  $>2.5 \leq 4.4$  mg/dl and  $>4.4 \leq 5.4$  mg/dl. The Results are tabulated and graphically analyzed. Ionized calcium level is normal in only 4.74 % of the total 190 cases. Irrespective of the acid base Disturbances ionized calcium level is lowered in critically ill patients.

**Keywords:** Acid-Base Imbalances, Ionized Calcium, Severely Ill Patients, pH.

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**Introduction**

Acid Base disturbances are frequently noticed in critically ill patients. The Acid Base disorders like metabolic acidosis, metabolic alkalosis, respiratory alkalosis, and respiratory acidosis are seen with necessary respiratory or renal compensations or combined together as mixed disorders [1,2]. pH has a significant impact on the concentration of ionized calcium. .

Ionized calcium levels play an important role for identification of disturbances in calcium homeostasis. This is due to the fact that deviation in Serum protein levels and blood pH will alter the Serum total calcium levels. Critically ill patients frequently encountered hypocalcemia. Alteration in protein levels and changes in Blood pH are commonly observed in critically ill patients, so calcium homeostasis cannot be assessed in these patients using their Serum total calcium levels. [3]

Three distinct fractions of calcium are present in the bloodstream: the protein-bound, anion-bound, and free, or "ionized," form. The calcium present in

each of these fractions is determined by the quantity of hydrogen ions, anions, and plasma proteins. The Plasma Proteins (albumin and globulins) and anions (phosphate, lactate, free fatty acids, and citrate) bind to the serum calcium. [4,5] Free ionized calcium pool contributes 45–50% of the total calcium in circulation which represent physiologically active portion. [4,5,6]

The concentration of the proteins directly correlates with the amount of protein bound calcium in the serum. Increase in serum protein concentration will Increase both the concentration of protein-bound calcium and total calcium. Similarly decrease in serum protein concentration will decrease both the concentration of protein-bound calcium and total calcium. When the concentration of plasma protein drops, so does the level of total plasma calcium. [4,5]

The changes in Protein concentration have greater effect on total calcium levels but not on ionized calcium. The albumin is the most important plasma

protein that changes in critically ill patients. There are many formulas available to correct the total calcium concentration for variations in protein level but it does not reflect ionized calcium level due to multiple factors that influence critically ill patients. [7,8,9]

pH has a significant impact on the concentration of ionized calcium. The positively charged hydrogen and ionized calcium (iCa<sup>2+</sup>) compete for the same binding at the negatively charged binding sites on the protein molecules and this binding is pH dependant. Decreased hydrogen ions or an increase in pH favor more protein binding that decreases the levels of free calcium.

Conversely, acidosis reduces protein binding thereby increasing the free calcium levels. For every 0.1 pH change, the change in ionized calcium is 0.05 mmol/L and inversely related. The total calcium concentration is not changed and remains the same but there is a shift in calcium from one fraction to another which is clinically important. [4,5,10] The goal of the present study is to analyse and correlate

the ionized calcium levels in the arterial blood gas from critically ill patients with acid-base disturbances.

**Materials and Methods**

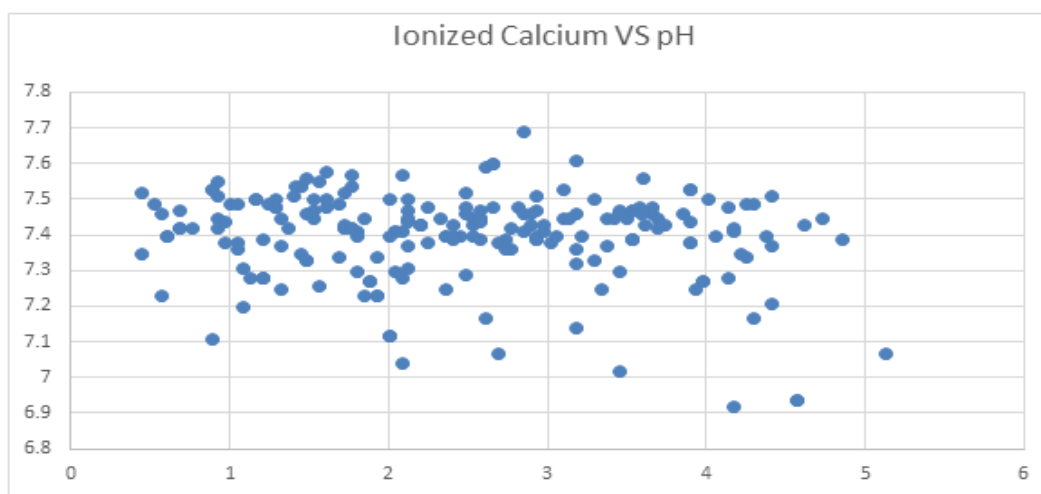
190 arterial blood gas analysis sample data's were utilized. The study was conducted at the Shri Sathya Sai Medical College and Research Institute for the period of September 2023 to November 2023 using the Blood gas Analyzer. Extreme care was taken to prevent pre-analytical mistakes and the Modified Henderson Equation was used to verify the consistency of the ABG report. [11,12] Key parameters were recorded, including measured pH, pCO<sub>2</sub>, and HCO<sub>3</sub> and Standard Base Excess values were noted. Using pCO<sub>2</sub>, the concentration of carbonic acid was computed (H<sub>2</sub>CO<sub>3</sub>=0.03 X pCO<sub>2</sub>) [11, 12] Corrected ionized calcium was calculated. Delta calcium is the difference between ionized calcium and calculated calcium (at pH 7.4) [4,5,13]

**Formula to calculate Corrected Ionized Calcium (atpH7.4):** Corrected ionized calcium = Measured iCa x (1 - 0.53 x (7.4-pH))

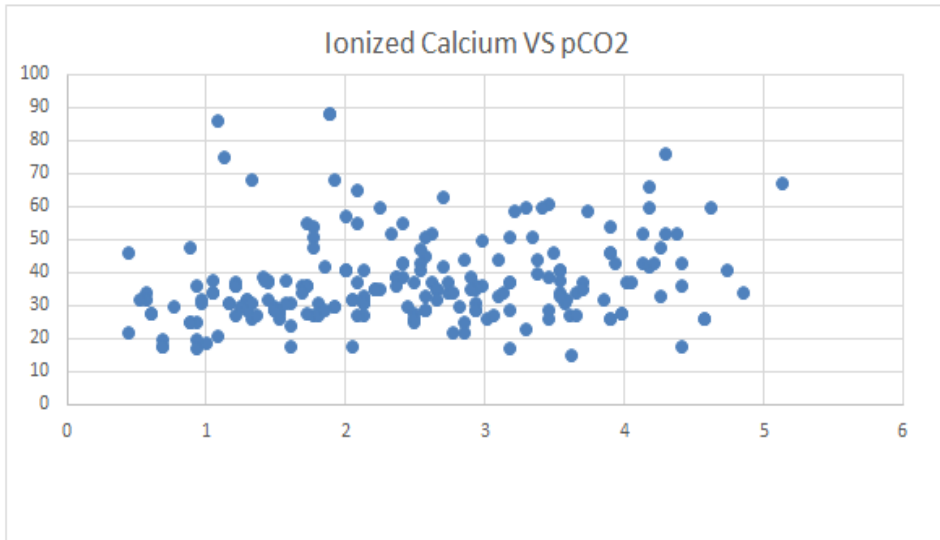
**Table 1: Ionized Calcium Levels in Various Acid-Base Disorders**

Ionized calcium Levels(mg/dL)	Normal	Respiratory acidosis	Respiratory alkalosis	Metabolic acidosis	Metabolic alkalosis	Mixed disorder	Total	Percentage (%)
≤1	1	0	9	2	1	8	21	11.05
>1.0≤2.5	9	3	19	19	11	16	77	40.53
>2.5≤4.4	9	4	21	11	17	21	83	43.68
>4.4≤5.4 (Normal Range)	1	1	1	3	1	2	9	4.74
<b>Total (Number of cases)</b>	20	8	50	35	30	47	190	100.00
<b>Percentage</b>	10.53	4.21	26.32	18.42	15.79	24.74	100.00	
<b>Mean</b>	2.68	3.11	2.23	2.18	2.69	2.42		
<b>Std.dev</b>	0.99	1.38	1.14	1.09	1.02	1.09		

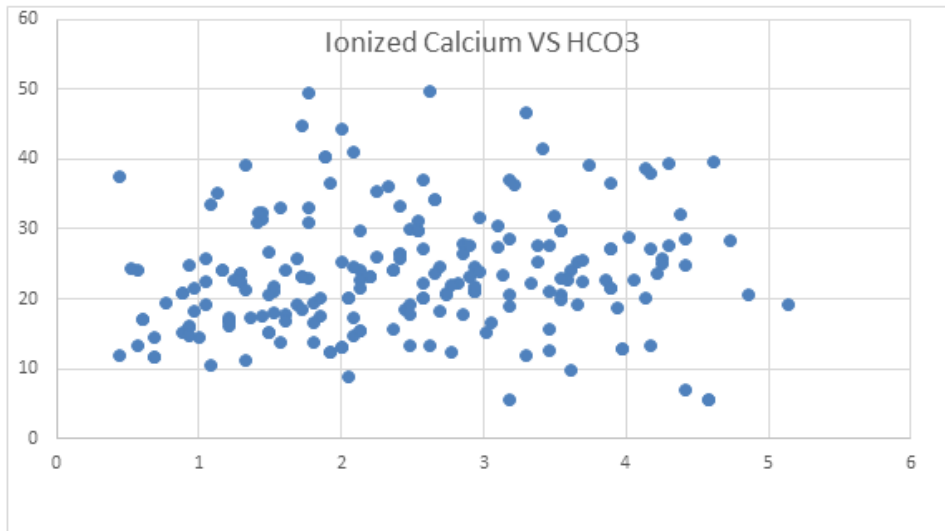
The Normal range of ionized calcium is >4.4≤5.4mg/dl.



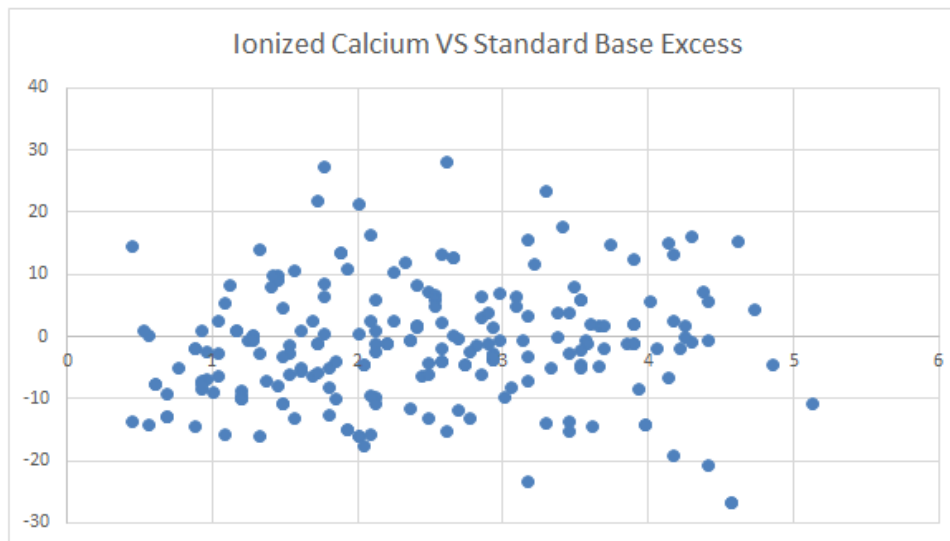
**Graph 1: Ionized calcium vs pH**



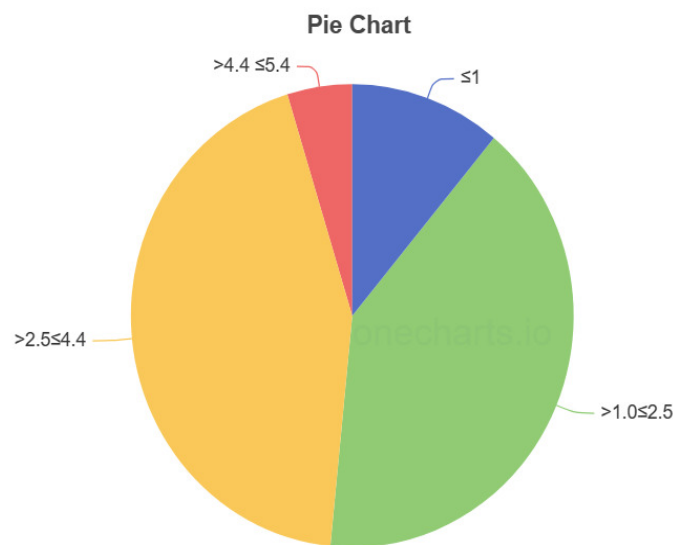
Graph 2: Ionized calcium vs pCO2



Graph 3: Ionized calcium vs HCO<sub>3</sub>



Graph 4: Ionized calcium vs Standard Base Excess



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**Graph 5: Distribution of ionized calcium in various acid base disorders of Total 190 cases**

### Discussion

Low ionized calcium levels in critically ill patients are documented in many previous research studies and stated that most of them do not have abnormality in calcium homeostasis [3]. Unusual low levels of ionized calcium are probably a sign of a critical sickness and these values becomes normal once the patients diseased conditions is improved. [14,15,16] Ionized calcium levels have been suggested as a marker for prognosis and adverse outcomes in intensive care unit (ICU) patients. The homeostatic set point for ionized calcium is different for healthy individuals and critically ill patients and it is found to be resistant to treatment. [17,18,19]

The aim of the current research study is to determine the serum ionized calcium levels in critically ill patients for various acid-base disorders. The reference range of ionized calcium is  $>4.4 \leq 5.4$  mg/dl. Ionized calcium levels were measured in the total 190 samples and divided into four groups based on the ionized calcium. Hemolyzed samples and samples with significant time delay between collection and  $iCa^{2+}$  measurement are rejected and not included in the study. Falsely low ionized calcium is caused by hemolysis. Delay in analysis causes an apparent hypercalcemia resulting from metabolic activity due to drop in pH. [19]

The four groups of the 190 samples were clearly tabulated in table 1. The relationships between pH,  $pCO_2$ , Bicarbonate and Standard Base Excess with ionized calcium were graphically displayed (Graphs 1,2,3,4) which indicated that there was no clear correlation for each sample separately. Pie chart is used to represent the distribution of ionized

calcium in various acid base disturbances. From this study it was found that only 4.74% of all cases have normal ionized calcium levels and it is clearly observed that ionized calcium is lowered in critically ill patient irrespective of the acid base disorders.

### Conclusion

Measurement and monitoring of ionized calcium levels in critically ill patients may provide an indication in assessing the prognosis and adverse events of the patients. Ionized calcium levels are found to be reduced in critically ill patients irrespective of the acid base disturbances.

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