Reliability of Albumin-Adjusted Calcium in Patients of Chronic Kidney Disease in a Tertiary Care Center

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Abstract:

Background*: Calcium circulates in the blood in 3 forms.Approximately 50% circulates as ionizedCa^{+2}.Most of the laboratories measure total calcium (TCa) and adjust it for albumin concentration if < 4 gm/dl to predict the true calcium status. However, this albumin-adjusted Ca(Adj-Ca)is less reliable predictor of true calcium in the patients of CKD. So,the present study was planned to compare the results of TCa and Adj-Ca with ionizedCa^{+2}in control & CRF patients and assess whether Adj-Ca is a reliable indicator of true Ca^{+2}in patients of CKD or not?*

Materials and Methods*: This study was carried out in SSG Hospital,Vadodaraon patients attending medicine OPD having normal renal function(RFT) as controls &patients of CKDas cases. S.Creatinine,S.albumin,S.TCa was measured on fully auto-analyzer ERBA- XL-640 and S.IonizedCa^{+2} by ISE analyzer and Adj-Ca was calculated by modified payne formula in both the groups.Statistical analysis was done by pearson's coefficient correlation.*

Results*: This study was done in the month of September-2021 recruited 150 controls and 137 cases.It was observed that in control group(albumin 3.5 ± 0.15gm/dl)Adj-Ca shows better correlation with ionized Ca^{+2}(r=0.7944,p<0.0001) as compared to TCa (r=0.7671,p<0.0001, while in case group(albumin 2.3 ± 0.35gm/dl)even Adj-Ca shows weak correlation (r=0.3417,p=<0.0001) with ionizedCa^{+2}.*

Conclusion*: This study concludes that Adj-Ca is a reliable indicator of true-Cain patients having normal RFT. However,in patients of CKD, Adj-Ca is overestimated thus not a reliable indicator to reflect the true calciumvalues. So, in these patient's measurement of ionizedCa^{+2} by direct ISE method seems to be the only choice despite its cost.*

Key Words: *Total calcium,Albumin adjusted calcium,Ionized Ca^{+2} ,chronic kidney disease (CKD)*.

I. Introduction

Chronic kidney disease (CKD) is a common condition that refers to a long-term loss of kidney function.[1]Patients with chronic kidney disease (CKD) have marked disruption in bone and mineral metabolism. Kidney failure is known to disrupt a number of homeostatic mechanisms that control serum calcium and normal bone metabolism.[2]

Calcium circulates in the blood in 3 forms. Approximately 13% calcium is bound to organic and inorganic anions,around 40% is bound to albumin and remaining 47% is available as biologically active ionized calcium (free calcium).[3,4]

The measurement of calcium in blood is one of the most commonly requested laboratory test. Most of the clinical laboratories measure total serum calcium (TCa) and then adjusts for albumin concentrations (if needed)to predict actual calcium statusas TCa is affected by albumin concentration and other bound anions without affecting the free ionized Ca^{+2}levels.[5] However, this albumin-adjusted Ca(Adj-Ca)is less reliable predictor of actual calcium in the patients of chronic kidney disease (CKD).[3]As calcium ions bound to serum albumin and organic and inorganic anions are subjected to variation in their values, there has always been a debate as to whether estimation of TCa or calcium adjustedfor serum albumin reflects actual value or free ionized calcium measured by direct ISE is the only suitable method to reflect true values in clinical laboratories.[5]So in our study we have compared the total and adjusted calcium (Adj-Ca) with ionized calcium (Ca^{+2}) to know the reliability of albumin-adjusted calcium in patients of CKD.

II. Material And Methods

This case-control study was carried out in SSG Hospital, Vadodara, Gujarat. We recruited 150 healthy controls having albumin concentration >3.5 gm/dland serum creatinine <1.2 mg/dl& 137 cases of CKD (stage 4&5)on haemodialysis from the medicine department. Age and Sex were matched in both the groups. Written informed consent was obtained from all the patients recruited in this study. Biochemical parameters like S.Urea, S.Creatinine,S.albumin,S.TCa was measured on fully automated analyzer ERBA- XL-640 and S.Ionized Ca^{+2} on ISE analyzer .Albumin-Adjusted Ca was calculated by modified payne formula in both the groups.

Modified payne formula: Adj-Ca[mg/dl] = TCa[mg/dl]+0.8[4-albumin{gm/dl}][6]
Total calcium also calculated using formula(Calculated **TCa = 2 * Ionized calcium**)[5]

Statistical analysis was done by pearson's coefficient correlation and unpaired t-test(p value <0.05=statistically significant).The Bland-Altman plots were plotted to evaluate the level of agreement between albumin adjusted calcium and calculated TCa using MedCalc software.

Study Design: Case-control study
Study Location: Medical college and S.S.G Hospital, Vadodara, Gujarat, India.
Study Duration: August 2021 to September 2021.
Sample size: 287 (150 controls and 137 cases)

ANALYTICAL METHODS
The serum samples were analyzed for serum for following parameters:
* S. Urea: GLDH method
* S. Creatinine: Modified IFCC method
* S. Albumin: Bromocresol Green (BCG) method
* S. Total Calcium: Arsenazo-III method
* Serum Ionized calcium were directly measured by Ion Selective Electrode (ISE) method

Inclusion criteria:
1. Healthy individuals as controls with albumin concentration >3.5 gm/dl
2. CKD patients as cases with stage 4 and 5

Exclusion criteria:

1. Healthy individuals with albumin concentration <3.5 gm/dl
2. CKD patients of early stage (stage 1-3)
3. *Any patients with other complications*

III. Result

This study was done in the month of August & September 2021, recruited 150 controls and 137 cases.It was observed that there is significant difference of mean of all parameters between both the groups (Table-1) and p value <0.001 is considered as statistically significant.Pearson's correlation coefficient wasapplied to show relation of albumin adjusted calcium (Adj-Ca) and total calcium (TCa) with Ionized -Ca. It was observed that in control group (albumin 3.6+0.10gm/dl) Adj-Ca shows better correlation with ionized Ca^{+2}(r=0.7944, p<0.0001) as compared to TCa (r=0.7671, p<0.0001. While, in case group (albumin 2.3+0.35gm/dl) even Adj-Ca shows weak correlation (r=0.3417, p=<0.0001) with ionizedCa^{+2}.(Table-2,Figure1-2))

The Bland–Altman plot was used to find agreements between total calcium and Adj-Ca in both the groups and it shows that in control group there is an equal distribution of values on both the sides of meanwhile in case group there is positive biasness suggesting that this adjusted calcium is overestimated. (Figure 3-4)

Table no :1 All parameters mean + SD in both the groups (p<0.001 statistically significant)

Parameters	Controls (150)	Cases (137)	P value
Urea(mg/dl)	27.67 +7.14	86.64+39.63	<0.0001
Creatinine(mg/dl)	0.88 +0.16	4.63 +2.13	<0.0001
Albumin(gm/dl)	3.57+0.16	2.28+0.35	<0.0001

Total Calcium(mg/dl)	9.39 ± 0.55	8.65 ± 0.55	<0.0001
Albumin-Adjusted Ca^{+2}(mg/dl)	9.73 ± 0.57	10.03 ± 0.62	<0.0001
Ionized Calcium(mg/dl)	4.68 ± 0.31	4.58 ± 0.38	0.0144
Cal-Tca^{+2} from I.ca^{+2}	9.36 ± 0.62	9.16 ± 0.75	0.0144

Table-2: Pearson's correlation coefficient

	Controls	**Cases**
Total Ca^{+2} & Ionized Ca^{+2}	r=0.7671 p= <0.0001	r= 0.3405 p=<0.0001
Adjusted Ca^{+2} & Ionized Ca^{+2}	r= 0.7944 p=<0.0001	r=0.3417 p=<0.0001
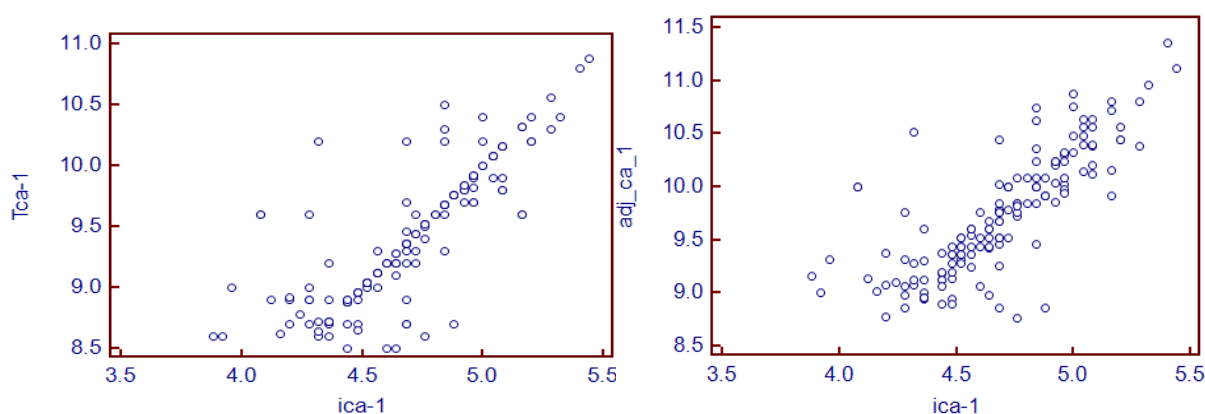
Figure:1 Pearson's correlation coefficient between Total Ca^{+2} & Ionized Ca^{+2} andAdjusted Ca^{+2} & Ionized Ca^{+2} (Control group)
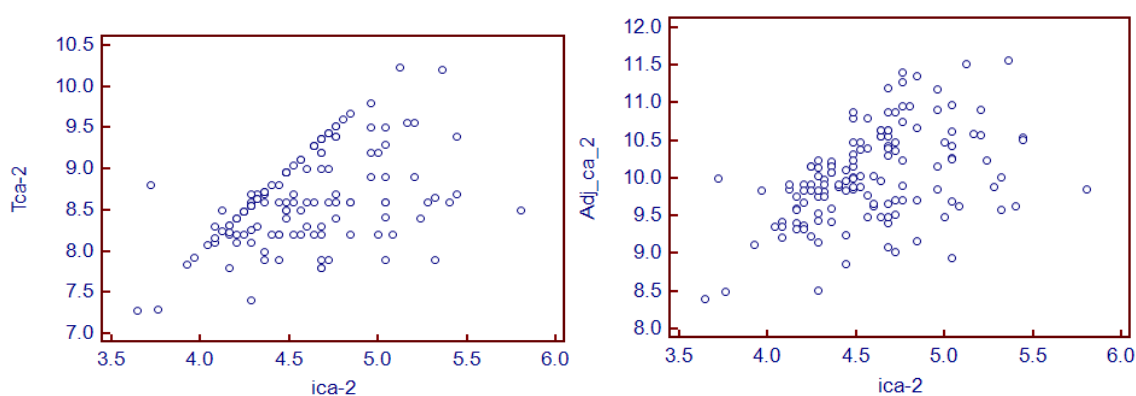
Figure:2 Pearson's correlation coefficient between Total Ca^{+2} & Ionized Ca^{+2} andAdjusted Ca^{+2} & Ionized Ca^{+2} (Case group)

Figure: 3-4: Blant-altman plot showing agreement between albumin adjusted calcium and calculated TCa
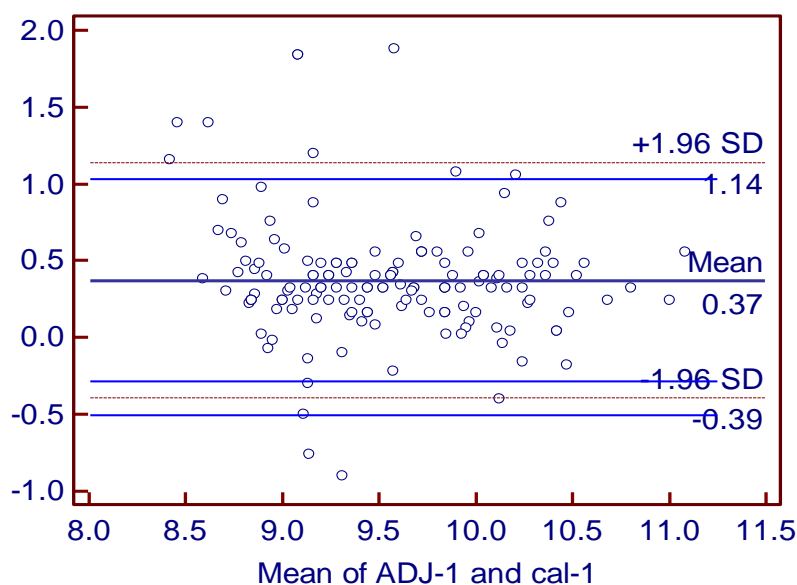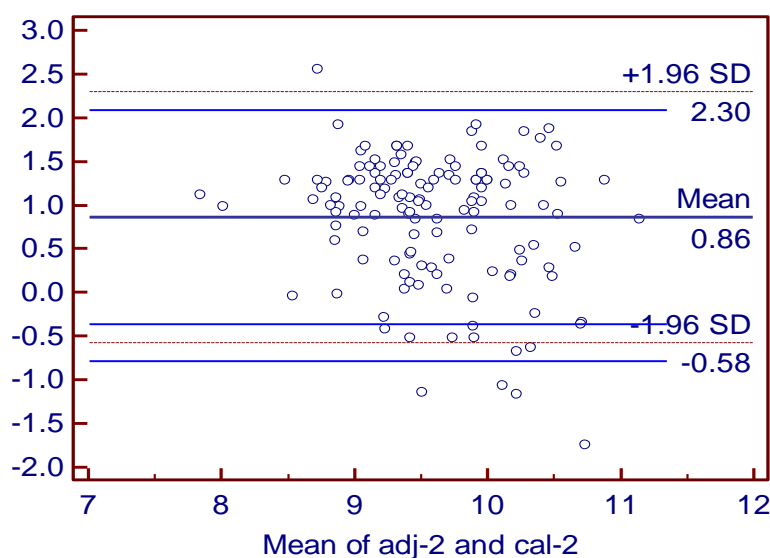

Figure-3

Figure-4

IV.   Discussion

In this study we have observed that in control patients(albumin concentrations >3.5 g/dl and serum creatinine <1.20 mg/dl) Adj-Ca shows better correlation with ionized Ca^{+2}as compared to total calcium while in CKD patients (albumin concentration <3.0 g/dl) both Adj-Ca and TCa shows weak correlation with ionized calcium.[5]In control group there is good agreement between albumin adjusted calcium and calculated TCa while in CKD patients there is positive biasness suggesting that this adjusted calcium is overestimated and does not show the actual calcium status. So, adjusted calcium levels are weak predictors of actual calcium levels in these patients.[6]

Many factors such as calcium supplementation, pH, serum phosphate and serum albumin levelsmay lead to underestimation or overestimation of the calcium values in patients with CKD.[4]Some studies were reported that total calcium(un-adjusted) and albumin adjusted calcium levels are weak predictors of actual calcium levels in CKD patients.[3] Similar findings were observed in our present studyalso.

C. Suvarna Devi et al. found that direct measurement of ionized calcium may be a better predictor of actual calcium levels in patients with CKD rather thantotal and albumin adjusted calcium, which is similar to our findings.[4]
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V.   Conclusion

This study concludes that albumin adjusted calcium (Adj-Ca) is a reliable indicator of actual Ca^{+2} status in normal healthy individual. However, in patients of CKD, Adj-Ca is overestimated thus not a reliable indicator to reflect the actual calcium status.So,in these patient's measurement of ionized Ca^{+2} by direct ISE method seems to be the only choice despite its cost.

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