IOSR Journal of Dental and Medical Sciences (IOSR-JDMS)
e-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 16, Issue 6 Ver. I (June. 2017), PP 01-10
www.iosrjournals.org

A Study of "Potassium Dip and Severity of Acute Ischemic Stress In Patients with Acute Coronary Syndrome"

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Abstract
Background: *Acute coronary syndrome (ACS) is highly prevalent throughout the world .Transient decrease in serum potassium level is common, demonstrating its occurrence in ACS and its significance on disease severity. AIM: To study the prevalence of potassium dip and its significance on disease severity among ACS patients.*
Materials & Methods: *This is an observational cross-sectional study with hundred newly diagnosed ACS patient. Potassium dip is assessed by DELTA POTASSIUM. Severity of ACS is assessed with duration of hospital stay, LV function status by 2D Echo and cardiac biomarker. Collected data are analyzed with SPSS 15 software.*
Results: *Among ACS, STEMI constitutes 65%,NSTEMI 18% and UA in 17%. With duration of hospital stay 46% over 6-7 days,31% over 5 days and 23% stayed beyond 7 days. Severe, moderate, mild LV dysfuntion and normal LV function are seen in 14 %, 42%, 27% and17% respectively. Analyzes of serum delta potassium with the variables shows significant correlation with respect to duration of hospital stay, LV dysfunction status and among various group of ACS having p value of 0.001.*
Conclusion: *Our study shows that the prevalence of potassium dip is common among ACS and delta potassium is positively correlating with disease severity.*
Keywords: *Acute coronary syndrome, Acute ischemic stress, Δk - Delta potassium (serum potassium level at discharge-level at admission), Left ventricular function, Potassium dip*

I. Introduction

ACS is highly prevalent in both developing and developed countries though many modifiable and non-modifiable risk factors are identified and addressed. ACS has sympathetic stress and manifests clinically with excessive sweating, tachycardia and anxiety. Hypokalemia is considered as an acute phase response to sympathetic activation which occurs following myocardial ischemia and this subsequently activates sodium potassium-ATP ase enzyme which is present on the cell membrane and shifts the K^+ intracellularly[1]. Hypokalemia is a serious condition that has implications in cardiovascular disease including arrhythmias, ACS, hypertension and sudden cardiac death . Studies have shown that hypokalemia during episode of acute coronary syndrome can be associated with poor prognosis and adverse outcome as the decrease in potassium level induces vasoconstriction which leads to further ischemia producing a vicious cycle there by the importance of potassium homeostasis during ischemic attack is clarified[2] . To see the potassium dip during ischemic episodes, it is of use to observe the change in levels during an attack to those during the stable period (delta potassium) because the mean value of potassium on admission will be around 4meq/l which does not come under hypokalemia. A larger delta potassium indicates a greater decrease in serum potassium during ischemic phase in comparison with that seen during stable phase. Prognosis in patients with acute coronary syndrome depends on factors like associated failure signs, ejection fraction and raised biomarkers. Thus delta potassium (Δ K) is defined as the difference in discharge and admission serum potassium level. $\Delta K = K^+$ at discharge - K^+ on admission. There are number of factors modifying the extent of the potassium dip as indicated by Δk. Serum glucose concentration during the period of ischemia is a factor which is positively correlated with Δk whereas HbA1c level is inversely correlated[3]. The other mechanism responsible for hypokalemia in ACS is reactive increase in insulin which occurs in response to adrenergic drive secondary to increase serum glucose. It is thought that the potassium which is a intracellular cation leak outside when cardiac cells are damaged by ischemic attacks and leads to a rise in serum potassium level during period of ischemia [thereby ΔK reduction] similar to cardiac markers like creatine kinase MB, but it is observed that a higher peak CK level occurs in patients with a greater ΔK and a lower potassium ($K < 4.1$) at the time of admission. However, further analysis with myocardial infarction demonstrated that ΔK was not significantly associated with peak CK level, thus it is

concluded that delta potassium reflects the severity of ischemic stress but not the extent of myocardial injury[4] .Patients with severe ischemia has lower K level on admission and was found to have a greater delta potassium[5,6]. But the patients who have with lower potassium level during ischemic attack did not have low potassium concentration during stable period. All these indicate that patients with lower potassium are more prone to have larger potassium dip and it indicates disease severity [7,8,9]. The findings of stable blood glucose values in patients without diabetes during the early periods after the onset of chest pain, during which potassium concentrations varies rapidly, suggest that sympathetic mechanisms were more important than insulin in shifting potassium across the cell membrane [10,11].

II. Aim Of The Study

To study the prevalence of delta potassium , its distribution among various group of ACS and also to find out the correlation between delta potassium and disease severity in patients with ACS.

III. Methods And Materials

Done as observational cross sectional study with detailed history including demographic details , Physical examination, serial ECGs, 2D Echocardiography, Chest x-ray, Complete Haemogram, blood sugar, urea, Serum Creatinine, Serum potassium level at admission and at discharge, cardiac enzyme CPK-MB, Urine routine, lipid profile at our institute after obtaining informed consent**.** Potassium dip is assessed by Δk-potassium at the time of discharge – potassium at the time of admission. Severity of ACS is assessed with type of ACS STEMI,NSTEMI, or UA ,duration of hospital stay and 2D echocardiography for LV function.

1.1. Inclusion criteria: All patients above 35 years of age admitted with first episode of acute coronary syndrome.

1.2. Exclusion criteria: Previous history of CAD, Patients with CKD, Patients on potassium sparing agents .

The data of each patient is collected and analysis is done to identify the prevalence ,significance and correlation between potassium dip and severity of acute ischemic stress in patients with acute coronary syndrome. Statistical analysis is done using Statistics Products Services Solutions (SPSS 15) software. Univariate analysis is done with paired t test and Pearson product moment correlation coefficient. A chi square test is used to analyze the probability of differences in frequency distributions between the groups and p value of <0.05 is taken to be statistically significant in all calculations.

IV. Results

With a sample size of 100 ACS patients who got admitted in our ICU we could observe 19% are in the age group of 35-45 years, 33% between 45-55 and 48% are beyond 55 years of age(Table 1/Fig 1). According to gender distribution 64% are males and 36% are females(Table 2/ Fig 2). Considering the co-morbid illness, 49% are diabetic and 51% are non-diabetic(Table 3 / Fig 3). Pre –existing hypertension history is present in 52% of cases and 48% are normotensives. Considering the pattern of ACS, 65% are suffering from STEMI,18% are with NSTEMI and 17% with UA. These patients had a stay of 5 days in 31%;5-7 days in 46%; and >7 days in 23%. On assessing the left ventricular (LV) function with 2D echocardiography 17% had normal function,27% had mild LV dysfunction ,42% had moderate LV dysfunction and 14% with severe LV dysfunction. During the study period the outcome is 90%(got recovered and discharged) and the mortality is seen in 10%. When analysis is done for Δk and its correlation among ACS groups , 72% of STEMI (47/65) has delta potassium greater than 0.5 and remaining has low delta potassium, with NSTEMI 67% (12/18) has potassium dip more than 0.5 and 24%(4 /17) of the unstable angina patients have potassium dip of more than 0.5. Overall 63% has potassium dip and the p value is 0.001,a significant one as shown in Table 4 / Fig 4. From the above it is clear that delta potassium is greater in STEMI group compared to others. Of the 31 patients who stayed less than 5 days, only 19% (6/31)has delta potassium greater than 0.5 and remaining(25/31) has normal delta potassium. But 76% (35/ 46) of the population who stayed for 5 to 7 days has delta potassium greater than 0.5. In those who stayed for more than 7 days, 95%(22/23) of patients has delta potassium more than 0.5% with a significant p value of 0.001 as shown in Table 5 / Fig 5. According to echocardiography assessment of left ventricular function Only 12% (2/17) of the patients with normal LV function has delta potassium greater than 0.5.On the other hand 33% of the patients with mild LV dysfunction have delta potassium more than 0.5. Of the 42 patients with moderate LV dysfunction 93% (39/ 42) has significant delta potassium. In patients with severe LV dysfunction 93% (13/14) has significant delta potassium and the significant calculated p value is 0.001 as shown in Table 6 /Fig 6. Above parameters shows that the patient with greater left ventricular dysfunction has larger delta potassium .Considering the admission level potassium as variable 38%(8/21) of the patients with potassium less than 4 at admission have significant delta potassium and 70%(55/79) of the patients with no potassium dip (admission $k^+ > 4$) has significant delta potassium and the p value is 0.08, an insignificant observation Table 7 / Fig 7. When analysis is done for Δk and its correlation with the variables like age, gender, diabetic status they did not show significant p values **.**

Admission level serum potassium values less than or equal to 4 and values more than 4 is the cutoff for analyzing the severity of ischemic stress and its correlation with variables like diabetes, age, gender, stay duration, among various group of ACS, LV dysfunction status , hypertension and outcome which showed no significant p values.

V. Discussion

ACS, a medical emergency is an important cause of morbidity and mortality all over the world. . Risk stratification and management of patients with suspected IHD (chronic stable angina, &ACS) is usually done with clinical finding starting from atypical chest pain , exertional pain, rest pain and ongoing pain, ECG changes from negative/normal to subtle ST-T changes and or frank ST segment elevation, cardiac markers either positive or negative and finally concluded as probability of having low risk, high risk or ST elevation MI. Based on the above risk stratification the patients are either discharged , medically treated with anticoagulants, antiplatelet or thrombolysis and directed for early interventional treatment like primary PCI. In this study among 100 patients admitted with the diagnosis of acute coronary syndrome we analyzed the delta potassium ,admission level potassium with the severity of ischemic stress and also its correlation with variables. Majority of the study group(48%) were more than 55 years of age . Among various group of ACS 65% had STEMI, 18% had NSTEMI and 17% had UA. *CORRELATION BETWEEN DELTA POTASSIUM AND SEVERITY OF ISCHEMIC STRESS;* Among 65 patients with STEMI 47 had delta potassium value more than 0.5 which constitute 72%. In patients with NSTEMI 66% has significant delta potassium. But in UNSTABLE ANGINA group only 23% has delta potassium more than 0.5. This finding is consistent with the study by herlitz j, hjalmarson a et al [12].Delta potassium has also shown to be positively correlated with duration of stay in hospital as detailed ; In patient who stayed for 5 days or less- 19% has significant delta potassium, In the patient who stayed for 5 to 7 days- 76% has delta potassium more than 0.5 and In patients who stayed for more than 7 days- 96% has significant delta potassium. The relationship between delta potassium and LV dysfunction also correlated positively. In 17 patients with normal LV function only 2 has delta potassium more than 0.5. In patients with mild LV dysfunction 33% has significant delta potassium. But 92% of patients with moderate and 93% of patients with severe LV dysfunction has delta potassium more than 0.5. This is also supported by the study published by hiroshi sekiyama1, tomohisa nagoshi1 et al[5] The present study assessed and found to have significant correlation between delta potassium and severity of ischemic stress with factors like type of ACS, LV Ejection fraction and duration of hospital stay. Other variables like age, gender, diabetes, hypertension and admission potassium values did not have significant correlation with delta potassium. *CORRELATION BETWEEN POTASSIUM VALUE AT THE OF ADMISSION AND SEVERITY OF ISCHEMIC STRESS*: In patients with diabetes mellitus the initial decrease in potassium value is not seen. This may be due to autonomic dysfunction associated with diabetes mellitus. This is is supported by the study by Jarman PR, Kehley AM, Mather HM et al [13]. Among various groups of ACS ,in STEMI patients only 21% has low potassium value. In NSTEMI patients only 5% has absolute potassium value less than 4 at the time of admission. In UNSTABLE ANGINA 35% has low potassium value. This shows that there is no correlation between potassium value at the time of admission and disease severity. This may be due to difference in the time of admission which has impact on the potassium value at the time of admission. Only patients admitted earlier has low potassium value which gradually increases over time. This is supported with the study by K Foo, N Sekhri, A Deaner, C Knight, A Suliman, K Ranjadayalan, A D Timmis[3].

VI. Conclusion

The study showed that the delta potassium is positively correlating with the severity of ischemic stress in patients with ACS in the form of prolonged stay in the hospital, more prevalent among STEMI group and also associated with poor outcome in the form of moderate to severe LV dysfunction This study also promotes awareness of monitoring significant change in serum potassium values among ACS patients there by protocol management towards heart failure, arrhythmias and sudden cardiac death prevention is addressed for good quality of life.

Acknowledgement

We the authors respectfully thank the participants, their care- takers, intensive care staff nurses, technicians and the statistician for their involvement and contribution towards this scientific study.

Limitation Of The Study

This study did not analyse the time of onset of pain and admission time which may have an impact in the potassium value at the time of admission and only few studies are available to compare the results**.**

Conflict Of Interest

We the authors contributed equally towards the development and revision of this manuscript.

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Figures And Tables

Table 1 : Delta Potassium Age Wise Distribution

Age		Delta potassium ΔK [meq/l]		Total	p value
		>0.5	<0.5		
35-45	Count	12	7	19	
	% within age	63.2%	36.8%	100.0%	
	% within ΔK	19%	19%	19%	
45-55	Count	17	16	33	
	% within age	51.5%	48.5%	100.0%	
	% within ΔK	27%	43.2%	33%	0.209
>55	Count	34	14	48	
	% within age	70.8%	29.2%	100.0%	
	% within ΔK	54%	37.8%	48%	
TOTAL	Count	63	37	100	
	% within age	63.0%	37.0%	100.0%	
	% within ΔK	100%	100%	100%	

FIG 1: Delta K^+ In Various Age Group

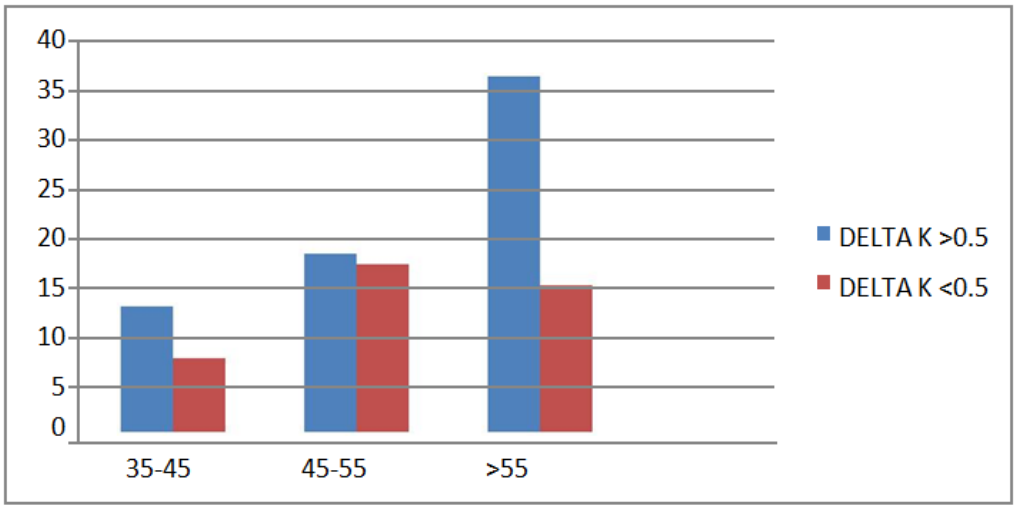

Table 2: Delta Potassium And Sex Of The Patients

Sex		Delta potassium [mEq/l]		Total	P value
		>0.5	<0.5		
Male	Count	40	24	64	
	% within Sex	62.5%	37.5%	100.0%	
	% within Potassium - Difference	63.5%	64.9%	64.0%	
Female	Count	23	13	36	
	% within Sex	63.9%	36.1%	100.0%	0.89
	% within Potassium - Difference	36.5%	35.1%	36.0%	
Total	Count	63	37	100	
	% within Sex	63.0%	37.0%	100.0%	
	% within Potassium - Difference	100.0%	100.0%	100.0%	

Fig 2: Delta K and Sex of the Patients

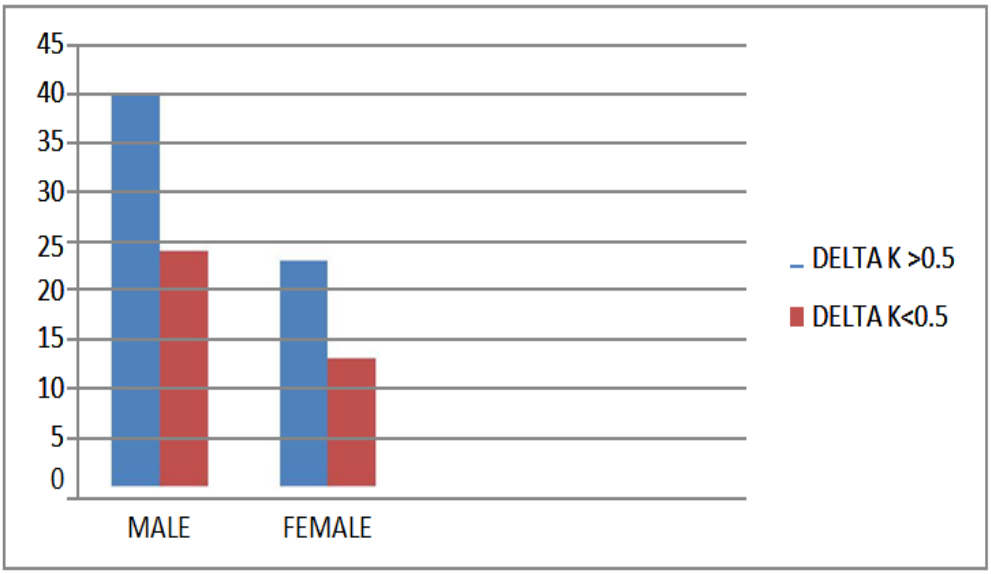

Table 3: Delta Potassium In Diabetic And Non Diabetic Group

Diabetes Mellitus		Delta potassium [meq/l]		Total	P value
		>0.5	<0.5		
Yes	Count	31	18	49	
	% within diabetes	63%	37%	100.0%	
	% within Potassium - Difference	49.2%	48.6%	49%	
No	Count	32	19	51	
	% within non diabetic	63%	37%	100.0%	0.957
	% within Potassium - Difference	50.8%	51.4%	51%	
Total	Count	63	37	100	
	% within diabetes	63.0%	37.0%	100.0%	
	% within Potassium - Difference	100.0%	100.0%	100.0%	

Fig 3: Delta K And Dm

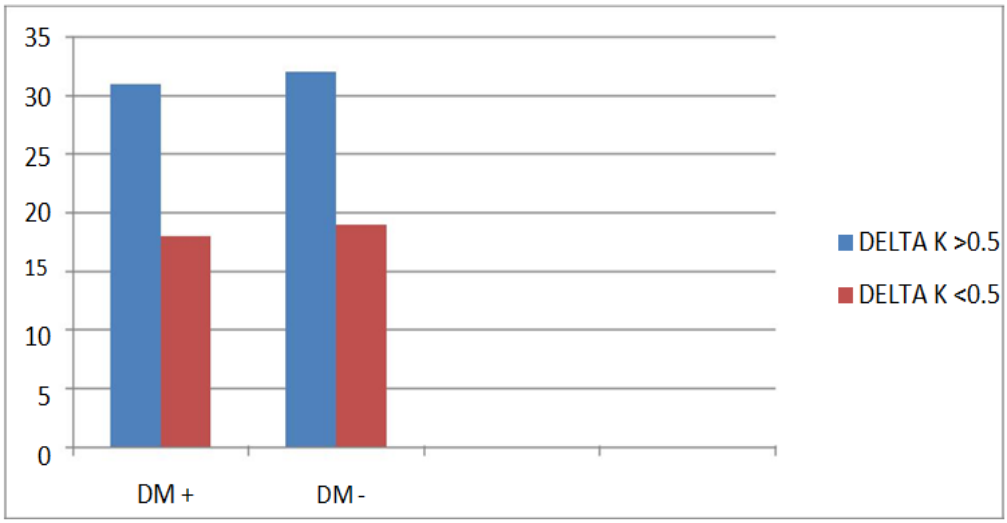

Table 4: Delta Potassium In Various Groups

Diagnosis		Delta potassium ΔK [meq/l]		Total	p value
		>0.5	<0.5		
STEMI	Count	47	18	65	0.001
	% within Diagnosis % within ΔK	72.3% 74.6%	27.7% 48.6%	100.0% 65%	
NSTEMI	Count	12	6	18	
	% within Diagnosis % within ΔK	66.7% 19.1%	33.3% 16.2%	100.0% 18%	
UA	Count	4	13	17	
	% within Diagnosis % within ΔK	23.5% 6.3%	76.5% 35%	100.0% 17%	
TOTAL	Count	63	37	100	
	% within Diagnosis % within ΔK	63.0% 100%	37.0% 100%	100.0% 100%	

Fig 4: Delta Potassium And Diagnosis

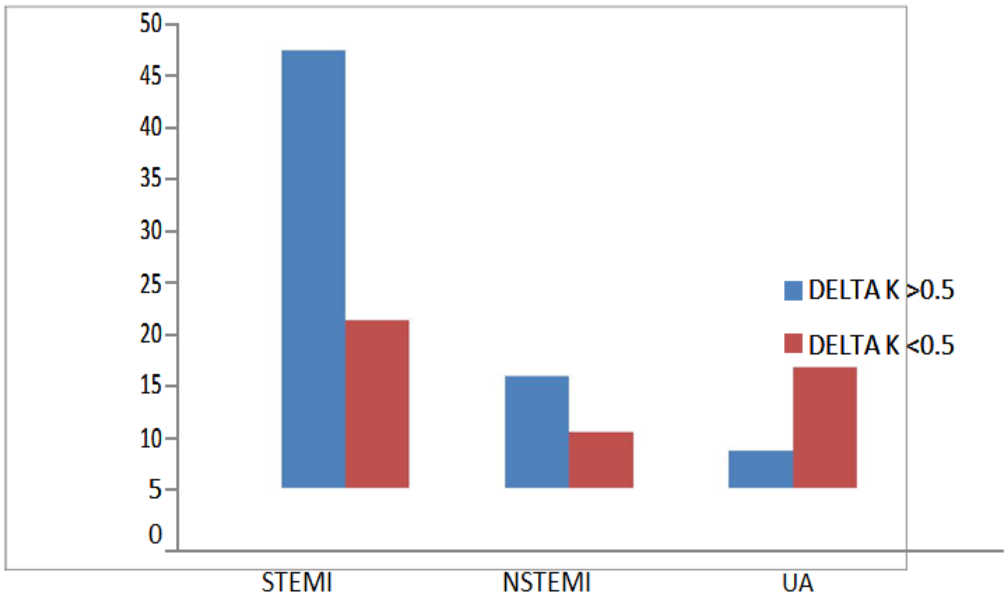

Table 5 : Delta Potassium And Duration Of Stay In Hospital

Duration of stay		Delta potassium ΔK [meq/l]		Total	p value
		>0.5	<0.5		
5 days	Count	6	25	31	0.001
	% within Duration of stay % within ΔK	19% 9.5%	81% 67.6%	100.0% 31%	
6-7 days	Count	35	11	46	
	% within Duration of stay % within ΔK	76% 55.6%	24% 29.7%	100.0% 46%	
>7days	Count	22	1	23	
	% within Duration of stay % within ΔK	95% 34.9%	5% 2.7%	100.0% 23%	
TOTAL	Count	63	37	100	
	% within Duration of stay % within ΔK	63.0% 100%	37.0% 100%	100.0% 100%	

Fig 5: Delta Potassium and Duration of Stay

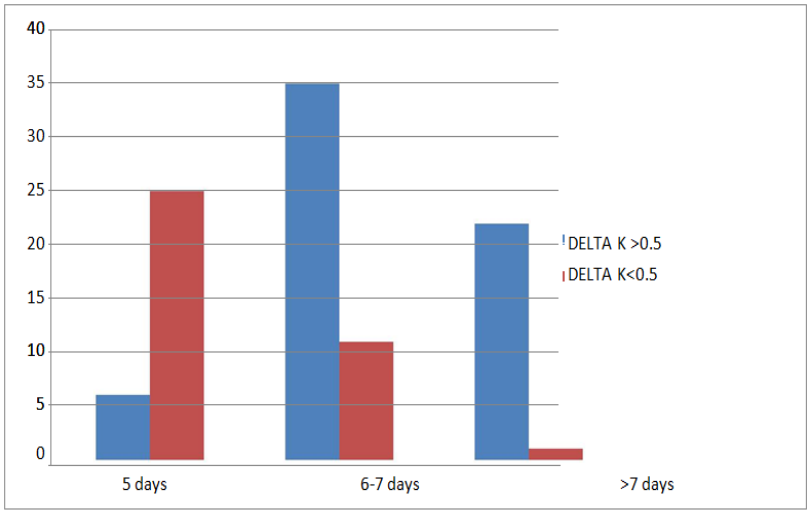

Table 6: Delta Potassium And Lv Dysfunction

LV Dysfunction			Delta potassium ΔK [meq/l]		Total	p value
			>0.5	<0.5		
A]	Normal	count %within LV function %within ΔK	2 12% 3.2%	15 88% 40.5%	17 100% 17%	0.001
B]	Mild	Count %within LV function %within ΔK	9 33% 14.3%	18 67% 48.6%	27 100% 27%	
C]	Moderate	Count %within LV function %within ΔK	39 93% 61.9%	3 7% 8.1%	42 100% 42%	
D]	Severe	Count %within LV function %within ΔK	13 93% 20.6%	1 7% 2.7%	14 100% 14%	
Total		Count %within LV function % within ΔK	63 63% 100%	37 37% 100%	100 100% 100%	

Fig 6: Delta K and LV Dysfunction

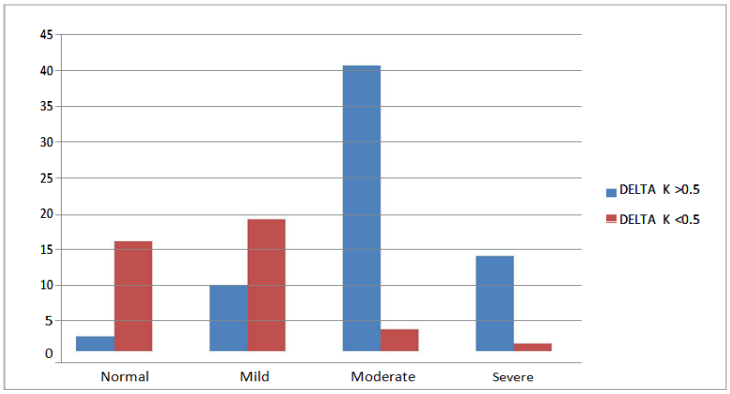

Table 7: Relationship Between Delta Potassium And Potassium At Admission

ΔPotassium – Admission K+ (mEq/L)		Delta potassium [meq/l]		Total	P value
		>0.5	<0.5		
<=4	Count	8	13	21	
	% within admission K+	38%	62%	100.0%	
	% within Potassium - Difference	12.7%	35.1%	21%	
>4	Count	55	24	79	
	% within admission K+	70%	30%	100.0%	0.08
	% within Potassium - Difference	87.3%	64.9%	79%	
Total	Count	63	37	100	
	% within admission K+	63.0%	37.0%	100.0%	
	% within Potassium - Difference	100.0%	100.0%	100.0%	

Fig 7: Delta K And K+ At Admission