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A study on the effect of biochemical parameters on the outcome and risk stratification of patients with cardiogenic shock following acute myocardial infarction in a Tertiary Care Hospital in South India

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Abstract

Introduction: *Cardiogenic shock (CS) is the most extreme complication of myocardial infarction and it is the initial presentation of at least 1 in 15 patients admitted to ICCU. Despite heroic efforts, the in-hospital mortality due to CS is still very high.*

Aims

1. *To determine the prognosis of patients admitted with cardiogenic shock as a complication of acute MI*
2. *To stratify the risk in the above patients with respect to the levels of admission day random blood glucose, thyroid hormone levels- T3,T4,TSH, Lipid profile- Total cholesterol, triglycerides, HDL,LDL, serum uric acid, blood urea and serum creatinine.*

Methodology: *We conducted a prospective, observational, descriptive, intention to treat study of patients presenting with cardiogenic shock as a result of acute MI presenting to the ICCU of Government Medical College, Coimbatore. The outcome and the multiple variables (hematological and biochemical parameters) were studied so as to stratify the risk of poor prognosis.*

Results & Discussion: *Out of the 200 cases of cardiogenic shock included in the study, 170 cases survived and 30 patients died attributing to 15%. The mean age in the death group was 53.13 years and in the survival group was 59.7 years. Most patients presented within a window period of 6-12 hrs. Admission blood pressure <40 mmhg was associated with early mortality despite use of vasopressor agents. EF <40% was associated with early death. Thrombolytic therapy didn't show to improve the outcome of cardiogenic shock. Age, smoking, past history of hypertension, window period, admission blood pressure < 60 mmHg , anterior wall STEMI were found to be statistically significant determinants of death. An RBS >200 mg/dl, urea >40 mg/dl, creatinine >2 mg/dl, TC >200 mg/dl, TG >150 mg/dl, HDL <40 mg/dl predicts MACE in acute MI patients. The admission time blood pressure, uric acid and urea were independently associated with bad outcomes in cardiogenic shock.*

Conclusion: *The prognosis of cardiogenic shock is poor despite effective early intervention methods. Early identification of risk factors can prompt prevention of MACE and hence help early treatment initiation to avoid bad prognosis in CS.*

Keywords: *Myocardial Infarction, ST elevation Myocardial Infarction, Shock, Coronary artery disease.*

Introduction

Cardiogenic shock is the most extreme complication of myocardial infarction and it is the initial presentation of at least 1 in 15 patients admitted to ICCU[1]. The clinical presentation is due to decreased myocardial contractility and pump failure which can develop early or late in the course of MI. This in turn leads to inadequate stroke volume and insufficient end organ perfusion .5-10% of patients with myocardial infarction develop cardiogenic shock and 2/3 rd among these are expected to die within 2-3 weeks[2]. Cardiogenic shock (CS) is the syndrome of primary cardiac dysfunction causing hypoperfusion of the organs and tissues leading to progressive multi-organ failure. CS contributes to be a major cause of circulatory shock only next to sepsis owing to 16% of admissions to intensive care[1]. Cardiogenic shock is thus characterized by a low systolic blood pressure in combination with poor end organ perfusion like cold clammy extremities, decreased urine output and acidosis.

Risk factors in the context of MI include older age, anterior wall MI, systemic hypertension, Diabetes mellitus, multivessel CAD, prior MI or prior angina, prior diagnosis of heart failure, STEMI and left bundle branch block[3].

Even in the era of prompt revascularization as therapy of choice, for patients with delayed cardiogenic shock as well as for patients with cardiogenic shock on admission, the in-hospital mortality is still approximately 50% [3].

Importance of the Study

The risk stratification and prognostication of acute MI have been successfully assessed using TIMI score and GRACE score for a long time. Early identification and subsequent revascularization has indeed reduced the incidence of death due to cardiogenic shock to a great extent, still the number of patients presenting with cardiogenic shock remains stable. This study aims to find out the prognosis of cardiogenic shock from the day of admission to ICU in our hospital with reference to the following biochemical variables- random blood glucose, blood urea , serum creatinine, serum T3,T4,TSH, serum uric acid and lipid profile and to stratify the risk in these patients with respect to these variables.

Objectives

1. To determine the prognosis of patients admitted with cardiogenic shock as a complication of acute MI
2. To stratify the risk in the above patients with respect to the levels of admission day random blood glucose, thyroid hormone levels- T3,T4,TSH, Lipid profile- Total cholesterol, triglycerides, HDL,LDL, serum uric acid, blood urea and serum creatinine.

Methodology

We conducted a prospective, observational, descriptive, intention to treat study of patients presenting with cardiogenic shock as a result of acute MI who got admitted to the ICCU of Government Medical College, Coimbatore Tamil Nadu. 200 patients of cardiogenic shock who are admitted to the ICCU with evidence of a recent (within 24hrs) MI and who have not received any sort of treatment elsewhere and who have not received mechanical ventilation from outside hospital were included. The period of the study was one year (july2016-june 2017). Consent of the patient was taken.

All patients in the study underwent the following: Detailed history of presenting symptoms- chest pain, duration of the index pain; Clinical examination- pulse rate, blood pressure, peripheral pulses, JVP, pedal edema, urine output.; Clinical system examination- cvs, respiratory system , git and cns; Details of past history of diabetes, hypertension, kidney disease, bleeding disorders. 12 lead echocardiogram was used to diagnose acute myocardial infarction.

Following Biochemical Parameters were assessed-

1. Random blood glucose at the time of admission to ICU from the capillary blood Blood

2. Urea and Serum createinine levels from venous blood by Jaffe's method.
3. Thyroid hormone levels- T3,T4 and TSH
4. Fasting Lipid Profile- Total cholesterol, Triglycerides, HDL, LDL
5. Serum Uric acid from venous blood.

End point of each case was death or complete recovery. Patients already diagnosed as case of cardiogenic shock and treated with mechanical ventilator support outside, Patients who had cardiac arrest prior to arrival in casualty, Patients who had renal failure prior to onset of the current episode of acute myocardial infarction,Patients with shock due to other systemic causes, Patients in whom blood samples could not be taken before giving medications & Patients who were already on statin therapy were excluded from the study.

Data Management and Analysis

Data was entered into Microsoft Excel. Statistical Analysis was done using software SPSS-version 21. Numerical values were reported using mean and standard deviation or median. Categorical values are reported using number and percentages. Probability value (p) value less than 0.05 was considered a statistically significant

Results

Out of the 200 cases of cardiogenic shock included in the study, 170 cases survived and 30 patients died attributing to 15%.

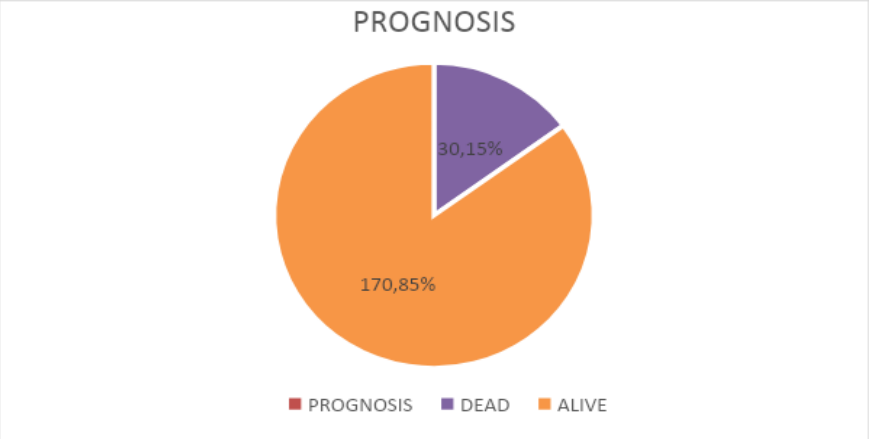

Fig 1- Pie chart showing prognosis of cardiogenic shock

Majority of the cases were males in the age group of 51-70 years. The mean age in the death group was 53.13 years and in the survival group was 59.7years.

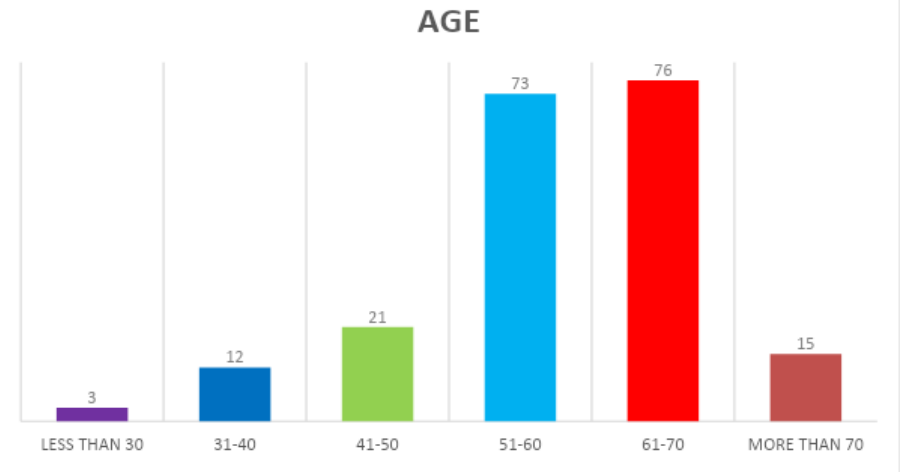

Fig 2 - Histogram showing age distribution in the study population

Smoking and alcoholism were much prevalent in the study population- 123/200. The incidence of smoking was greater in the death group than the survival group. Prevalence of alcoholism showed a similar trend owing to 61% and 28% respectively. A total of 78 patients (39%) were hypertensives, of which 19 patients were from the death group and rest from the survival group. A family history of CAD was present in 16.5 % of patients.Most of the patients presented in the window period of 6-12 hr- 59%, followed by >12 hrs by 26.5% patients and <6hrs by 14.5%.Cases were divided into STEMI , NSTEMI and others based on the ECG findings. Anterior wall STEMI dominated the group by 50.5%, followed by posterior/inferior wall STEMI 35% and NSTEMI contributed to 14.5%. STEMI contributed to the majority of deaths, in which anterior wall infarction was the commonest. Among the STEMI group, Anterior wall infarction contributed to 23/ 30 patients of the dead group and posterior/inferior wall infarction in 5 /30 patients.At presentation, 66.5% of patients had systolic blood pressure between 60-90 mmhg. 22% between 40-60 mmhg and 11.5 % <40 mmhg. Majority of the patients in the death group had systolic bp <60 mmhg.

Admission time heart rate was assessed in all patients. Mean heart rate in the death group was 122.96 and in the survival group was 124.38. Among the STEMI patients, 55.5% underwent lytic therapy, 20 out of the 30 patients in the death group underwent lytic therapy. Vasopressors were used in 96% of the total study group including all the patients in the death group. Ejection fraction was also analyzed by echocardiogram. 30% of the dead patients (10/30) had an EF <30%, 20% had EF between 30-45% and the rest had EF between 45-50%.

Univariate regression analysis showed that gender, alcoholism, family history of CAD ,past history of hypertension, admission heart rate rate and use of vasopressor agent was not statistically significant.

However age (p value- 0.001), smoking(p value- 0.0014), window period (p value - 0.001), admission blood pressure < 60 mmHg (p value- 0.001) , anterior wall STEMI (p value- 0.022) were found to be statistically significant determinants of death in Cardiogenic shock.

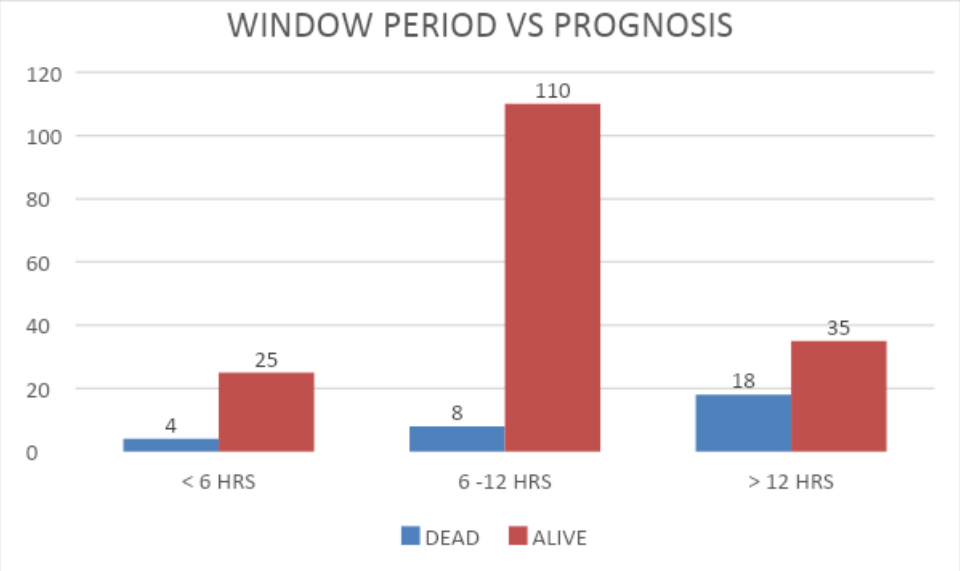

Fig 3- Histogram showing outcome in different window period

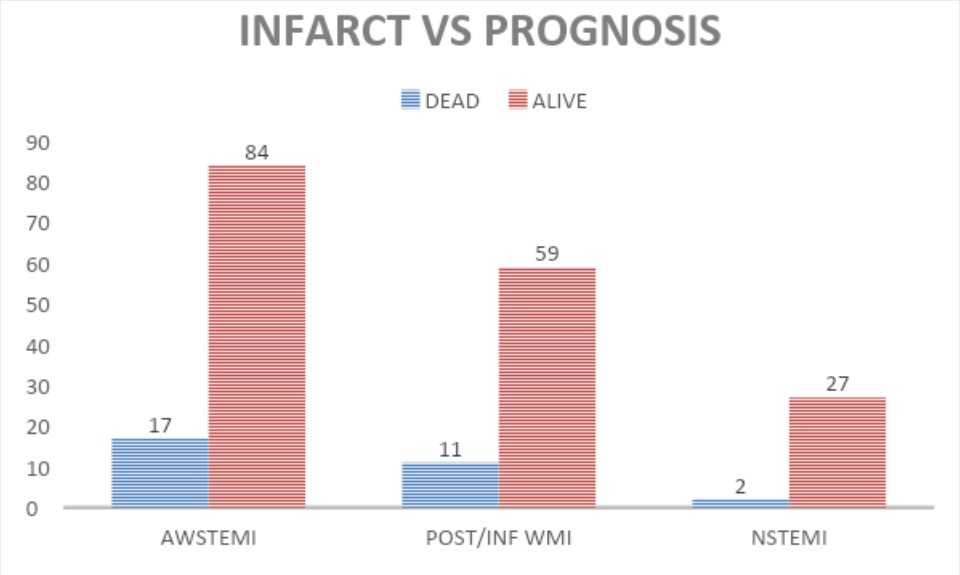

Fig 4-Histogram showing outcome in different MI

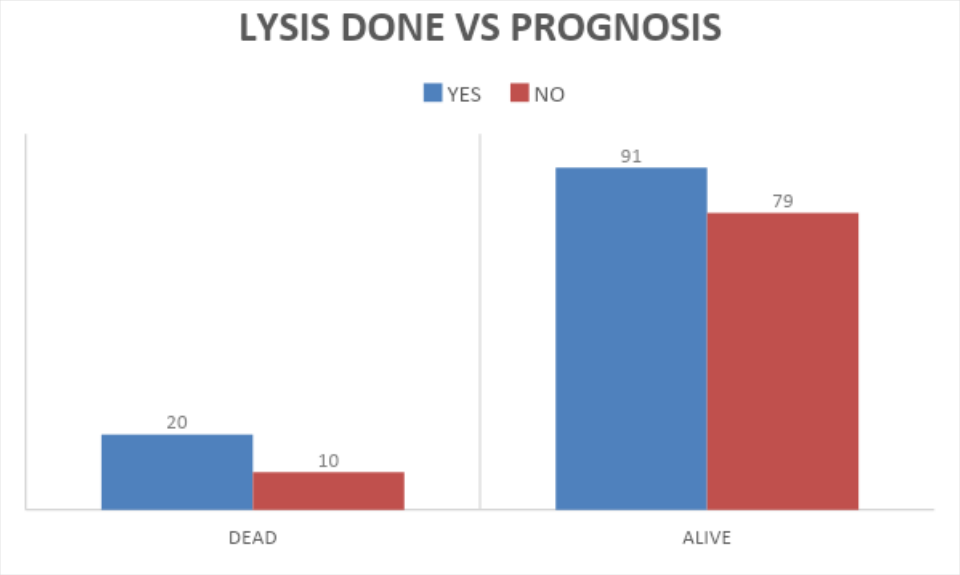

Fig 5- Histogram showing Prognosis in Lysis underwent patients

The following biochemical variables were then analyzed

1. Random blood sugar- patients were divided into 3 groups - <140 mg/dl, 140-200 mg/dl and >200 mg/dl. 56.5% of patients had hyperglycemia. The mean RBS in the death group was 208.46 and in the survival group was 154.05. The incidence of hyperglycemia was higher in the death group. Hyperglycemia had a negative association with survival and MACE with a significant p value of 0.001.f

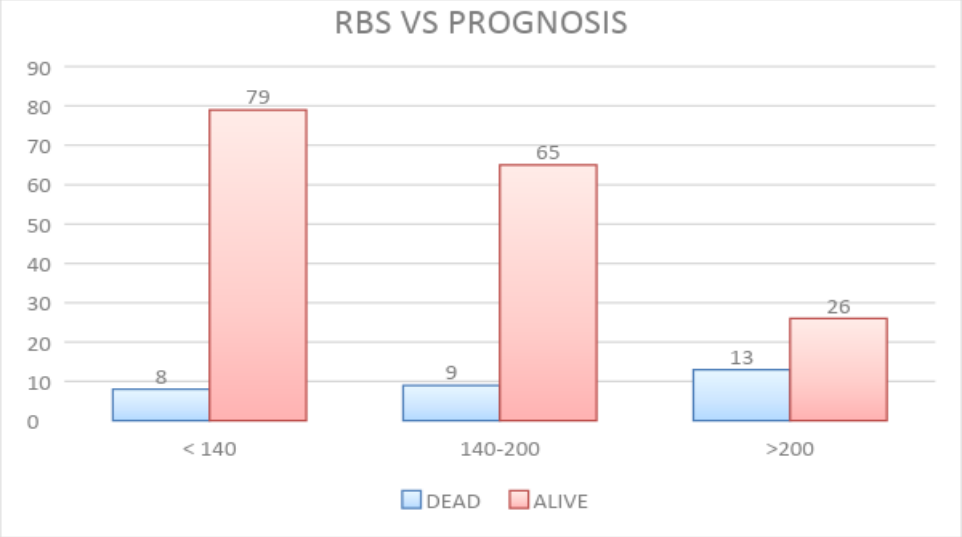

Fig 6- Histogram showing Distribution of RBS in study population

2. Serum uric acid - the mean uric acid level in the death group was 6 mg/ dl and in the survival group was 5.33. Serum uric acid was found to have a positive correlation with prognosis with a significant p value of 0.017.

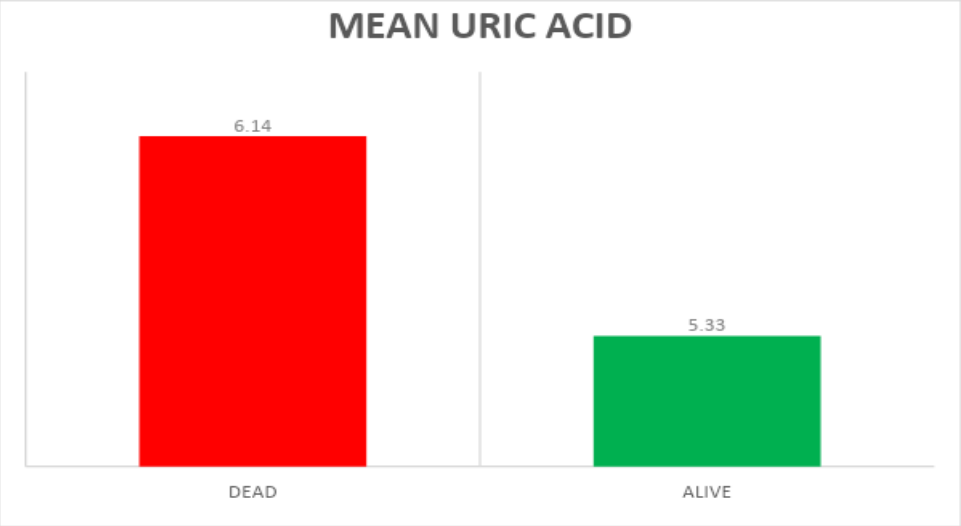

Fig 7- Mean uric acid in study population

3. Blood urea- the mean blood urea level in the death group was 40.26mg/dl and in the survival group was 28.67. 12/30 patients in the death group had urea more than 40 mg/dl and the mortality was considerably high in this group with a significant p value of 0.001

Table 1- Distribution of Blood Urea in study population

BLOOD UREA		
	MEAN	STANDARD DEVIATION
DEAD	40.26	4.31
ALIVE	28.67	6.16
P VALUE = 0.001		
SIGNIFICANT		

4. Serum creatinine- the mean creatinine value in the death group was 1.65 and in the survival group was 1.19 with a standard deviation of 0.48 and 0.4 respectively. Creatine >2 was observed in 2/30 patients in the death group. On analysis a serum creatinine level more than 2 was significantly associated with mortality with a p value of 0.001.

Table 2 - Distribution of Serum Creatinine in study population

SERUM CREATININE		
	MEAN	STANDARD DEVIATION
DEAD	1.65	0.48
ALIVE	1.19	0.4
P VALUE = 0.001		
SIGNIFICANT		

5. T3 level- the mean T3 levels were almost the same in both the survival and death group . About 22/200 patients had a low T3 level accounting to about 11% . This difference was not found to be statistically significant with respect to the prognosis(p value- 0.875)

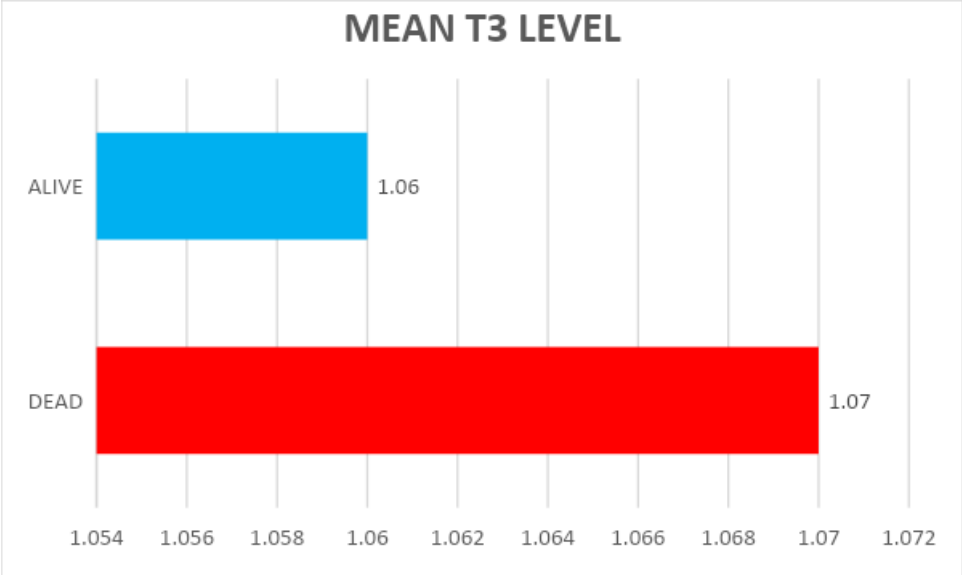

Fig 8- Distribution of T3 levels in study population

6. T4 level- the mean T4 levels wre 8.71 and 8.85 with standard deviation of 1.58 and 1.74 in the alive and the death group respectively. There was not much difference between the two groups. P value was 0.685 (not significant) when analyzing the T4 value with the prognosis.

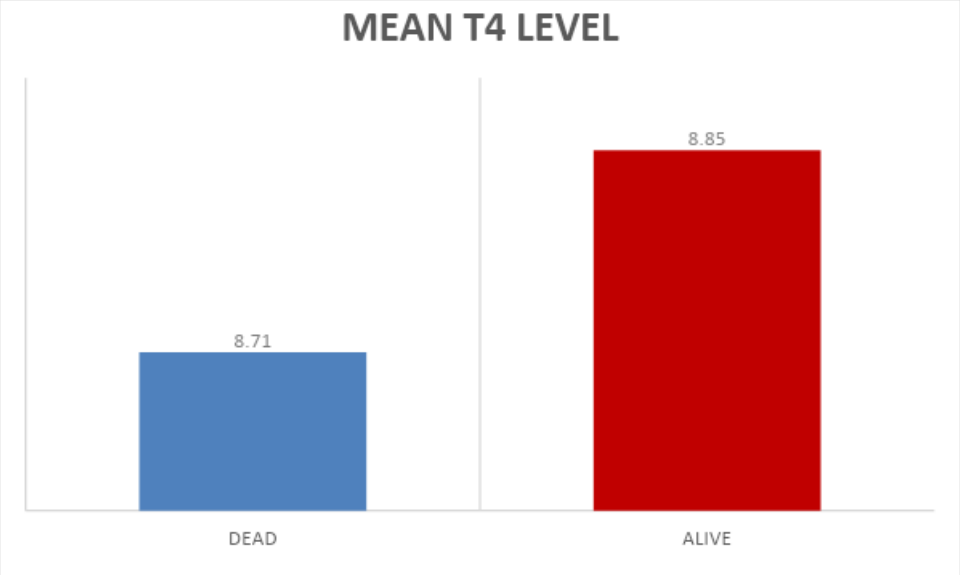

Fig 9- Distribution of T4 levels in the study population

7. TSH level- the mean TSH values were 2.32 and 2.19 with standard deviation of 0.68 and 0.7 in the alive and the death group respectively. The p value was found to be non significant when analyzing the effect of TSH level on the prognosis(0.349)

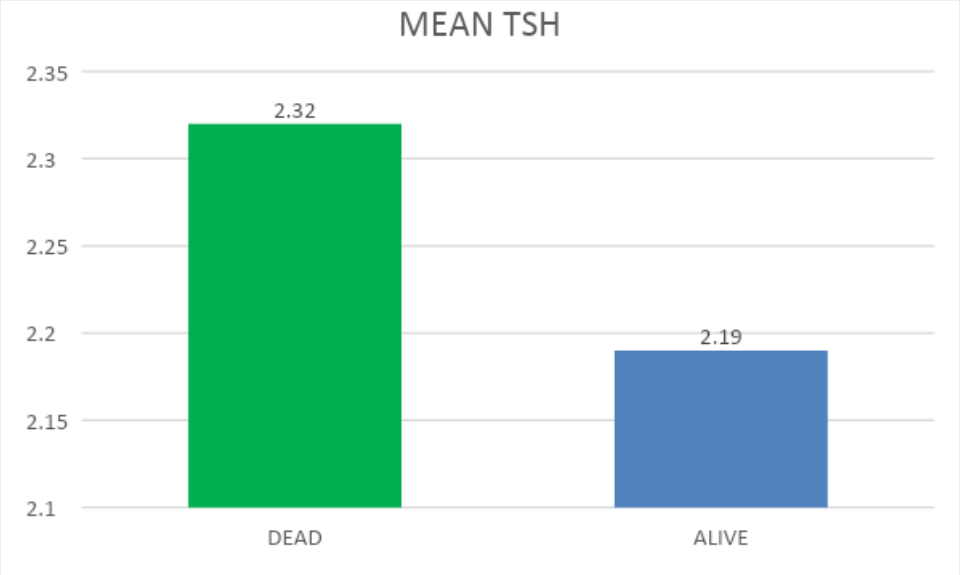

Fig 10- Distribution of TSH levels in the study population

8. Total Cholesterol- the mean values were 171.1 and 171.14 mg/dl with standard deviation of 16.01 and 14.7 respectively in the alive and death group. This shows that there was no significant difference in the two groups. 2/30 patients in the death group and 13/ 170 patients in the alive group had a TC value of >200. The p value was found to be non-significant (0.989).

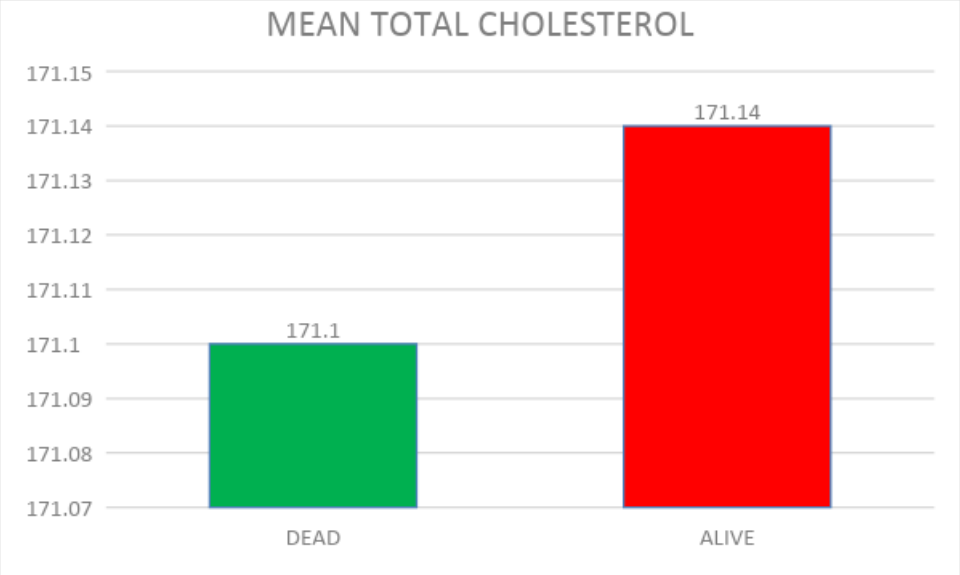

Fig 11- Distribution of Total cholesterol levels in the study population

9. Triglycerides- there was significant difference in the mean values in the alive group and death group- 186.23 and 222.56 with standard deviation of 16.69 and 21.16 respectively. All the patients in the death group had TG value >150 mg/dl. The p value(0.001) was found to be statistically significant.

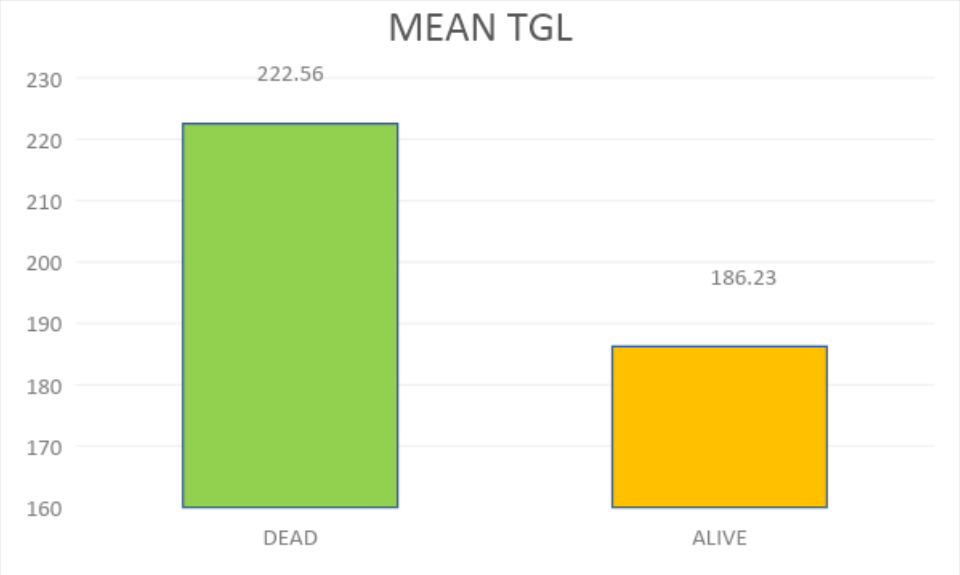

Fig 12- Distribution of Mean Triglyceride levels in the study population

10. HDL cholesterol- the mean values were not much different in the two groups 41.26 and 42.44. 17/30 patients in the death group and 62/170 patients in the survival group had a HDL value <40 mg/dl . The p value was found to be non-significant(0.037).

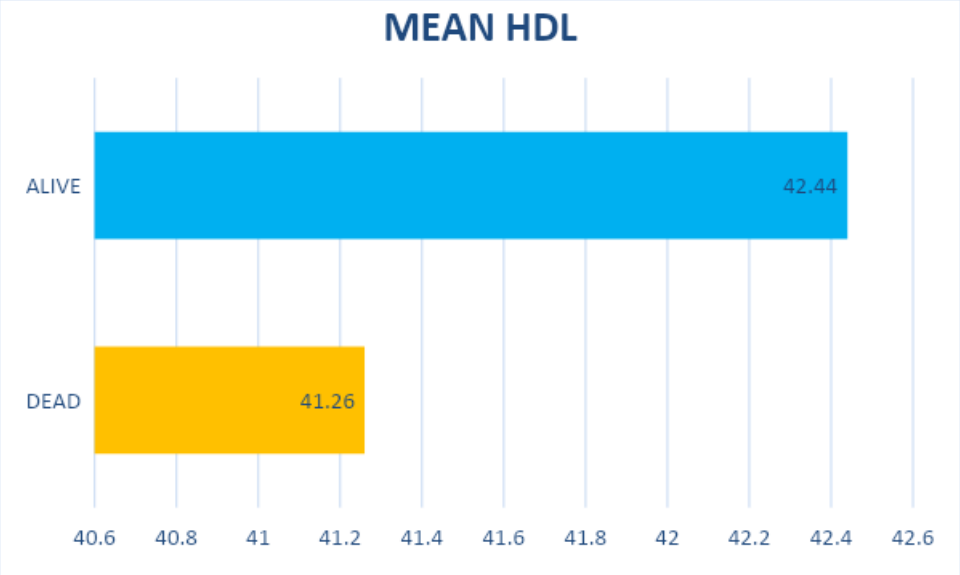

Fig 13- Distribution of HDL levels in the study population

Discussion

The prognosis of cardiogenic shock is poor despite early effective intervention methods. From the 200 cases who underwent the study, 170 patients survived and 30 patients had died. The mortality rate was 15%. 69 % were males and 31% were females. Neither of the sex had an adverse effect on the prognosis. Most of them fell into the age group of 61-70yrs closely followed by the 51-60 age groups. The extremes of age group constituted only a small percentage. Increasing age denoted a worse prognosis.

The percentage of smokers and alcoholics were higher in the death group. A family history of CAD was present in 16.5 % of patients and this didn't affect the prognosis in any way.

Most of the patients in the survival group presented in the window period of 6-12 hrs and death group >12 hrs, this indicated that the delay in getting the medical care / in hospital management increased the death in cardiogenic patients. STEMI patients constituted the major bulk in the dead group with anterior wall MI contributing to the majority of deaths. A low blood pressure of <40 mmhg and an initial heart rate of >120/min was a bad prognostic factor despite the use of vasopressor agents in our study. Similarly a depressed ejection fraction of <30 % was associated with more mortality. The use of thrombolytic therapy was not found to reduce the mortality rate in cardiogenic shock patients in our study. This might be attributed to the low sample size or the advantage of primary PCI over lytic therapy.

Results from the SHOCK trial showed that systemic hypotension, age >/= 75 years, baseline serum creatinine >1.9 mmol/l and past history of hypertension had significant impact on outcome of cardiogenic shock and our results are consistent with these results.

Among the various biochemical variables studied, hyperglycemia was observed in 56.5%. A random blood sugar level >200 mg/dl was found to adversely affect the outcome and related to MACE. In critically ill patients, mean blood glucose correlated with mortality only in the nondiabetic cohort and not in the diabetic cohort [5.] This suggests that hyperglycemia has more deleterious effects on short-term mortality of non diabetic patients. This may be because the already known diabetic patients are likely to be on insulin or oral hypoglycemic agents which decreases the severity of stress hyperglycemia.[6]. It is also proposed that diabetic patients may develop, with time, a resistance to hyperglycemia making them capable of tolerating a wide range of hyperglycemia without developing any toxic effects[7.]

The most widespread tools available are the GRACE risk score and the TIMI risk score. [8,9.]. The addition of admission BG level to existing models can help in better risk stratification. Iwakuar et al found that a blood sugar ≥8.9 mmol/L was found to be an independent prognostic factor [10].Ishihara et al. found a similar correlation with a blood sugar level > 11.1 mmol/L.. In a study conducted by Tada et al. a blood glucose level of 9.2 mmol/L was put forth as one of the strongest indicators of prognosis and death. In a study by Yang et al. [10] it was confirmed that STEMI Cardiogenic shock with an elevated BG level was definitely associated with an absolute risk of 30-day mortality.

Serum uric acid was elevated in 30% of patients and a value > 6 mg/dl was associated with adverse outcome in MI. Data from First National Health & Nutrition Examination Study (NHANES) suggest that an increase of blood uric acid level by 1 mg/dl increases the risk of CAD by 48% in women.[13] . They have a 3.7 fold increased mortality rate than the general population. Although the Framingham Heart Study failed to establish such a relationship, recent studies show the opposite fact. The admission time serum uric acid levels are correlated with MAC in ACS patients . Male gender, serum creatinine, BMI and hypertension correlates with uric acid levels. Studies in Beijing that involved 502 STEMI patients stated that those with hyperuricemia tend to experience MACE more frequently (consisting of HF and cardiogenic shock) during hospitalization.

Elevated blood urea was observed in 40% of the patients. A value >40 mg/dl was associated with a bad outcome . Serum creatinine was significantly found to be elevated in the dead group and a value more than 2 mg/dl was negatively associated with outcome. In the GRACE registry, an increase of 1 mg/dL from the baseline creatinine was associated with a 1.2-fold increase in risk for hospital death..In another GRACE registry publication, using the National and Kidney Foundation recommendations, patients with severely depressed baseline CrCl has a very poor prognosis[4]. Patients with baseline CrCl between 30-60 mL/min, CrCl < 30 mL/min have two fold and four fold mortality than CrCl >60 mL/min. [12]

Lipid profile analysis showed elevated triglycerides, elevated total cholesterol and reduced HDL in the majority of the patients. Among these, a TC level > 200 mg/dl, TG >150 mg/dl and HDL <40 mg/dl were found to be associated with adverse outcome in cardiogenic shock. Study done by Yokokawa et al. demonstrated elevated total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C) and reduced high density lipoprotein cholesterol (HDL-C). Early treatment of dyslipidemia definitely reduces the morbidity and MACE in myocardial infarction. However, the change in lipid & lipoprotein levels due to tissue necrosis change during acute myocardial infarction which contributes to the delay in treatment. (Balci, 2011).[14]

Sick euthyroid syndrome ie. A low T3, normal TSH and normal T4 levels were observed in 14.6% of the patients, with almost same prevalence in both the survival and death group.This is in line with the study by Pimentel et al, who found an association of abnormal thyroid hormones alterations with worse prognosis. Two further larger studies involving consecutive STEMI patients undergoing PCI also have related the low T3 syndrome to increased mortality. [15] Available data suggest that thyroid hormone replacement therapy aiming to reverse the abnormal thyroid state occurring during AMI may improve hemodynamics, ventricular function, and cardiac remodeling.[16]

Following regression analysis, a low blood pressure <90 mmhg, a serum uric acid level >8 mg/dl, urea level>40 mg/dl were found independently to be statistically significant in determining the outcome of cardiogenic shock.

Conclusions

The prognosis of cardiogenic shock is poor despite effective early intervention methods. The

in-hospital mortality ranges from 50-70% in cardiogenic shock following acute myocardial infarction. Age is a significant risk factor- increasing age- indicates a bad prognosis. Smokers have a bad prognosis. Most patients present within a window period of 6-12 hrs and this has a significant impact on the outcome. Admission blood pressure <40 mmhg was associated with early mortality despite use of vasopressor agents. Majority of anterior wall STEMI have a bad prognosis. EF <40% was associated with early death. Thrombolytic therapy didn't show to improve the outcome of cardiogenic shock, this points to the fact that primary PCI is the best treatment for MI presenting with cardiogenic shock when compared with early thrombolysis. An RBS >200 mg/dl, urea >40 mg/dl, creatinine >2 mg/dl, TOtal cholesterol >200 mg/dl, Triglycerides >150 mg/dl, HDL <40 mg/dl predicts MACE in acute MI patients. Among these, the admission time blood pressure, uric acid and urea were independently associated with bad outcomes in cardiogenic shock.

Limitations of the Study

Our study had few limitations. Cardiac enzymes were not done in the study. Infarct type was decided with the ECG changes and angiogram study was not done. Echocardiography was done in the recovering stages of the shock, hence accurate assessment of ejection fraction could not be made. Long term mortality could not be assessed.

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