Original Research Article

# A study on coagulation profile of patients thrombolysed with streptokinase in acute st-elevation myocardial infarction

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**Received: 08-07-2020 / Revised: 07-09-2020 / Accepted: 20-09-2020**

## Abstract

**Introduction**: a study on coagulation profile of patients thrombolysed with streptokinase in acute st-elevation myocardial infarction.aims and objectives of study1.To find the changes in the coagulation system after thrombolysis with streptokinase in st elevation myocardial infarction. 2.To postulate about the timing of starting heparinisation after thrombolysis with streptokinase in st elevation myocardial infarction. **Materials and methods**-is a cross sectional observational study of patients admitted with acute st elevation myocardial infarction(stemi) who were candidates for thrombolysis. Coagulation assay protocol-Whole blood is collected at baseline and at intervals of 3, 6, & 9hrs following initiation of thrombolysis. **Results and conclusion**: Early heparinisation may be considered in those patients who have non resolving st segment 90 minutes after thrombolysis , or those patients who have continuing pain even after thrombolysis..A significant correlation was found between aptt at 6hours and aptt at 9 hours that is patients who were in the therapeutic range at the end of 6 hours were also maintained at the end of 9 hours probably due to heparinisation at the end of 6 hours after thrombolysis.3.There is suboptimal anticoagulation in MI.

**Keywords:** coagulation,myocardial,CAD,factors,burden.



## Introduction

Global Burden of Diseases (GBD) study reported the estimated mortality from CAD(coronary artery disease) in India at 1.6 million in the year 20001. It has been predicted that by 2020 there would be 11% increase in CV deaths in India[1-4].According to data from Registrar General of India Coronary heart disease (CHD) mortality is greater in south India while stroke is more common in the eastern Indian states. CHD prevalence is higher in urban Indian populations while stroke mortality is similar in urban and rural regions.WHO(World Health Organization) has predicted that from years 2000 to 2020 disability-adjusted life years lost (DALYs) from CHD in India [6-8].

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shall double in both men and women from 7.7 and 5.5 million.The mortality is highest in south Indian states, eastern and north-eastern states and Punjab in both men and women, while mortality is the lowest in the central Indian states of Rajasthan, Uttar Pradesh and Bihar[9-12].Several risk factors have been associated with CAD .A risk factor is a feature of an individual or population that is present early in life and is associated with an increased risk of developing future disease. Apart from multiple conventional risk factors other factors such as abnormalities of inflammation, hemostasis, and/or thrombosis appear to contribute decisively Smoking is a major risk factor for CAD[13]There are significant state and regional level variations. Smoking was highest in eastern Indian states and lowest in Punjab.The major conventional risk factors include hypertension, diabetes, smoking, hyperlipidemia and obesity. The non conventional risk factors include hsCRP, lipoprotein (a),homocysteine, fibrinogen, D-dimer, tissue plasminogen activator (t- PA) and plasminogen activator inhibitor (PAI- 1).Hypertension, diabetes and

metabolic syndrome were significantly more common risk factors in females whereas males were more likely to be smokers. The prevalence of smoking and tobacco chewing was significantly higher in patients presenting with premature CAD than in elderly patients with CAD . STEMI was more common than UA(Unstable Angina)/NSTEMI(Non ST Elevation Myocardial Infarction) in smokers than non smokers[14]. Both the incidence and prevalence of CAD are increased in patients who are affected with periodontal disease. Association of premature CAD is seen with dyslipidemia, family history of CAD, smoking and tobacco chewing.The higher prevalence of cardiovascular risk factors in urban areas in India is in contrast to high income countries where the CVD risk factors are equal in urban and rural areas. There is recent evidence that, in more developed states of India, the rural-urban differences in cardio metabolic risk factors have largely disappeared and the risk factors are equal or slightly greater in rural subjects. In the last 30 years, the prevalence of hypertension and hypercholesterolemia has doubled in India while that of diabetes has trebled.

**Aims and objectives of study**

1.To find the changes in the coagulation system after thrombolysis with streptokinase in st elevation myocardial infarction.

2.To postulate about the timing of starting heparinisation after thrombolysis with streptokinase in st elevation myocardial infarction[15-18].

## Materials and methods

**Setting:**The study was conducted in medicine department of KAPV govt medical college Trichy.The total duration of study was 1 year.

**Design:**Is a Cross sectional observational study of patients admitted with Acute ST Elevation Myocardial Infarction(STEMI) who were candidates for thrombolysis. Coagulation assay protocol

Whole blood is collected at baseline and at intervals of 3, 6, & 9hrs following initiation of thrombolysis[19-21].

**Obtaining the sample:**Whole blood is collected into citrated anticoagulant tube containing a fixed amount of citrate as anticoagulant in ratio of one part citrate solution to nine parts of whole blood. Sample is sent to laboratory immediately.Patient is heparinized at 6 hours irrespective of the results of PT (prothrombin time)/APTT(activated partial thromboplastin time) with UFH(unfractionated heparin) with a loading dose of 5000IU followed by 5000 units q6th hourly for 5 days[22-28].

**Method of collection of data**

A written informed consent was taken for participation after explaining the purpose and design of the study to each subject. The patient prior to consent was informed that refusal to participate in the study would not lead to any detrimental consequences or affect the treatment there of. A detailed medical history, physical examination and ECG was recorded at the time of arrival of the patient and 90 minutes after thrombolysis[29-31].

**Inclusion criteria**

All patients presenting with acute st segment elevation myocardial infarction presenting within the window period[32-34].

**Exclusion criteria**

1.Those patients with contraindications for thrombolysis.

2.Those on anticoagulants.

3.Those thrombolysed earlier.

**Statistical analysis**

The collected data was summarized in terms of tables, diagrams and charts. Statistical analysis was done using Epi-Info software, version 7.1.2.0. Continuous variables were presented as mean values with Standard Deviation. Categorical variables were compared using Chi square test. A probability value of $< 0.05$ was considered statistically significant.

**Tools used**

1.Clinical proforma

2.ECG

3.Measurement of PT/APTT [35-38]

**Results**

486 patients were thrombolysed during the time period July 2016 to June 2017. Analysis could be done on 54 patients based on our inclusion criteria.Mean age ranges between 39 to 87 with mean age 63.69 and standard deviation 11.86.

**Table 1: Age wise Classification**

| Age group | Frequency | Percent |
|---|---|---|
| ≤ 50 | 13 | 24.1 |
| 51-60 | 4 | 7.4 |
| 61-70 | 19 | 35.2 |
| 71-80 | 17 | 31.5 |
| Above 80 | 1 | 1.9 |
| Total | 54 | 100.0 |

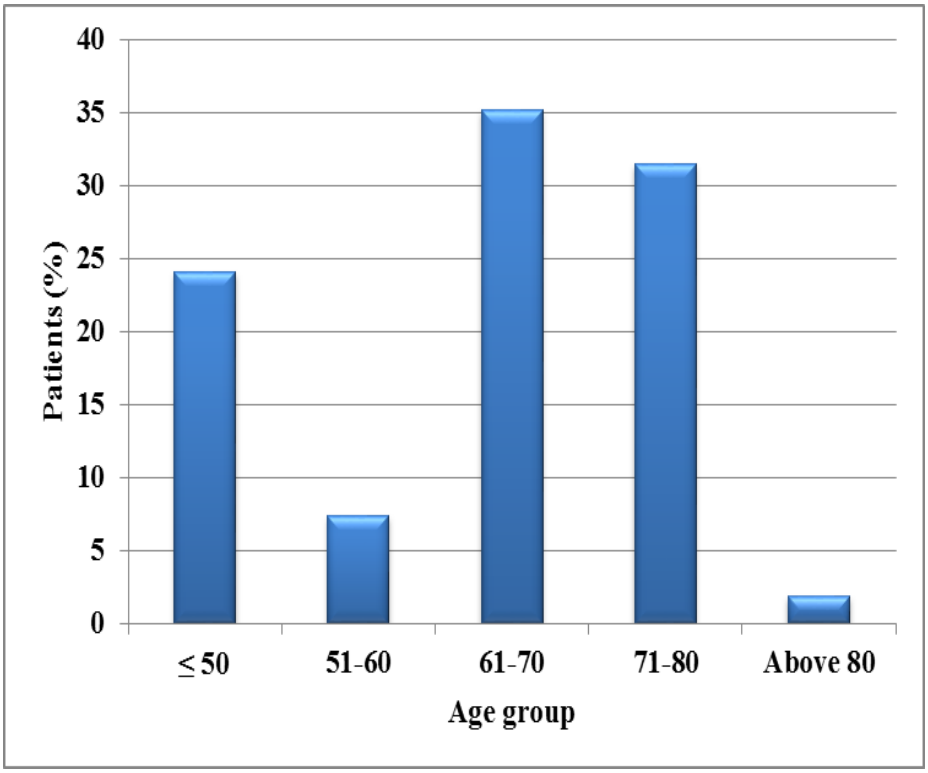



**Fig 1:Age wise classification**

**Table 2:Gender wise Classification**

| Gender | Frequency | Percent |
|---|---|---|
| Female | 19 | 35.2 |
| Male | 35 | 64.8 |
| Total | 54 | 100.0 |

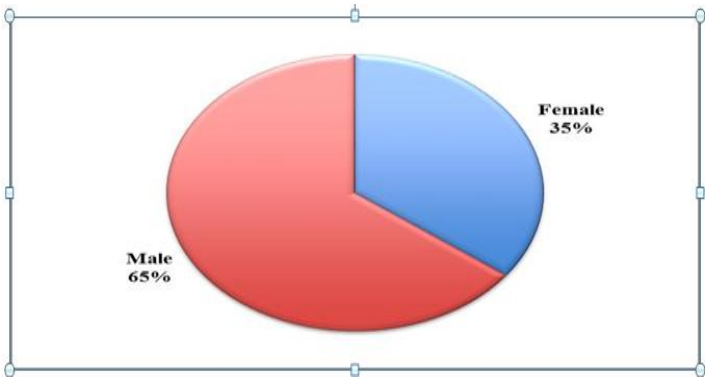



**Fig 2:Gender wise classification**

**Table 3:Classification based on myocardial wall involvement**

| ECG | Frequency | Percent |
|---|---|---|
| AWMI | 16 | 29.63% |
| IWMI | 28 | 51.85% |
| AIWMI | 3 | 5.56% |
| LWMI | 3 | 5.56% |
| PIWMI | 2 | 3.70% |
| ALWMI | 2 | 3.70% |
| **TOTAL** | **54** | **100.00%** |

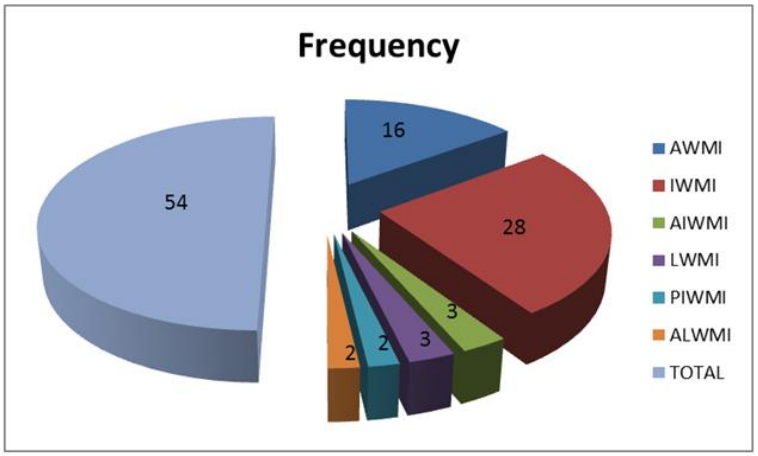



**Fig 3:Myocardial wall involvement**

The time of thrombolysis after onset of pain was as follows. 33 patients (61.11%) presented within 6 hours of symptom onset. 16 patients within 6 - 12 hours of symptom onset. And 5 patients presented after 12 hours of symptom onset.

**Table 4:Classification based symptom onset to thrombolysis time**

| Index pain to thrombolysis interval | Frequency | Percent |
|---|---|---|
| < 6hours | 33 | 61.11% |
| 6 - 12 hours | 16 | 29.63% |
| > 12 hours | 5 | 9.26% |
| **TOTAL** | **54** | **100.00%** |

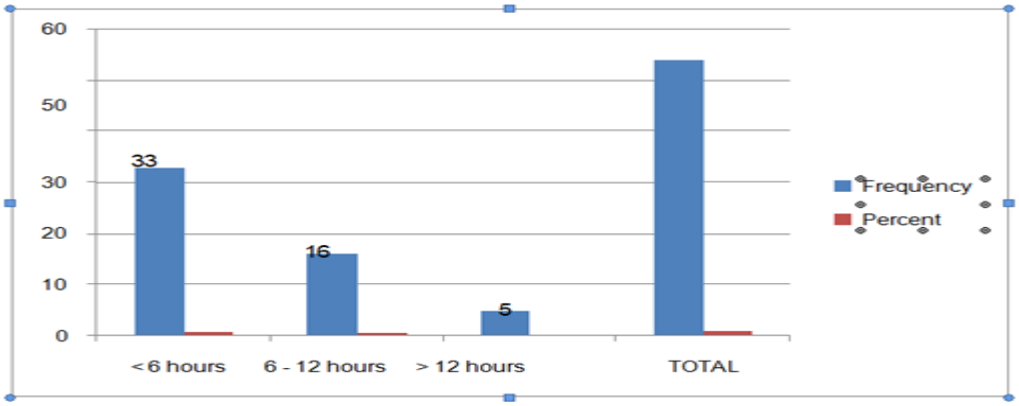



**Fig 4: symptom onset to thrombolysis time**

Out of 54 patients thrombolysed, 42 patients(77.78%) had successful thrombolysis and 12 patients(22.22%) had failed thrombolysis.

**Table 5:Classification based on Thrombolysis outcome**

| Thrombolysis result | Frequency | Percent |
|---|---|---|
| Successful | 42 | 77.78% |
| Failed | 12 | 22.22% |
| **TOTAL** | **54** | **100.00%** |

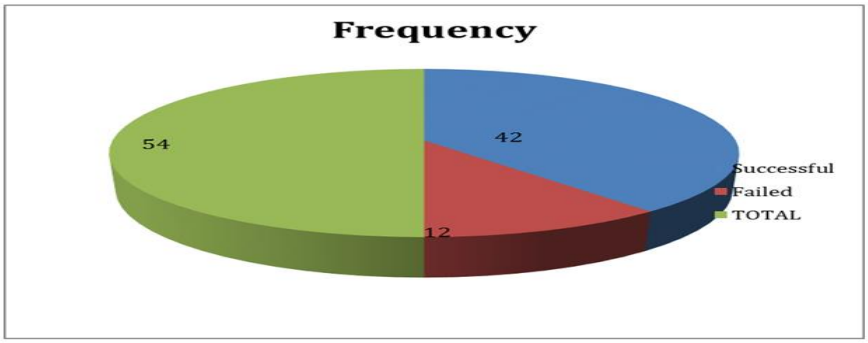



**Fig 5:Thrombolysis outcome**

Successful thrombolysis based on time of presentation – 33 patients presented within 6 hours of symptom onset of which 30 patients(90.91%) had successful thrombolysis, and 3 patients(9.09%) had failed thrombolysis.

**Table 6:Index pain to thrombolysis time < 6 hours and thrombolysis outcome**

| Thrombolysis result | Frequency | Percent |
|---|---|---|
| Successful | 30 | 90.91% |
| Failed | 3 | 9.09% |
| **TOTAL** | **33** | **100.00%** |

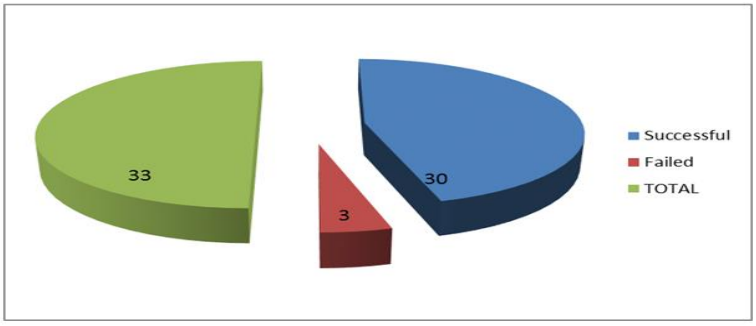



**Fig 6: Index pain to thrombolysis Interval < 6 hours frequency**

16 patients presented within 6 – 12 hours of symptom onset of which 10 patients(62.50%) had successful thrombolysis , and 6 patients(37.50%) had failed thrombolysis.

**Table 7:Index pain to thrombolysis interval 6 - 12 hours and thrombolysis outcomes**

| Thrombolysis result | Frequency | Percent |
|---|---|---|
| Successful | 10 | 62.50% |
| Failed | 6 | 37.50% |
| **Total** | **16** | **100.00%** |

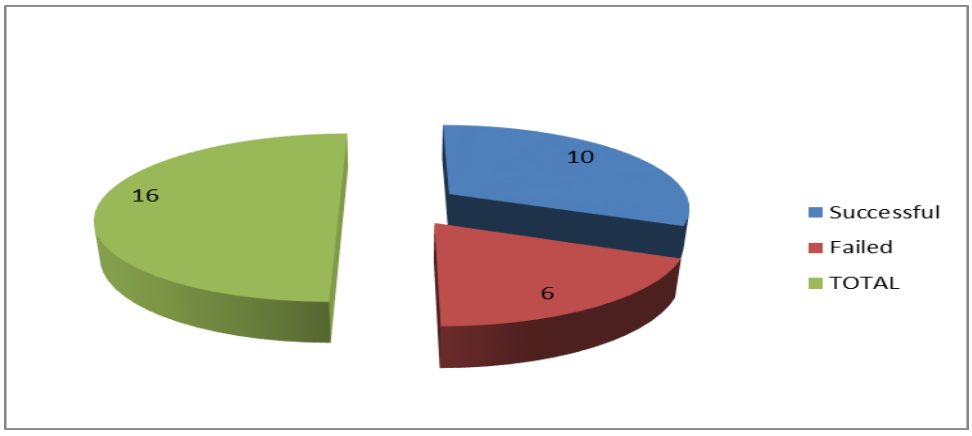



**Fig 7:Index pain to thrombolysis interval 6 - 12 hours and thrombolysis outcome**

5 patients were thrombolysed after 12 hours of symptom onset of which 2 patients (40%) had successful thrombolysis, and 3 patients(60%) had failed thrombolysis.

**Table 8:Index pain to thrombolysis time >12 hours and thrombolysis outcome**

| Thrombolysis result | Frequency | Percent |
|---|---|---|
| Successful | 2 | 40.00% |
| Failed | 3 | 60.00% |
| **TOTAL** | **5** | **100.00%** |

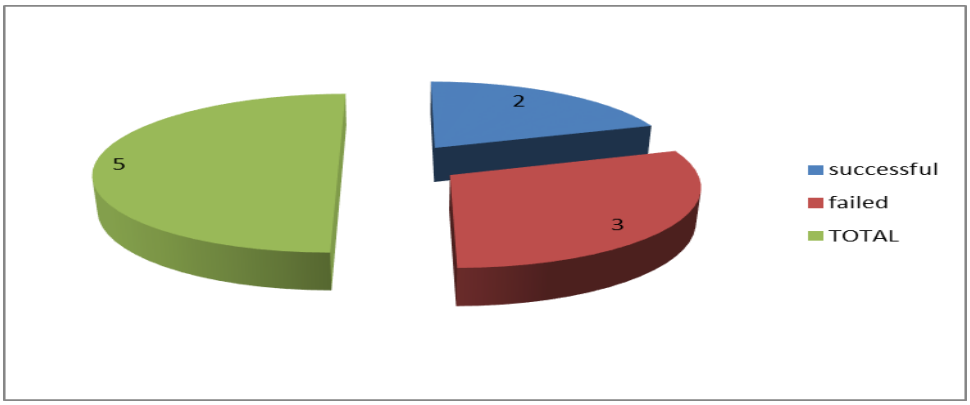


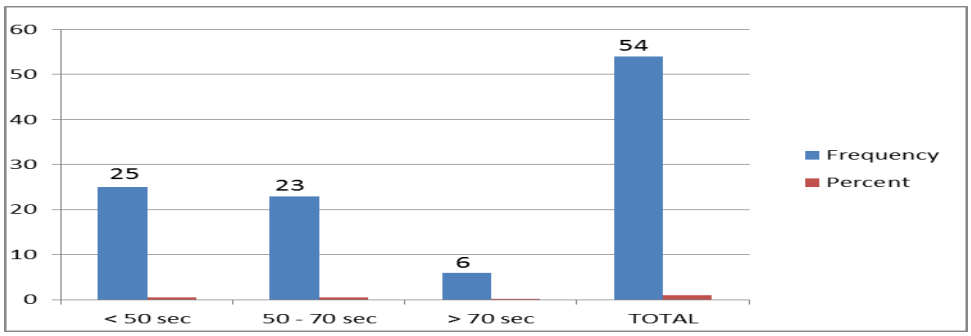

**Fig 8:Index pain to thrombolysis time >12 hours and thrombolysis outcome**

50 – 70 seconds is the ideal APTT to maintain and to prevent reoclussion. As streptokinase was available in our hospital we wanted to know how many patients were in the therapeutic range of APTT after administration of streptokinase.23 patients (42.59%) had APTT in the desired level of 50-70 seconds at the end of 3 hours of thrombolysis. 25 patients (46.30%) had APTT below the desired level. 6 patients(11.11%) had APTT above the desired level.

**Table 9:Classification of patients based on APTT level at 3 hours**

| APTT at 3hrs | Frequency | Percent |
|---|---|---|
| < 50 sec | 25 | 46.30% |
| 50 - 70 sec | 23 | 42.59% |
| > 70 sec | 6 | 11.11% |
| **TOTAL** | **54** | **100.00%** |

**Fig 9:Classification of patients based on APTT level at 3 hours**




**APTT at 6 hours after thrombolysis**

16 patients(29.63%) had APTT within the desired therapeutic level at the end of 6 hours after thrombolysis.

**Table 10:Classification of APTT at the end of 6 hours**

| APTT at 6 hrs | Frequency | Percent |
|---|---|---|
| < 50 sec | 26 | 48.15% |
| 50 - 70 sec | 16 | 29.63% |
| > 70 sec | 12 | 22.22% |
| **Total** | **54** | **100.00%** |

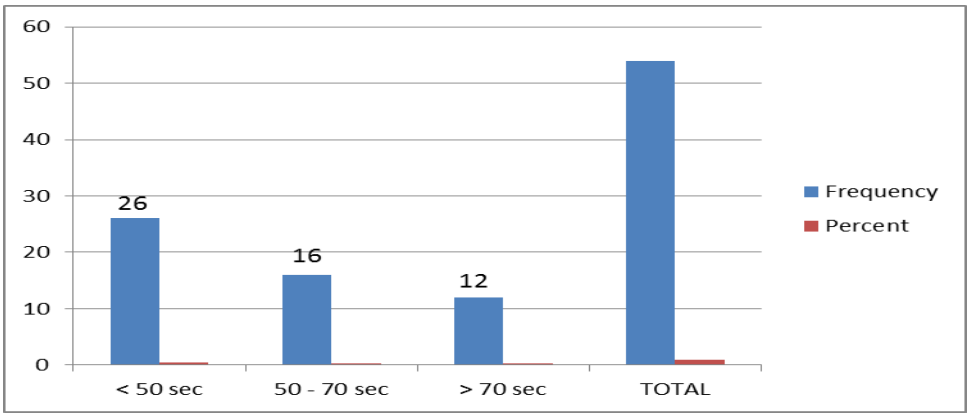



**Fig 10:Classification of APTT at the end of 6 hours**

**APTT at the end of 9 hours**

19 patients were in the desired APTT value of 50 – 70 seconds.

**Table 11:Classification of patients based on APTT values at 9 hours**

| APTT at 9 hrs | Frequency | Percent |
|---|---|---|
| < 50 sec | 28 | 51.85% |
| 50 - 70 sec | 19 | 35.19% |
| > 70 sec | 7 | 12.96% |
| **Total** | **54** | **100.00%** |

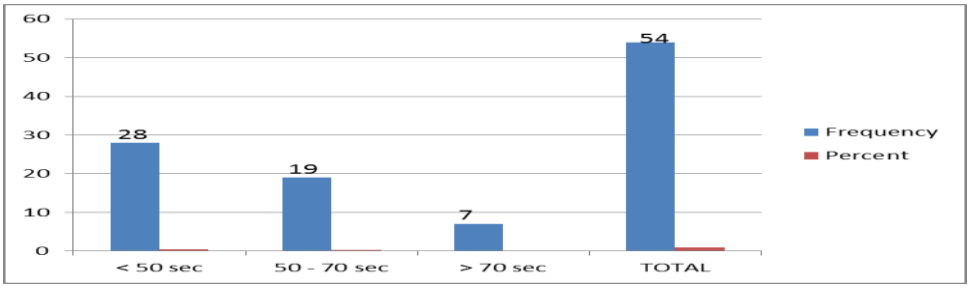



**Fig 11:Classification of APTT at the end of 9 hours**

23 patients had PT below 30 seconds, 24 patients had between 30-60 seconds and 7 patients had >60 seconds.

**Table 12:Classification of patients based on PT at 3,6 and 9 hours**

| PT | 3hr | | 6hr | | 9hr | |
|---|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | Frequency | Percent |
| < 30 | 25 | 46.3 | 23 | 42.6 | 30 | 55.6 |
| 30-60 | 23 | 42.6 | 24 | 44.4 | 19 | 35.2 |
| > 60 | 6 | 11.1 | 7 | 13.0 | 5 | 9.3 |
| Total | 54 | 100 | 54 | 100 | 54 | 100 |

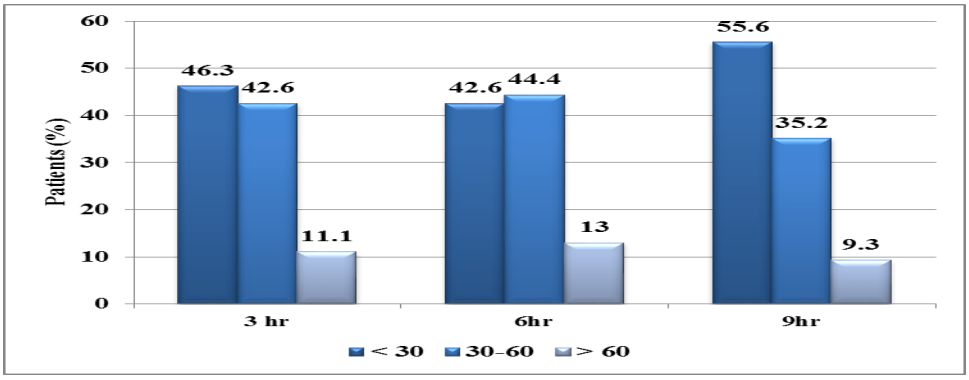



**Fig 12:Classification of patients based on PT at 3,6 and 9 hours**

**Table 13:Classification of patients based on APTT at 3, 6 and 9 hours**

| APTT | 3hr | | 6hr | | 9hr | |
|---|---|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent | Frequency | Percent |
| < 50 | 25 | 46.3 | 26 | 48.1 | 28 | 51.9 |
| 50-70 | 23 | 42.6 | 16 | 29.6 | 19 | 35.2 |
| > 70 | 6 | 11.1 | 12 | 22.2 | 7 | 13.0 |
| Total | 54 | 100 | 54 | 100 | 54 | 100 |

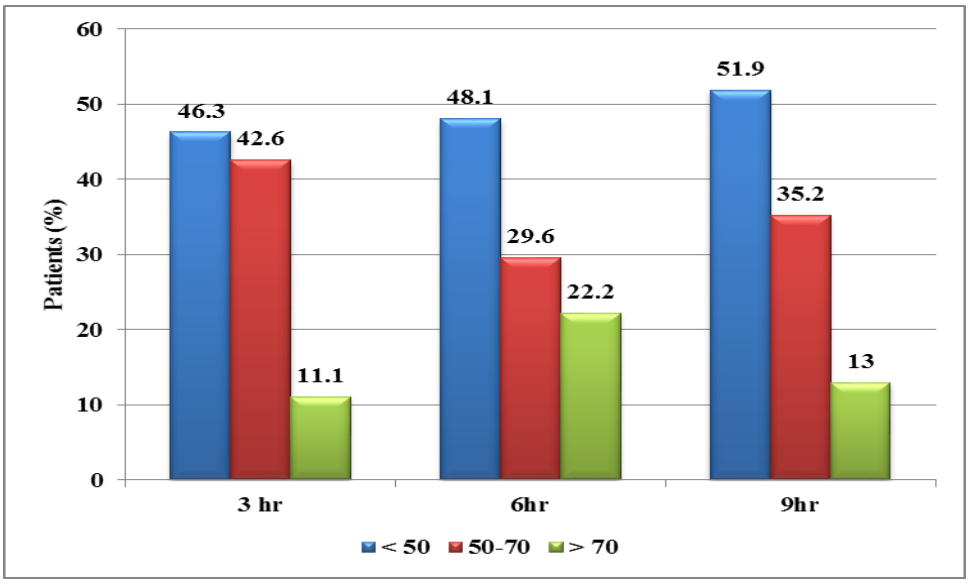



**Fig 13:Classification of patients based on APTT at 3, 6 and 9 hours**

Comparison between APTT values of patients consuming alcohol and who do not consume alcohol.17 patients were consuming alcohol and 37 patients were not consuming alcohol.P = 0.025.

**Table 14:Comparison of alcohol habit and APTT values**

| APTT | Alcoholic | | Non alcoholic | |
|---|---|---|---|---|
| | Frequency | Percent | Frequency | Percent |
| < 50 | 4 | 23.5 | 22 | 59.5 |
| 50-70 | 6 | 35.3 | 10 | 27.0 |
| > 70 | 7 | 41.2 | 5 | 13.5 |

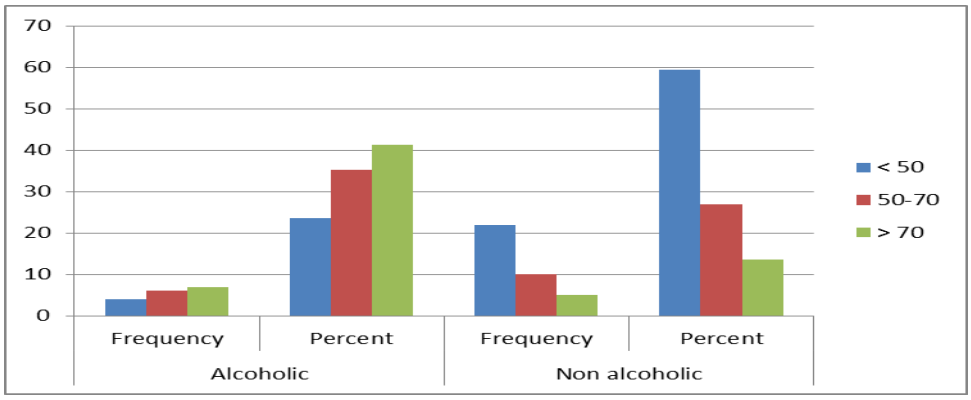



**Fig 14:Comparison of alcohol habit and APTT values**

Relationship between successful thrombolysis and APTT value at 6 hours Out of 42 successful thrombolysis patients , 19 patients (45.24%) had APTT values below the therapeutic range , 13 patients (30.95%) were in the therapeutic range , and 10 patients (23.81%) were in the supratherapeutic range.

**Table 15:APTT values and success of thrombolysis**

| APTT at 6 hrs | Frequency | Percent |
|---|---|---|
| < 50 sec | 19 | 45.24% |
| 50 - 70 sec | 13 | 30.95% |
| > 70 sec | 10 | 23.81% |
| TOTAL | 42 | 100.00% |

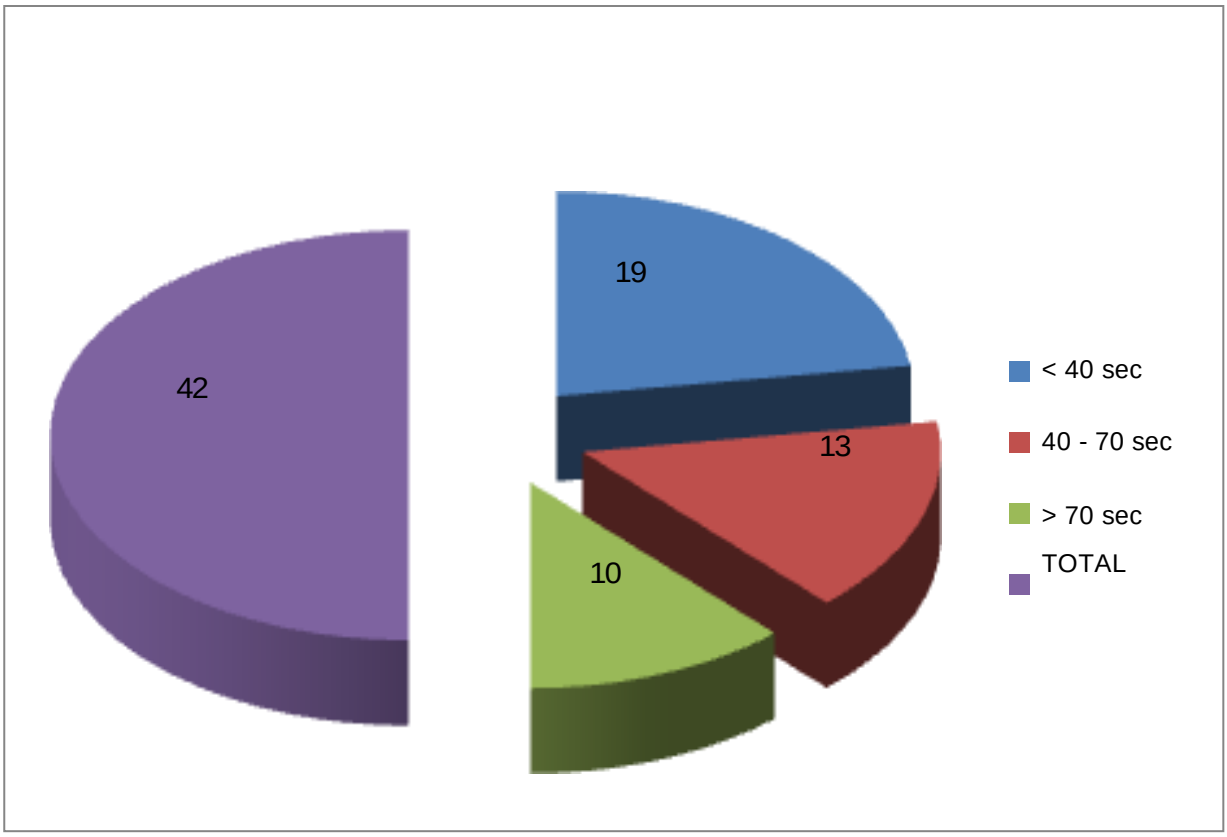



**Fig 15:APTT values and success of thrombolysis**

**Relationship between failed thrombolysis and APTT**

12 patients had failed thrombolysis , out of which 7 patients (58.33%) were in the sub therapeutic range, 3 patients (25%) were in the therapeutic range and 2 patients (16.67%) were in the supra therapeutic range.

**Table 16:Failed thrombolysis and APTT at 6 hours**

| APTT at 6 hrs | Frequency | Percent |
|---|---|---|
| < 50 sec | 7 | 58.33% |
| 50 - 70 sec | 3 | 25.00% |
| > 70 sec | 2 | 16.67% |
| **TOTAL** | **12** | **100.00%** |

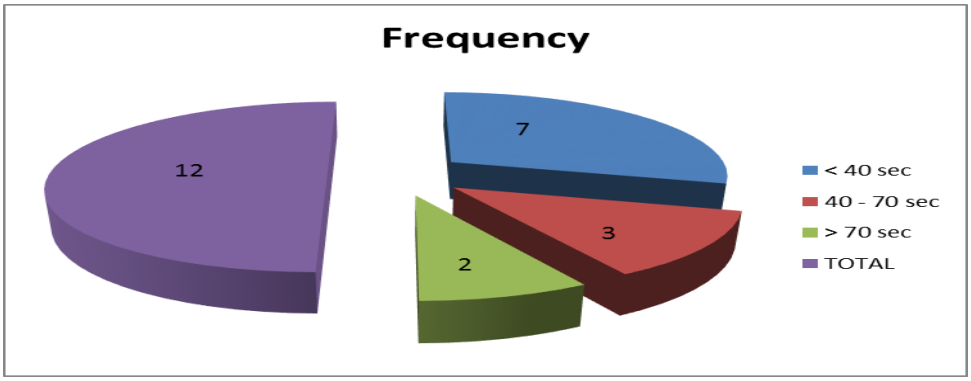



**Fig 16: Failed thrombolysis and APTT at 6 hours**

**Table 17:Comparison of patients with APTT at 6 hours and APTT at 9 hours**

| APTT at 9 hrs | APTT at 6 hrs | | | | | |
|---|---|---|---|---|---|---|
| | APTT < 50 | | APTT 50-70 | | APTT > 70 | |
| | Frequency | Percent | Frequency | Percent | Frequency | Percent |
| < 50 | 24 | 92.3 | 3 | 18.8 | 1 | 8.3 |
| 50-70 | 2 | 7.7 | 12 | 75.0 | 5 | 41.7 |
| > 70 | 0 | 0 | 1 | 6.3 | 6 | 50.0 |
| Total | 26 | 100 | 16 | 100 | 12 | 100 |

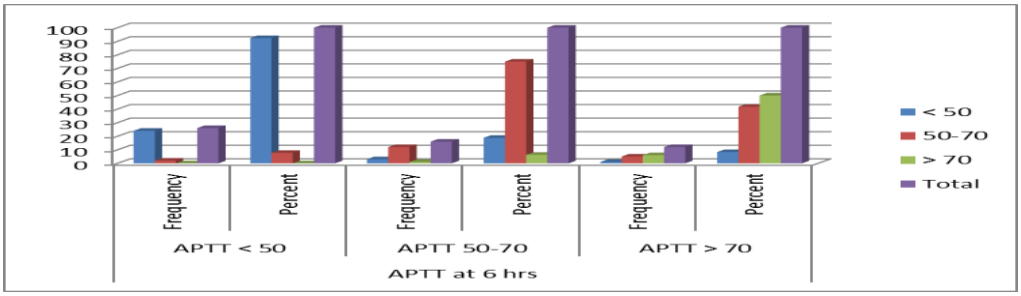



**Fig 17:Comparison of patients with APTT at 6 hours and APTT at 9 hours**

$\chi^2 = 45.533$ $P < 0.001$.

Kappa score for the agreement between APTT at 6 hours and 9hours is 0.640.

**Discussion**

Most patients were in the age group of 61 – 70 years. Of the 54 patients 19 were females and 35 were males, male female ratio was 1.8:1. 51.85% patients had isolated inferior wall involvement based on ecg criteria , < 30% patients had involvement of anterior wall, rest of them had overlapping involvement.61% patients were thrombolysed within 6 hours of symptom onset, 9.26% patients were thrombolysed after 12 hours of symptom onset.42(77.78%) patients had successful thrombolysis and 12(22.22%) patients had failed thrombolysis. A study by L Bhatia et al found ST segment resolution in 53% of patients.90% patients had successful thrombolysis when thrombolysis was initated within 6

hours of symptom onset.60% patients had failed thrombolysis when they were thrombolysed after 12 hours of symptom onset. So early thrombolysis has more chances of a successful thrombolysis.In our study only 29.63% patients had APTT in the therapeutic level of 50 – 70 seconds which was similar to study by Arnout J et al where 32% patients were in the therapeutic range. No association was found between alcohol use and APTT values. 17(31.48%) patients were using alcohol in our study.There was a significant relation between APTT at the end of 6 hours and APTT at the end of 9 hours and may be due to heparinisation at the end of 6 hours.Based on the above data 48.15% patients had their APTT in the sub therapeutic level at the end of 6 hours after thrombolysis. These patients may have been benefited if they were heparinised at an earlier time. This needs further study by comparing two groups based on early heparinisation before 6 hours and at 6 hours (standard heparinisation), and comparing the outcome in these two group based on resolution of ECG , decrease in pain and angiographic findings.

## Conclusion

Early heparinisation may be considered in those patients who have non resolving ST segment 90 minutes after thrombolysis , or those patients who have continuing pain even after thrombolysis.A significant correlation was found between APTT at 6hours and APTT at 9 hours that is patients who were in the therapeutic range at the end of 6 hours were also maintained at the end of 9 hours probably due to heparinisation at the end of 6 hours after thrombolysis.

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**Source of Support:Nil**
**Conflict of Interest: Nil**