

# “ STUDY OF REPERFUSION ARRHYTHMIAS IN POST-THROMBOLYTIC THERAPY IN ACUTE MYOCARDIAL INFARCTION ”

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## ABSTRACT:

**Objective:** Early intervention in myocardial infarction leads to decrease in mortality. The main treatment methods used today to provide myocardial reperfusion are thrombolytic therapy and percutaneous coronary intervention. current study aims at studying prevalence of Reperfusion arrhythmias by electrocardiogram during and within 48 hours of thrombolysis and its relation to mortality.

**Methods:** 100 Patients admitted with acute STEMI in DR PSIMS & RF who are more than 18 yrs of age including both males and females, with features suggestive of acute myocardial infarction who have underwent thrombolytic therapy are selected for the study. Assessment of reperfusion arrhythmias during and within 48 hrs of thrombolytic therapy using ECG is performed. The relation between reperfusion arrhythmias and survival outcome after thrombolytic therapy were assessed.

**Results:** In this study Maximum incidence of acute STEMI was seen between 45-75 years with male predominance. There was no statistically significant difference between the two groups in the frequency of reperfusion arrhythmias ( $P = 0.014$ ). Although angiographic vessel patency was higher in patients undergoing percutaneous coronary intervention, there was no significant difference between the patency rates of each group with and without reperfusion arrhythmias.

**Conclusion:** There is no significant relation between mortality and reperfusion arrhythmias, there was no significant p value between them, indicating Reperfusion arrhythmias are benign, and should be used as a marker of successful thrombolysis. Thus RA is not an event of serious concern as they are usually well tolerated and are amenable to treatment. Early streptokinase therapy has a favorable impact on mortality in MI and hence should be tried in all the Acute MI patients who do not have contraindications for streptokinase therapy.

**Keywords:** ST segment elevation MI(STEMI), Ventricular Tachycardia(VT), Ventricular Fibrillation(VF), Reperfusion Arrhythmias(RA), Thrombolytics.

## INTRODUCTION

Rapid rise is seen in the incidence of non communicable diseases after a decline in the incidence of communicable diseases. At the beginning of third millennium, the prevalence of non communicable diseases is rising across the globe. By 2020, non communicable disease will cause 70% of deaths in developing countries. The major non- communicable diseases are cardiovascular disease (ischemic heart disease-IHD and hypertension), diabetes, cancer and chronic pulmonary disease, these conditions affects countries worldwide but with a growing trend in developing countries. Diabetes and hypertension, apart from other disabilities, can lead to IHD. IHD is the most common, serious, chronic, life-threatening illness in the United States, where 13 million persons have IHD of which >6 million have angina pectoris, and >7 million have sustained myocardial infarction<sup>[1]</sup>

These conditions are also a major cause of mortality and morbidity in the Asia-Pacific region and account for around half of the global burden i.e. around seven million deaths and 129 million disability-adjusted life years (DALYs) annually from 1990 to 2010. (WHO)<sup>[2][3][4][5][6]</sup>. The epidemiologic characteristics of acute myocardial infarction(AMI) have changed dramatically over the past three to four decades. Since 1987, the adjusted incidence rate of hospitalization for acute myocardial infarction or fatal coronary artery disease in the United States has declined by 4 to 5% per year<sup>[7][8]</sup> Nevertheless, approximately 5,50,000 first episodes and 200,000 recurrent episodes of acute myocardial infarction occur annually. Globally, ischemic heart disease has become the leading contributor to the burden of disease as assessed on the basis of disability-adjusted life-years.<sup>[9]</sup> Use of thrombolytic strategies like Streptokinase has been prevalent since decades, and there was significant reduction of mortality after the thrombolytic therapy. Reperfusion arrhythmias has been considered as successful markers of reperfusion. And the studies regarding consideration of

reperfusion arrhythmias as a marker of reperfusion has been going on since decades. So the main aim of this study is regarding whether reperfusion arrhythmias can be considered as prognostic indicators for thrombolysis or not. Thus aim of this study is to know the prevalence of reperfusion arrhythmias during and within 48 hrs of i.v streptokinase therapy. To assess the prognosis of MI secondary to thrombolytic therapy, To assess whether reperfusion arrhythmias are the non invasive markers of successful thrombolysis by means of the electrocardiogram.

Material and Methods

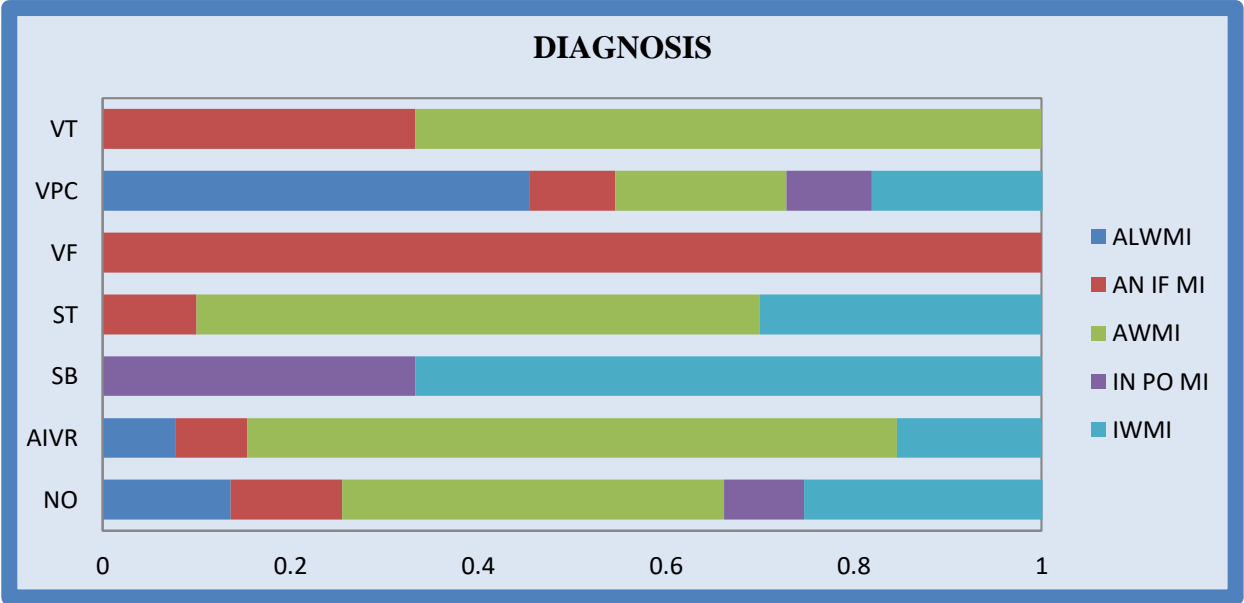
The data of patients treated by either thrombolysis or percutaneous coronary intervention with a diagnosis of acute ST elevation myocardial infarction followed in Dr.Pinnamaneni Siddhartha Institute of Medical Sciences and Research Foundation, Chinnaoutpalli tertiary care, teaching hospital in South India between the years November 2015and November 2017, 100 patients were evaluated retrospectively in this study. Patients with non-ST elevation myocardial infarction, unstable angina pectoris, cardiac conduction system disorders, permanent pacemakers, mechanical ventilation support, cardiogenic shock, and survivors of cardiac arrest due to acute myocardial infarction were excluded from the study group in addition to the individuals to whom rescue PCI was performed following the first 24 hours of thrombolytic therapy. The diagnosis of STEMI was based on recently published criteria of the European guidelines [4]. Time of diagnosis, patient age, gender, height, weight, hypertension, diabetes mellitus, history of previous MI, smoking, ECG, lipid profile, urea, creatinine, blood glucose, troponin I, and potassium values were recorded. Assessment of reperfusion arrhythmias during and within 48 hrs of thrombolytic therapy using ECG.

RESULTS

Total numbers of patients were 100 and were divided into 5 age groups and each age group to two sex groups. 35-45,46-55,56-65,66-75 and 76-85years. Relation of reperfusion arrhythmias with age groups in study group. There was no relation as p value is insignificant, age, sex, smoking, alcohol consumption, diabetes, hypertension, with window period and types of MI has no influence in the occurrence of reperfusion arrhythmias

DIAGNOSIS	Reperfusion Arrhythmias				Total	
	No		Yes			
	Count	%	Count	%	Count	%
ALWMI	8	13.6%	6	14.6%	14	14.0%
AN IF MI	3	5.1%	2	4.9%	5	5.0%
AN INF MI	4	6.8%	3	7.3%	7	7.0%
AWMI	24	40.7%	19	46.3%	43	43.0%
IN PO MI	5	8.5%	1	2.4%	6	6.0%
IN POSTMI	0	0.0%	1	2.4%	1	1.0%
IWMI	15	25.4%	9	22.0%	24	24.0%
Total	59	100.0%	41	100.0%	100	100.0%
Chi-square value = 3.24; df= 6; P=0.778						

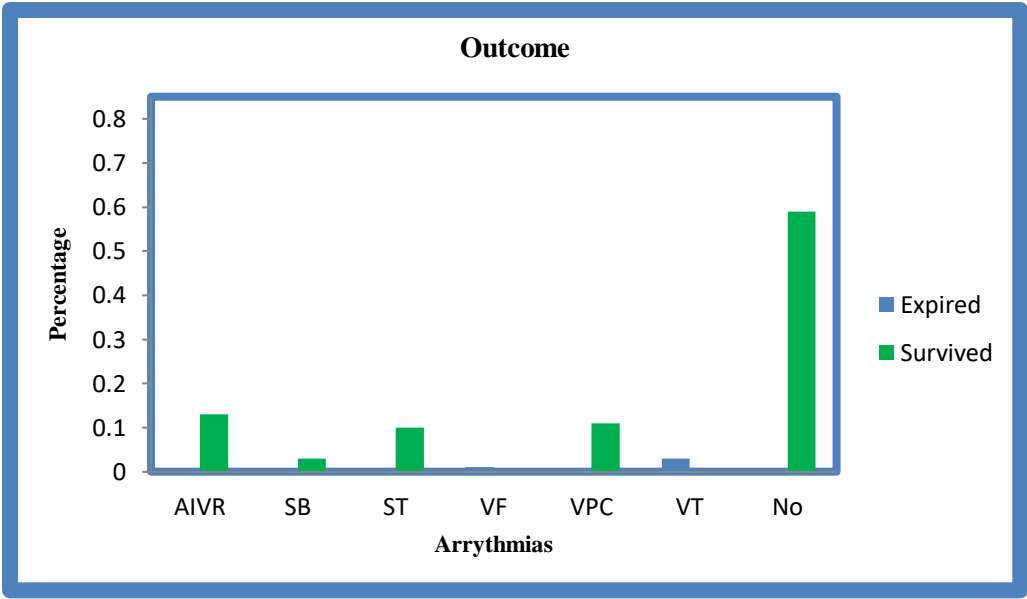
**Table 1:** Relation of reperfusion arrhythmias with Type of MI in study group. There was no relation as p value is insignificant, Type of MI has no influence in the occurrence of reperfusion arrhythmias



**Graph 1:** Distribution of various reperfusion arrhythmias in different types of Myocardial infarction

**Table 2:** Distribution of various reperfusion arrhythmias in different types of Myocardial infarction

DIAG NOSI S	ARRYTHMIAS														Total	
	N		AIVR		SB		ST		VF		VPC		VT			
	Co un t	%	Co un t	%	Co un t	%	C o u nt	%	C o un t	%	Co un t	%	Co un t	%	Cou nt	%
ALW MI	8	13.6%	1	7.7%	0	0.0%	0	0.0%	0	0.0%	5	45.5%	0	0.0%	14	14.0%
AN IF MI	7	11.9%	1	7.7%	0	0.0%	1	10.0%	1	100.0%	1	9.1%	1	33.3%	12	12.0%
AWM I	24	40.7%	9	69.2%	0	0.0%	6	60.0%	0	0.0%	2	18.2%	2	66.7%	43	43.0%
IN PO MI	5	8.5%	0	0.0%	1	33.3%	0	0.0%	0	0.0%	1	9.1%	0	0.0%	7	7.0%
IWMI	15	25.4%	2	15.4%	2	66.7%	3	30.0%	0	0.0%	2	18.2%	0	0.0%	24	24.0%
Total	59	100.0%	13	100.0%	3	100.0%	10	100.0%	1	100.0%	11	100.0%	3	100.0%	100	100.0%



**Graph 2:** Types of Reperfusion Arrhythmias and their relation to outcome in study group

OUTCOME	Reperfusion Arrhythmias				Total	
	No		Yes			
	Count	%	Count	%	Count	%
Expired	0	0.0%	4	9.8%	4	4.0%
Survived	59	100.0%	37	90.2%	96	96.0%
Total	59	100.0%	41	100.0%	100	100.0%
Chi-square value = 5.99; df= 1; P=0.014						

**Table 3:** Relation of reperfusion Arrhythmias to out come in study group.  
There was significant relation to reperfusion arrhythmias and outcome of the study group as P value was significant.

**DISCUSSION**

Arrhythmias and conduction disturbances are common during the early hours after an acute MI and a major cause of death in the pre-hospital phase. The occurrence at greatest frequency before or during thrombolysis indicates that ongoing myocardial ischemia and reperfusion injury are major determinants for arrhythmias and conduction disturbances.

STEMI is treated during early window period of 8hrs with streptokinase or primary percutaneous intervention. Early thrombolysis is associated with good prognostic outcome of Acute MI. According to various studies and literature reperfusion arrhythmias during and within 48 hrs of thrombolysis is associated with good prognosis.

This study was done to show prevalence of reperfusion arrhythmias in STEMI during and within 48hrs of streptokinase therapy in different age and sex groups. The study population were divided into 5 different age groups. 35-45,46-55,56-65,66-75,76-85 age groups. 28% of people belong to 46-55,26% to 66-75,16% belongs to 56-65,15% to 35-45 and 76-85 years. This is comparable with study done by Kakade SV et al. <sup>[10]</sup> The Maximum incidence of acute STEMI was seen between 45-75 years was 70%. Incidence of this study almost compares well with incidence being 85% between 35 years and 75 years of age as reported by Martin TC et al in (2007) Age incidence is probably more common because of life style, economic status and multiple risk factors and life expectancy, In this study there are 57% males and 43% females in contrary with study done by <sup>[11]</sup> Martin TC et al, where incidence was 72% in males and 28% in females, and by Kock HL et al <sup>[12]</sup> where 72% were males and 24% were females. It is more common among males because of life style and more risk factors like hypertension, smoking, diabetes mellitus and alcohol.

In this study 70% of patients presented with chest pain, 15 % with SOB, 15% with both. It is compared to study by Mhatre MA et al. <sup>[13]</sup> which shows the pattern and incidence of various symptoms of acute MI in which Chest pain was the most common presenting symptom which was present in 80% of patients and another 15% had all together epigastric pain and pain in left arm alone. Sweating was 2nd most common symptom (64%) followed by dyspnea (43%). Vomiting was present in 28% and palpitation in 11% Another 8% of patients presented with giddiness/syncope.

**RISK FACTOR AND MI**

Incidence of type 2 diabetes mellitus was 38% in the present study as compared to 19% in Svensson AM et al <sup>[14]</sup> study of 2007, study shows a higher incidence of Type2 DM in Acute MI pts, indicating DM is a major risk factor in MI. In the present study, 53% had hypertension showing higher prevalence of Acute MI in disease groups which is in agreement with Kokubo Y et al <sup>[15]</sup> study in 2008. According to study done by DUNN 1983. Both systolic and diastolic hypertension increase the risk of a myocardial infarction and the higher the pressure, the greater the risk. Even when other major risk factors are absent, the increased risk still exists. The immediate and long-term mortality after infarction in patients with hypertension is increased. 23% of patients are associated with Smoking, which is a risk factor for acute MI, 38% are associated with alcohol consumption, however several studies show that mild alcohol consumption has a protective role in ACS(Acute Coronary Syndrome) where as large amounts and binge intake is associated with acute MI. Role of alcohol as a risk factor is still controversial.

**TYPES OF MI**

5 different groups of STEMI -AWMI -43%,IWMI- 24% ALWMI-14%, AN INF MI-12%, IN PO MI-7% are in our study group. When compared to study done by Sarala. H. Tippannavar <sup>[16]</sup> in which most of patients (83%) had ST segment elevation MI of which 34% had extensive anterior wall MI, 23% had inferior wall MI, 14% had anteroseptal wall MI, 6% had inferior wall with RV extension, 3% had lateral and anterolateral wall MI each, and non-ST elevation MI patients were 17%.

All patients in the study group were given streptokinase 1.5 million units i.v for thrombolysis after excluding the contra indications and were monitored during and at 48 hrs for arrhythmias, limitation of study was it doesn't includes all the types of MI, like lateral septal MI

Due to random sample collection, percentage of people in the groups were also not the same.

**REPERFUSION ARRHYTHMIAS AND THROMBOLYSIS**

The term, reperfusion arrhythmias, was used in the first studies of thrombolytic therapy guided revascularization in acute myocardial infarction. To confirm the presence of vessel patency and successful reperfusion of the myocardium following thrombolytic therapy, electrocardiographic data in addition to clinical and laboratory measures are used by the clinicians. These include normalization or more than 50% regression of ST elevation, T-wave inversion, and any other arrhythmia observed in electrocardiography. The most frequently observed arrhythmias that are defined as reperfusion arrhythmias are ventricular premature contractions, sustained or non sustained episodes of ventricular tachycardia, accelerated idioventricular rhythm, atrial fibrillation, and ventricular fibrillation. These arrhythmias are thought to be indicators of successful reperfusion.

According Jurkovicová O, Cagán S <sup>[17]</sup> study, Reperfusion arrhythmias originate as a consequence of the complex of cellular and humoral reactions accompanying the opening of coronary artery. As the primary cause of their generation are considered the chemically defined substances that are produced and accumulated in myocardium during reperfusion. The key role is oxygen radicals but of importance are also other substances such as calcium, thrombin, platelet activating factor, inositol triphosphate, angiotensin II and others. ascribed to free These chemical mediators of reperfusion arrhythmias operate as modulators of cellular electrophysiology causing the complex changes at the level of ion channels.

It is supposed that in the genesis of reperfusion arrhythmias unlike ischemic arrhythmias operate nonreentrant mechanisms such as abnormal or enhanced automaticity and triggered activity due to after depolarizations. Reperfusion arrhythmias are an important noninvasive marker of successful recanalization of infarction-related coronary artery.

**INCIDENCE AND RISK FACTORS RELATION**

In this study, incidence of REPERFUSION ARRHYTHMIAS are 41% As compared to Ersan Tatli et al study <sup>[18]</sup> which shows (88.7%) reperfusion which were lesser incidence in this study group, the maximum incidence of reperfusion arrhythmias was present in age group of 46-55 years i.e 28% followed by 66-75 i.e 26%,56-65-16%, 35-45 and 76-85-15%, and the p value for age groups was not significant. This study shows there was no statistical significance between age group and arrhythmias.

RA is present in 57% males and 43% females the p value was not significant for sex, there was no statistical significance between sex group and arrhythmias. Where as reperfusion arrhythmias in diabetics are 38%, the p value was significant for DM. This study shows there was statistical significance between Diabetics and arrhythmias. Incidence of RA in hypertension are 53%, although HTN is a risk factor for MI, the p value was not significant between reperfusion arrhythmias and HTN, hence no statistical significance. In alcoholics the incidence of RA was 9%, and the p value was not significant, in Smokers are 34%, and the p value was not significant between reperfusion arrhythmias and smoking. In this study type of MI and window period of hospital presentation and arrhythmias have no statistical significance

**TYPES OF ARRYTHMIAS**  
**ACCELERATED IDIO-VENTRICULAR RYTHMN(AIVR)**

In this study 13% of patients develops AIVR. It is most common type of reperfusion arrhythmias in this study group. it is most common in AWTMI Accelerated Idioventricular Rhythm (AIVR) was defined as ventricular rhythm with a rate of 60 to 125 beats/minute and frequent episodes of "slow ventricular tachycardia,"

As compared to Ersan Tatli et al <sup>[19]</sup> where there was 73.3% of AIVR in patients with thrombolytic group, in this study although the percentage is low, but it was most common arrhythmias noted in study group. In a study by Terkelsen et al., the most common arrhythmia observed was AIVR (42%). In a study by Chiladakis, <sup>[20]</sup> the presence of AIVR combined with normalization of ST segments was demonstrated to indicate successful reperfusion in patients treated with Thrombolytics

However <sup>[21]</sup> Gore et al and <sup>[22]</sup> Hacket et al. does not find AIVR to be associated with successful reperfusion indicating ventricular rhythm may be a marker of early reperfusion and continuing arterial patency. In a previous study, the presence of accelerated idioventricular rhythm combined with normalization of ST segments was demonstrated to indicate successful reperfusion in patients treated with thrombolytics and there was no requirement for emergency coronary angiography and rescue percutaneous coronary intervention (PCI) in this group of patients. Among these, AIVR was the most sensitive and specific arrhythmia in cases of successful reperfusion.

	Ersan Tatli et al	Terkelsen et al	Present study
AIVR	73.3%	42%	13%

**Table 4:** AIVR incidence post thrombolysis comparison studies in ST elevation MI

**SINUS TACHYCARDIA**

In this study sinus tachycardia was present in 10% which is mostly seen in AWTMI-6% IWMI-3%,as compared to Sarala. H. Tippannavar, study <sup>[16]</sup> where the incidence is 22%, it was so low in this study, there is no mortality in this patients with sinus tachycardia, in contrary to Crimma et al <sup>[23]</sup> were the mortality incidence was 23.72%,in which it was shown that sinus tachycardia is associated with adverse outcomes.

**SINUS BRADYCARDIA**

Sinus bradycardia was most commonly associated with inferior wall myocardial infarction. In the present study, 3%had sinus bradycardia, out of which 2% were of inferior wall MI  
Where as in study made by Michel Rotman et al. 1 (10-30%), Philip J Podrid, <sup>[24]</sup> where 16% to 25% patients had sinus bradycardia particularly of inferior wall MI and posterior wall MI. It was most often transient. Brady-arrhythmias and hypotension are common in proximal occlusion of right coronary artery commonly leading to Inferior myocardial infarction, because of reflexes arising from the ischemic right ventricle. In the present study 3% had SB, out of which 2 were purely in inferior and 1 in inferior + posterior wall MI. In all these patients, SB was transient and majority of the patients had normal sinus rhythm (NSR) by the end of 1 st day. All the patients had NSR at discharge. Similar observations were made by Swart G et al. <sup>[25]</sup> In the present study, there were no deaths in patients with SB and inferior wall MI, indicating a protective role of SB in inferior wall MI. Similar observations was made by Malla RR and Sayani A. <sup>[26]</sup> Occasionally they may progress to complete heart block, treatment with atropine and i.v fluids and inotropes may be needed, occasionally may need pacemaker implantation

**VENTRICULAR ARRYTHMIAS**

In this study over all 15% Ventricular arrhythmias are seen, VF 1%, VT 3%, VPC-11%, when compared to <sup>[27]</sup> Henkel DM, Witt BJ et al studies the incidence was low In Ravi Kumar Navsk study 2015, ba Ventricular arrhythmias were present in 32% of them of which 24% had Ventricular Tachycardia (VT) and 28% had Ventricular Premature Beats (VPB). In Sarala. H. Tippannavar et al <sup>[16]</sup> Ventricular arrhythmias were seen in 31 cases of which VPBs in 23 cases, VT in 6 cases, VF in 2 cases. Study conducted by Julain Villacastin <sup>[28]</sup> showed total incidence of VPC 12% and VT 18% and Mossimo Zoni Berisso et al<sup>[29]</sup> showed 19.7% VPCs and VT 6.8%. Mhatre MA et al. <sup>[13]</sup> shows the overall incidence of ventricular arrhythmias being 33% of which VT was 24%, VPC, were 8% and ventricular bigeminy being 1%. Also overall incidence is more in anterior and lateral wall MI than inferior wall alone

**VENTRICULAR PREMATURE COMPLEXES**

Data from the Gruppo Italiano per lo Studio della Sopravvivenza dell'infarto Miocardico study demonstrated that 64% of patients who had MI then had ventricular arrhythmia and 20% of patients had more than 10 VPCs per hour when 24-h Holter monitoring was used.

In this study, VPC s are present in 11% population, with 5% in ALWTMI,2%IWMI and AWTMI each, 1% in IN PO MI, AN IF MI. Which was of low incidence compared to Mohit J Shah et alla study in which VPCs were observed in 31% of the patients when they occurred alone. In Anterior wall MI VPCs were observed in 36.23% of the patient while 23.1% of the patients with Inferior wall MI had VPCs. There is no mortality in VPC s in this study group, which indicates VPC is has a good prognostic significance.



**VENTRICULAR TACHYCARDIA**

In this study incidence of VT is 3%, 2% in AWMi, 1% in AN IF MI. in contrary to study done by Horvat D et al.<sup>[30]</sup> Where VT was seen more in anterolateral MI than antero-septal MI, In another study, Gibson et al.<sup>[31]</sup> exhibited the development of VT and VF in 3491 patients with STEMI after thrombolytic therapy, mortality seen in patients with VT was 100% whereas study done by Metal GC and Al-Khatib S<sup>[32]</sup> was 25.2% and 24% respectively. This discrepancy could be explained by larger infarcts and older age in present study. In this study patients was given i.v lignocaine and D.C SHOCK, but patients didn't survive.

**VENTRICULAR FIBRILLATION**

In the Framingham Heart Study, the proportion of sudden CAD deaths was 62% in men aged 45-54 years, decreasing to 58% in men aged 55-64 years and to 42% in men aged 65-74 years. According to Kuller, 31% of deaths are sudden in people aged 20-29 years. In this study incidence of VF is 1% AN IF MI, the mortality is 1% Which Indicates that VF is associated with bad prognosis in relation to reperfusion in this study. In the study by Sarala. H. Tippannavarone patient developed VF after reperfusion expired This is consistent with Masood et al. Study that showed the worst arrhythmia after SK injection is ventricular fibrillation 1 Mohit J Shah et al ventricular fibrillation occurred only in 2 of the 100 patients, however with 100% mortality. This study shows a total mortality of 4% i.e associated with VT/VF as compared with the study by<sup>[33]</sup> Newby KH et al., showed that sustained VT and VF occur in up to 20% of patients with AMI and have been associated with poor prognosis, It is an established fact that primary VF, irrespective of timing, is an independent predictor of in hospital mortality. In the study by<sup>[34]</sup> Behar S et al., the incidence of secondary VF complicating AMI was 2.4%.

In conclusion there was no significant relation between mortality and reperfusion arrhythmias, there was no significant p value between them, indicating Reperfusion arrhythmias are benign, and was a marker of successful thrombolysis which was comparable with the study done by AVG huran and AJ. Cann.<sup>[35]</sup> Thus RA is not an event of serious concern as they are usually well tolerated and are amenable to treatment. They infarct indicate an effective reperfusion when present. Early streptokinase therapy has a favorable impact on mortality in MI and hence should be tried in all the Acute MI patients who do not have contraindications for streptokinase therapy.

**STUDY LIMITATIONS**

The major limitation of the study was that it was conducted in small population that may not represent entire population. The study was conducted in those population visiting hospital, Age groups were taken randomly in this study, so the mortality was shown in random sample distribution was not equal among different age groups.

**SUMMARY & CONCLUSION**

Out of 100 Cases of Acute MI admitted in the present study, 57% were males and 43% were females. Maximum incidence of Acute MI was seen between 4th to 7th Decade of life. Most predominant presenting symptoms are Chest pain (70%). Anterior wall MI(43%) was the most common MI seen in the study group. Inferior wall 24%, Anterolateral 14%, Antero inferior 12%, Infero-posterior 7%. Incidence of diabetes 38%, HTN 53%, Smoking 23% and alcohol 38% each. Reperfusion Arrhythmias shows significant correlation with DM, and no relation to HTN, alcohol, smoking, age groups and window period. Reperfusion arrhythmias were observed in 41% patients. AIVR 13% Most common, VPC 11%, Sinus tachycardia 10%, sinus bradycardia 3%, VT 3%, VF 1%. The Incidence of reperfusion arrhythmias were more in Anterior wall MI 19 Cases, Inferior wall MI 9 Cases, ALWMI 6 cases, Antero Inferior 5, Infero-posterior 2 cases. Mortality was seen in 4 Cases who had 3 VT and 1 VF. All patients who developed VT and VF were expired in this study, showing 100% mortality for these arrhythmias occurring commonly in AWMi and AN INF wall MI occurrence of these ventricular arrhythmias are associated with poor prognosis during and post thrombolytic therapy and should be intervened immediately. Patients who developed other arrhythmias like AIVR, VPC, ST, Sinus Bradycardia were reverted to normal without any intervention and survived, indicating these arrhythmias occurring in thrombolytic therapy are benign. In this study there was statistical significance between survival outcome and reperfusion arrhythmias showing an inference that reperfusion arrhythmias occur during and post thrombolytic therapy were mostly benign and indicate successful thrombolysis.

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