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Assessment of the co-relation between 1st set of Troponin I, age, duration of chest pain and LVEF in patients presenting with first stemi and treatment protocol followed

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Abstract: Coronary heart disease is the cause of 17.1 million deaths per year throughout the world. The rationale of this study was to determine the importance of 1st set of Troponin I in relation to age, duration of chest pain and left ventricular ejection fraction (LVEF) in patients presenting with acute ST elevation myocardial infarction along with the treatment protocol followed in emergency. It was a cross sectional prospective observational study which was conducted at a tertiary care hospital, at the Cardiology department for a period of 12 months. All patients regardless of gender, aged between 30-80 years with co-morbidities were included presenting with acute STEMI. A total of 150 patients were included in this study with a mean age of 61.2±10.3 years out of which males were (71%). Around 61% of the people presented to emergency >12 hours after onset of chest pain. There was non-significant difference in the treatment protocol given to all patients. For statistical analysis SPSS 21 was applied and significant relationship was observed between age, duration of chest pain and LVEF (p value <0.05). It was seen in our population that people older than 50 years tend to present to emergency department late with chest pain symptoms which results in a linear rising relationship with Troponin I and with increasing Troponin I there was significant reduction seen in LVEF.

Keywords: Acute ST elevation myocardial infarction, left ventricular ejection fraction,

INTRODUCTION

Coronary heart disease has not only impacted the mortality worldwide today only but it is predicted that it will continue to follow similar trends in the future as well (Wong *et al*., 2019). One of the most frequent causes listed in the United States (US) as a cause of admission in the hospital and contributing to both morbidity and mortality in the short and long run is acute myocardial infarction (AMI). According to an assessment the yearly occurrence of recurrent and new MI (myocardial infarctions) are 200,000 and 550,000. It has been reported that around one American suffers from AMI every 42 seconds (Mozaffarian *et al*., 2016).

The comparison in terms of race (Malays, Chinese and Europeans) shows that the Asians have an increased incidence of premature coronary artery disease (CAD and standardized mortality rates (Volgman *et al*., 2018). Due to multiple contributing factors of different food supplements, co-morbidities and versatility of life there is an increased tendency in the Asian people to develop MI (Geltsetzer *et al*., 2018; Shrivastava *et al*., 2017). Literature studies have shown that South Asian people tend to be at higher risk of suffering from MI (50%) in comparison to the United Kingdom (UK) white population (Ahmed *et al*., 2018).

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It is unfortunate that Pakistan is included in the list of countries in which there is data scarcity regarding CVS (cardio vascular diseases). The literature evaluation shows two studies done in 1965 and 1973 in Karachi which showed data regarding the incidence of IHD (Ischemic heart disease) in the countryside and metropolitan population which was around 0-1.5% and 0.7-3.7% respectively (Aziz *et al*., 2012; Syed *et al*., 1973). Globally CHD (coronary heart disease) is considered as one of the chief risks leading to mortality in Pakistani population. Approximately 30 to 40 per cent of all deaths in the country are reported to be due to cardiovascular diseases (CVD). The CHD deaths in Pakistan has reached about 200,000 per year that is 410/100,000 of the population (Fatema *et al*., 2016).

Included amongst the diseases responsible for a large number of illness and death, Acute ST-Elevation Myocardial Infarction is one of the most common cardiac emergency. The detection of cardiac biomarker is not only an important step in the detection of ischemia (Baker and Harrison, 2010). But also plays a role in the estimation of the infarct size. They have been utilized for this purpose since a long time especially Creatinine kinase MB and myoglobin but they need to be repeated during a small time window (Alvin *et al*., 2017; Kloner *et al*., 2017; Goins *et al*., 2018). For the estimation of myocardial injury the measurement of cardiac troponins is routinely performed after an acute myocardial infarction.

After acute myocardial infarction, the single best sole predictor of mortality is left ventricular function (Melendo-Viu *et al*., 2020). It has been shown that for early identification of patients with poor LV function , the cardiac biomarkers help to predict the left ventricular ejection fraction and that serum troponin-I concentration has been found to be inversely correlated with LVEF as a consequence of inverse relation between infarct size and LVEF (Gula *et al*., 2008).

The aim of this study was to associate age of the patient, the duration of chest pain and LVEF in patients presenting with first STEMI and assess their relationship with 1st set of Troponin I. Since the people of 3rd world countries tend to present to Accident and Emergency Departments much later then the time of actual onset of symptoms hence this study was conducted to assess the above as the Troponin I is not usually significant in people who present to accident and emergency earlier then 4 to 6 hours of their chest pain duration, also lack of data regarding this particular issue was observed hence this study was performed.

MATERIALS AND METHODS

Subject selection and study criteria

A randomized, observational, prospective study was conducted on 150 consecutive patients who presented to the ED (emergency department) of tertiary care hospital in Karachi from January 2018 to December 2018. Patients aged between 30 and 80 years, irrespective of whether they were males or females presenting with acute STEMI, with ST segment elevation of > 1 mm in precordial leads or presumably new onset LBBB (left bundle branch block) were included in this study after obtaining informed consent.

Diagnosis and evaluatory parameters

Based on the availability of prior electrocardiogram STEMI was identified by the existence of ST segment altitude of >1mm in precordial leads or new or presumably new onset LBBB (Hossain *et al*., 2019). Discomfort, heaviness in the chest along with squeezing pain travelling to arms, neck, lower jaw and epigastrium; shortness of breath; weakness; diaphoresis; nausea and lightheadedness were the common evaluator symptoms (Kingma, 2018).

Troponin-I levels were measured by the ELISA method at the laboratory (Chenevier-Gobeaux *et al*., 2011) after 12 and 24 hours of presentation and peak troponin levels were recorded. After 72 hours of hospitalization, LVEF was calculated by means of echocardiography through simplified Simpson's method (Ahmad *et al*., 2013; Minamino-Muta *et al*., 2019). The main outcome variable of the study was to determine the cut off values of serum troponin-I levels, which identifies LVEF of < 50% in patients primary PCI. Both ELISA and echocardiography was performed and recorded by a laboratory technician. In order to minimize bias, the staff physician was not involved in the study.

Treatment plan given

The treatment plan in the emergency department, comprised of 300mg aspirin, clopidogrel 600 mg, parenteral beta blockers as per indications and an initial weight-based bolus of unfractionated heparin (Antman *et al*., 2004). All 150 patients then underwent successful primary PCI and were admitted in the coronary care unit.

Variables included in performa

All the variables including age, gender, history of diabetes (defined as a fasting blood glucose ≥ 126 mg/dl or on treatment) (Raz *et al*., 2009), hyperlipidemia (fasting blood cholesterol ≥ 200mg/dl or on treatment) (Stone and Grundy, 2019), hypertension (systolic blood pressure ≥140/90 mmHg or on treatment) (James *et al*., 2014), smoking, peak troponin-I levels and LVEF (Khan *et al*., 2017) were recorded in the proforma.

Exclusion criteria

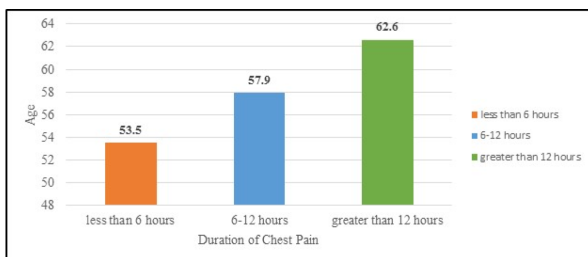
All those with previous history of any cardiac surgery were excluded along with those with any contraindication to reperfusion therapy and other co-morbidities including renal failure and sepsis etc.

STATISTICAL ANALYSIS

The data was analyzed using Statistical package for social sciences (SPSS version 22). The continuous variables to be analyzed from the descriptive statistics were presented as mean ± Standard deviation (S.D). Percentage values were shown for categorical variables. Paired Sample t-test was used for comparison between the dependent variables. After assessment of distribution one way analysis of variance (ANOVA) was done. Binomial testing was applied for relation with co-morbidities and significance of $p \leq 0.05$ was considered significant.

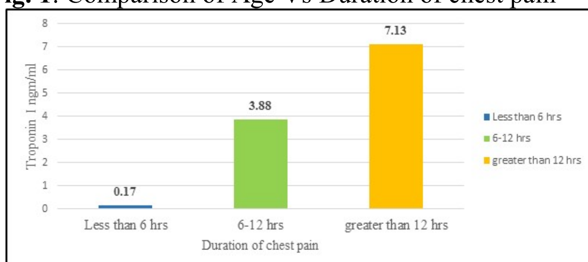
RESULTS

Table 1 shows that the mean ages of the patients enrolled were 59.4. Majority of the patients were male (71%) as compared to females. In terms of age demarcation 4% lied in the range of 20-40 years, 23% of the population lied in the range of 40-50 years and 73% were greater than 50 years. 45% of the population were diabetics, 59% population was hypertensive where as 52% of the population smoked. The data also showed that 60% of the patients reported at emergency department when their chest pain duration exceeded 12 hours. The ejection fraction of 60% population was in the range of 30-50 according to the data.



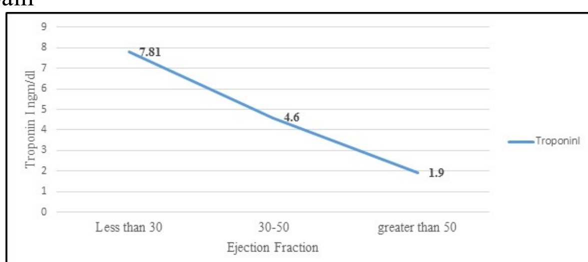
Paired t-test between age and DOA show significant $p \leq 0.05$ relationship

Fig. 1: Comparison of Age Vs Duration of chest pain



Paired t-test between Troponin I and DOC show significant $p \leq 0.05$ relationship

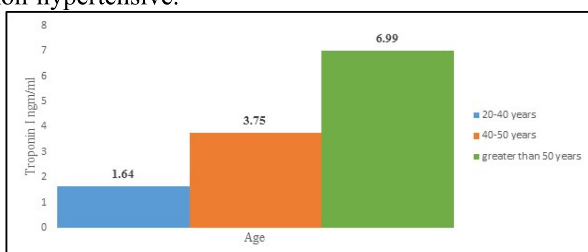
Fig. 2: Comparison of Troponin I Vs Duration of chest pain



Paired t-test between Troponin I and Ejection Fraction show significant $p \leq 0.05$ relationship

Fig. 3: Comparison of Troponin I Vs Ejection Fraction

Table 2 showed the comparison between different co-morbidities. According to the binomial testing applied it showed that the diabetic data was insignificant as compared to non-diabetic population. Similarly the data for smokers was insignificant as compared to non-smokers. However there was a significant difference $p \leq 0.05$ when hypertensive population was compared with non-hypertensive.



Paired t-test between Troponin I and Age show significant $p \leq 0.05$ relationship

Fig. 4: Comparison of Troponin I Vs Age

Table 3 showed the paired t-test comparison between different variables. According to it when duration of chest pain (DOC) was compared with Troponin I a significant relationship $p \leq 0.05$ was observed between them. This was further verified by fig. 2 which shows that as the DOC increases the Troponin I levels also increased. Linear relationship was observed between the two showing a level of 7.13ngm/ml when DOC was greater than 12 hours.

Similarly when Age and DOC were compared a significant $p \leq 0.05$ relationship was observed between the two. Fig. 1 also shows that with increasing age the DOC was higher. At mean age of 62.6 years the duration of chest pain reported was greater than 12 hours. Age was also compared with Troponin I and $p \leq 0.05$ was seen i.e there was a significant relationship reported. Fig. 4 shows a linear relationship between age and Troponin I. The level of Troponin I ascends as the age increases. 6.99 ngm/ml has been reported at age limit greater than 50 years. Ejection Fraction (EF) and Troponin I have also been compared in table III and showed a significant relation between the two variables $p \leq 0.05$. Fig. 3 shows that there is an inverse relationship between the two. As the value of Troponin I increases there is a decline in EF i.e when EF is less 30 the mean Troponin I level is 7.81ngm/ml.

There was insignificant difference between the emergency treatment protocols administered to all the patients. table 4 shows the treatment pattern followed:

DISCUSSION

Table 1 shows that male population was more prone to CHD as compared to female population according to the random population that was observed. Literature studies have also shown that male population are more prone to cardiovascular diseases as compared to female gender (Menotti and Puddu, 2019). Co-morbidities such as smoking (Mac Kenzie *et al*., 2017), diabetes (Rana *et al*., 2016) and hypertension (Chen *et al*., 2017) are considered as risk factors in the development of CHD. Our results show hypertensive data was of significance as compared to other co-morbid conditions.

Troponin I is 100% tissue-specific for myocardium and has been shown to be a highly delicate and specific AMI marker. After an acute coronary syndrome, ventricular function is the best predictor of death. It acts as a myocardial damage marker, providing data on systolic function, diagnosis and prognosis (Kinoshita *et al*., 2018). The diagnosis can be confirmed by recording the transient elevation of the ST-segment (>1mm) during angina on the ECG (Gakidou *et al*., 2017).

Fig. 1 shows comparison of Age versus Duration of Symptoms. Significantly, our result shows increase in the

Table 1: Patient history and demographics

Patients characteristics	MEAN ± S.D
Age (years)	59.4 ±10.7
Patients characteristics	Percentage (%)
Male	71
Age	
20-40 years	4
40-50 years	23
> 50 years	73
Co-morbidities	
Diabetics	45
Smokers	52
Hypertensives	59
Duration of chest pain	
< 6 hours	18
6-12 hours	22
> 12 hours	60
Ejection Fraction	
< 30	10
30-50	60
> 50	30

Table 2: Binomial testing showing effect of Co-morbidities

		Category	Observed Prop.	Test Prop.	Exact Sig. (2-tailed)
Dm	Group 1	Yes	.45	.50	.272
	Group 2	No	.55		
Smoker	Group 1	Yes	.51	.50	.800
	Group 2	No	.49		
Htn	Group 1	No	.41	.50	.034
	Group 2	yes	.59		

Table 3: Paired T-test comparison between the variables

Paired Groups	P- value
Duration of chest pain and Troponin I	0.001
Age and Duration of chest pain	0.003
Age and Troponin I	0.029
Ejection Fraction and Troponin I	0.017

Table 4: Treatment protocol followed in emergency for STEMI

Drug	Dosage
Aspirin	300mg stat
Ticagrelor	180mg stat
Heparin	70-100 units/kg/I/V stat
Atorvastatin	40-80mg stat

duration of symptoms of MI with increasing Age. Among old age population, events of Coronary heart disease (CHD) are well proven as a leading cause of death (Melgarejo-Moreno *et al*., 1999). Presenting acute MI symptoms differs from those present in younger patients than in elderly (Akshata, 2015). It is observed among older patients with acute myocardial infarction (AMI) that although chest pain is the most prevalent symptom, atypical symptoms such as dyspnea, vomiting, sweating, shoulder pain, and epigastric pain may also occur. Previously, several authors stressed the variability in the clinical presentation of AMI in elderly (Go *et al*., 2014).

Fig. 2 shows relation between Age and Troponin I. Age is a strong self-determining risk factor for the development of atherosclerotic disease (Sedighi *et al*., 2019). The

significance of cardiovascular troponin turns out to be considerably more conspicuous in elderly (Wanamaker *et al*., 2019), especially those >80 years of age, for whom secondary diagnostic attributes of ACS such as chest pain, electrocardiography, and biomarkers are frequently inconsistent when trying to eliminate AMI (Kwok *et al*., 2017; Rains *et al*., 2014). Relationship between age, comorbidities and the levels of cardiovascular biomarkers that serve as markers for cardiac events are still under discussion. One of these biomarkers, cardiac troponin, is the best biomarker for myocardial necrosis detection (Cho *et al*., 2020).

Fig. 3 shows relation between Troponin I and Duration of Symptoms. Our result shows Troponin levels of 0.17ng/ml in less than 6 hours, 3.88ng/ml in 6-12 hours and 7.13ng/ml in greater than 12 hours respectively. Cardiovascular Troponin levels are usually so low that they can't be recognized with most blood tests. Most heart attack patients have raised Troponin levels within 6. After 12 hours, nearly everyone who has had a heart attack will have raised levels (Al-Khatib *et al*., 2018). Angina attacks are typically short-lived (2-5 minutes, but sometimes only 30 sec) and more episodes are likely to recur within 20-30 minutes (Gurwitz *et al*., 2013).

Fig. 4 shows relation between Troponin I and Ejection Fraction. According to literature studies, approximately half of patients with clinical heart failure symptoms have a normal or near-normal left ventricular ejection fraction (LVEF), known as heart failure with preserved ejection fraction (HFpEF) (Brouwers *et al*., 2013; Chow *et al*., 2017). Cardiac troponin (cTn) has been recognized as an efficient predictive marker in several domains, together with acute HF exacerbation with a potentially reduced EF (Crespo-Leiro *et al*., 2018). In fig. 4, our result shows well defined reduction in ejection fraction with increased levels of Troponin I.

Table 4 shows treatment protocol given to the STEMI patients in the accident and emergency department. The GDMT (guide line directed medical therapy) was defined as administration of aspirin, a $P2Y_{12}$ inhibitor (clopidogrel, prasugrel, or ticagrelor), and an anticoagulant (low-molecular weight or unfractionated heparin before sheath; low-molecular weight heparin, unfractionated heparin, or bivalirudin before completion of PCI) and statin (high intensity either Atorvastatin 40-80mg p/o stat or Rosuvastatin 20-40mg p/o stat) (Huded *et al*., 2018). From our study it was determined that elderly population is at the highest stake since they do not take chest pain as seriously as it should be taken.

CONCLUSION

It was seen that in Pakistani population people greater than 50 years tend to present to emergency department late with chest pain symptoms which results in a linear rising relationship with Troponin I and with increasing Troponin I, there was a significant reduction seen in LVEF (p value <0.005)

The key message is to create awareness amongst population older than 50 years about the importance of chest pain and how it should be approached early in order to decrease coronary disease morbidity

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