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Elevation of Cardiac Biomarker Signposts the Risk on Renal Disease

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Abstract: *Myocardial infarction is a primary cause of death and disability in worldwide. Myocardial infarction may occur with atypical symptoms, or even without symptoms, being detected only by ECG, biomarker elevations, or cardiac imaging. The patients who are hospitalized for ST segment elevation of MI are subjective to several complications and interventional processes related with AKI, such as cardiogenic shock, heart failure, cardiac catheterization, and coronary artery bypass surgery. In this study to assess the ability of troponin-T and NT-pro BNP in primary detection of acute myocardial infarction and to assess the role of urea, creatinine and potassium to find out the risk factors of acute kidney injury in acute myocardial infarction. Randomly 60 myocardial infarction patients (40male: 20female) samples were analysed. The severity of MI compared the age between (50y-70y) found to be increased then the other age categories and it concludes that severity of myocardial infarction is based on the age but not gender biased. Development of acute kidney injury in acute myocardial infarction patients were based on the life style habits, stress and treatment based on procedures followed in the hospital.*

Key Words: *Cardiac Diseases, MI, NT-ProBNP, Renal Disease, Trop-T.*

1. INTRODUCTION:

Myocardial infarction (MI), typically called a heart attack, occurs when blood flows or ceases to a portion of the heart, causing heart muscle damage. Myocardial infarction is a primary cause of death and disability in worldwide. Coronary atherosclerosis is a long-standing disease with stable and unstable periods. Inflammation was activated in the vascular wall throughout unstable periods, the event it may unexposed, but the event it may be a primary catastrophic leading to sudden death or severe hemodynamic deterioration. However, the current clinical practice, health care delivery systems, as well as epidemiology and clinical trials all require understanding more about of the myocardial infarction. Identify of ever a smaller amount of myocardial necrosis precisely with the help of available serological specific biomarkers, the way of accuracy of detecting myocardial infarction has changed. Such changes occurred when glutamine-oxaloacetic transaminase (GOT) was replaced by lactate dehydrogenase (LDH) and later by Creatine kinase (CK) and the MB fraction of CreatineKinase(CKMB) activity and CKMB mass (Thygesen et al., 2018) The term myocardial infarction considers cell death of cardiac myocytes caused by ischaemia, which is caused by the perfusion imbalance between supply and demand. The clinical environment of Ischaemia can be identified from the history of patient‘s and also from the Electro Cardio Gram (ECG).Possible ischaemic signs include different combinations chest, upper extremity, jaw, or epigastric discomfort with exertion or at rest. The discomfort associated with acute myocardial infarction usually lasts at least 20 min (Thygesen et al., 2018). Myocardial infarction may occur with atypical symptoms, or even without symptoms, being detected only by ECG, biomarker elevations, or cardiac imaging (Tamis-Holland et al., 2019). Myocardial infarction classified into five types those are known as Type 1 Spontaneous Myocardial Infarction.Type 2 Secondary Myocardial Infarction of Ischaemic Imbalance. Type 3 Cardiac Death Due to Myocardial Infarction.Type 4a Percutaneous Coronary Intervention (PCI) associated Myocardial Infarction. Type 4b Stent thrombosis-associated Myocardial infarction as confirmed by angiography or autopsy. Type 5 Myocardial infarction associated with CABG (Tamis-Holland et al., 2019)

Biomarkers for myocardial cell death can be identified by the presence of specific proteins which released into the blood circulation from the damaged myocytes, which includes myoglobin, cardiac troponin T (first assessment 6–9 h later onset of symptoms) and I, CK, LDH, (12 and 24 h later onset of symptoms) as well as many others (Baker et al., 2019). Myocardial infarction is diagnosed when blood levels of sensitive and specific biomarkers increased in the clinical state of acute myocardial ischaemia (Thygesenet al., 2018). Diagnosis of Acute Myocardial infarction is critical for the initiation of effective evidence-based medical treatment and management (Aroesty et al., 2019). Electro cardiography (ECG) and measurement of cardiac troponins are the current diagnostic cornerstones (Hedayati et al., 2018; Aroesty et al., 2019). ECG by itself is often insufficient to diagnose an acute myocardial infarction, Cardiac troponins, which are structural proteins unique to the heart, are sensitive and specific biochemical markers of myocardial damage (Katus et al., 2018;Khan 2018).The major drawback of standard cardiac troponin assays is their poor sensitivity when presenting a patient, due to a delayed increase in cardiac troponin circulation levels (Khan 2018; Aroesty et al., 2019). They plays an important role in clinical practice to identifying acutecoronary syndromes patients, who are at high risk and benefits of early diagnostic strategy is to escape from the rich and glycoprotein IIb/IIIa blockage (Eggers et

al., 2017; Kocharet al., 2018; Thiele et al., 2019; Sorbets et al., 2020). In addition, cardiac troponin levels are higher than all other clinically available biomarkers, including myoglobin, Creatine kinase (CK-MB), myeloperoxidase, and cardiac fatty acid-binding protein, for the diagnosis of acute myocardial infarction (Eggers et al.,2017; Thiele et al., 2019; Klüser et al., 2019 and Wang et al., 2020). The diagnosis of acute myocardial infarction requires prolonged monitoring over a period of 6 to 12 hours and with the serial blood sampling. A delay in confirming a diagnosis of acute myocardial infarction may increase the risk of complications associated with the condition B-type natriuretic peptide (BNP) is a vasoactive hormone synthesized and secreted by the heart in response to increased left ventricular wall tension (Mclellan et al., 2016).The diagnostic and prognostic utility of BNP measures was first seen while setting heart failure, (Zile et al., 2016), Increased BNP concentrations are an free predictor of mortality in Acute Coronary Syndromes patients (Mclellan et al., 2016). After acute myocardial infarction, levels of B-type natriuretic peptide rise rapidly during the first 24 hours and then move to stabilize (Shiraishi et al., 2016 ; Olivier et al., 2017 ; Narang et al., 2018 ; Pandey 2019) the Risk factors for acute myocardial infarction individuals of south Asian descent (India, Pakistan, and Bangladesh) have an increased risk of ischaemic heart disease (IHD) compared with most other ethnic groups(Mongraw-Chaffin et al., 2018; Volgman et al., 2018; Narang et al., 2018). Because the prevalence of conventional risk factors such as smoking, hypertension, and hypercholesterolemia is no higher in south Asians than in other ethnic groups (Shridhar et al., 2018; Volgman et al., 2018 ; Leppert et al., 2019). High triglyceride concentrations, low concentrations of high density-lipoprotein (HDL) cholesterol, increased visceral fat, and insulin resistance are more prevalent among south Asians, and these factors have been proposed as reasons for the higher risk of (Volgman et al., 2018 ; Vaideeswar et al., 2019).

Treatment Blockage of the vessel is usually caused by thrombus formation and timely treatment with thrombolytic drugs such as streptokinase has enhanced the immediate and longer-term outlook following acute myocardial (Zhang et al., 2019 ; Safi et al., 2020). The global utilization of streptokinase and tPA for occluded arteries trial showed that tissue plasminogen activator may be better than streptokinase in those patients who are younger, present earlier, have anterior infarction, and who have been given streptokinase for a previous myocardial infarction (GUSTO Investigators., 1993). Aspirin can also use as thrombolytic drugs, although its action is unclear and may not be entirely related to its anticoagulant effects. Lifelong treatment with aspirin after myocardial infarction was generally accepted. Angioplasty is a new thrombolytic drug are available commercially now, it is unlikely that TIMI grade 3 patency rates will ever be greater than 70-80% nor that the high reocclusion rates will improve. Angioplasty undertaken within 12 hours of onset of chest pain has been shown to improve clinical outcome in comparison to thrombolysis. The present study is designed with this background to assess the role of cardiac markers in the risk assessment of acute myocardial infarction (AMI).

2. MATERIALS& METHODS:

AU480 Fully automated clinical chemistry analyzer (Beckman Coulter), h 232 Cardiac Biomarker analyzer (Cobas), Electrolyte analyzer (Biolyte2000), Centrifuge, Micropipettes, Becton Dickinson (BD) Vacutainers and BD eclipse needles.

3. SAMPLE COLLECTION:

Blood samples are collected from the age between (35y-85y) in Billroth Hospital as per the ISO 15189: 2012 protocol and the study is approved by the institutional Ethics committee BEC/2019 M.Sc.,/007. Blood samples were taken into the Becton Dickinson (BD) Vacutainer® plain gel and Heparinized tubes for highly sensitive parameters such as Troponin-T and NT-pro BNP. Samples are (plain tubes - Yellow) allowed to clot and centrifuged at 5000 rpm for 20 min; the obtained serum was used to analyse basic biochemical parameters such as Urea, Creatinine and potassium.

3.1. Estimation of Troponin-T by Roche Cardiac Quantitative Troponin-T (Wang et al., 2018):

The test strip consists of two monoclonal cardiac troponin T (cTnT) specific antibodies, one is gold-labeled and the other is biotinylated. With the cTnT in the blood, the antibodies form a sandwich complex. After the erythrocytes are separated from the sample, the plasma moves through the detection zone where the gold-labeled cTnT sandwich complexes accumulate and the positive signal is displayed. Excess gold labeled antibodies accumulate along the control line, signalling that the test was valid. The intensity of the signal line increases is proportion to the troponin T concentration. Cobas h232 optical device detects the two lines and tests the signal line strength. The integrated software converts the signal intensity to a quantitative result as value and displayed in screen.

3.2. *Estimation of N-terminal pro BNP with the Roche Cardiac Quantitative pro BNP:*

The test consists of one monoclonal and one polyclonal antibody counter epitopes of the NT-pro BNP molecule of which one was gold-labeled. The antibodies from a sandwich complex with the NT-pro BNP in the blood, which moves through the detection zone where the NT-pro BNP sandwich complexes marked with gold accumulate and the positive signal is shown as a reddish line (signal line). Excess gold-labeled antibodies accumulate along the control line then only the test was valid.The signal line strength increases in proportion to the NT-pro BNP concentration and which the optical device shows the effects on the screens detect.

3.3. ***Estimation of the urea by Urease:***

Urea is hydrolysed to create ammonia and carbon dioxide, in the presence of water and urease. The free ammonia in an alkaline pH and in the presence of markers produces a complex color in proportion to the concentration of urea in the specimen.

3.4. Estimation of Creatinine by the Jaffe's (Singh et al., 2019):

Picric acid combines with creatinine in an alkaline medium to form an orange colored complex with the alkaline picrate. Intensity of the color formed during the fixed time is directly proportional to the amount of Creatinine present in the sample.

3.5. Estimation of the potassium by Turbidimetric:

Potassium reacts with sodium tetra phenyl boron resulting in an insoluble turbid suspension. The formation of turbidity is measured at 630nm and is proportional to the concentration of the potassium in the sample.

4. RESULTS:

Results were obtained by the relevant methods, the ability of troponin-T and NT-pro BNP in detection of acute myocardial infarction was assessed

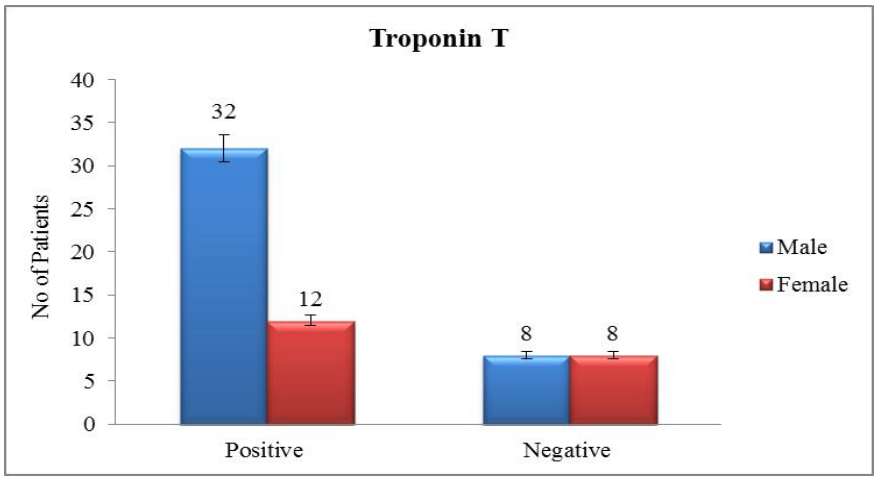

Figure 1: Assessment of Troponin-T values based on gender

Fig. 1: represents the difference of Troponin-T positive and negative for male and females. On X-axis indicates the troponin-T positive and troponin-T negative and Y-axis indicates total number of patients. On X-axis first bar represents 32 male patients (53%) and second bar represents 12 female patients (20%) are tested to troponin-T positive. Third and fourth bar represents respectively 8 male patients (13%) and 8 female patients (13%) are tested to troponin-T negative. Troponin-T positive male shows higher incidence while compare with the positive female. For negative Troponin-T shows no significant difference based on the gender bias

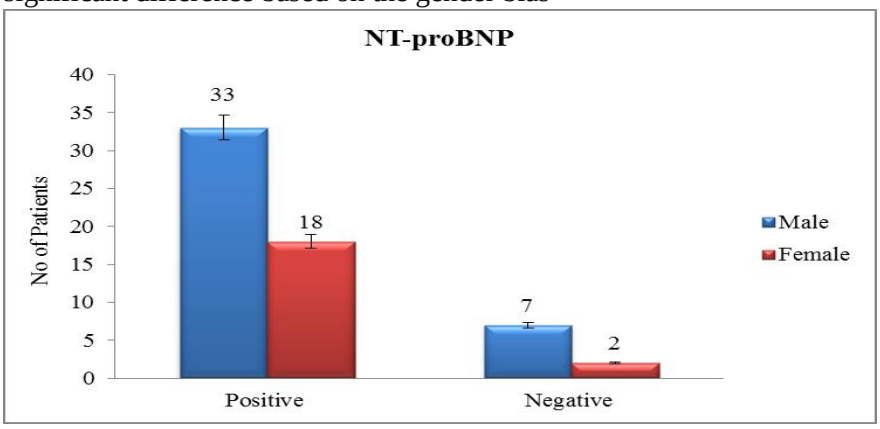

Figure 2: Assessment of NT-pro BNP values based on gender

Fig. 2: represents the difference of NT-pro BNP positive and negative for male and female patients. X- axis indicates positive and negative of NT-pro BNP. Y-axis indicates the total number of patients. On X- axis first bar represents 33 male patients (55%) are tested to positive of NT-pro BNP and second bar represents 18 female patients (30%) are tested to positive of NT-pro BNP. Third and fourth bar represents respectively 7 female patients (11%) and 2 female patients (3%) are tested to NT-pro BNP negative. NT- pro BNP positive for male shows higher incidence while compare with female positive cases whereas negative for NT-pro BNP have a significance difference while compare with male and female patients.

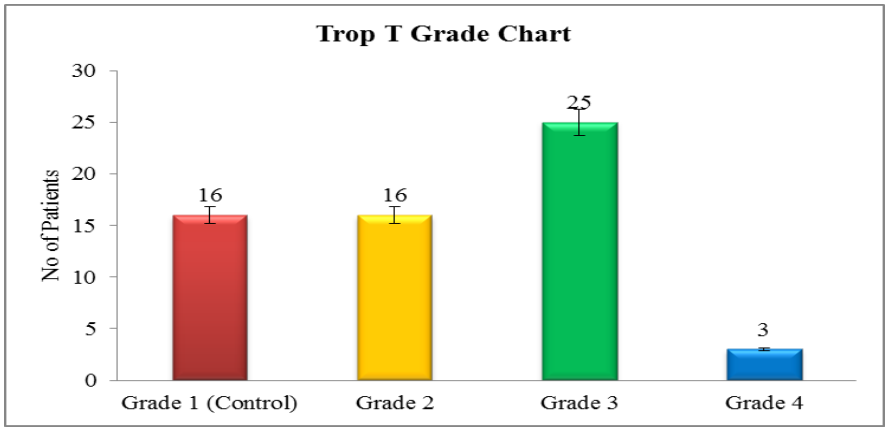

Figure 3: Evaluation and grading of Troponin T levels in a random Analysis of Cardiac risk patients

Fig. 3: represents the grading of Troponin-T positive as Grade I Considered as <50 ng/L Acute myocardial infarction not likely but still possible in context of clinical assessment repeat the test (eg: after 3-6h) to detect rising Troponin-T levels, Grade II Considered as 50100 ng/l AMI possible, Grade III Considered as 100-2000 ng/L AMI likely, Grade IV Considered as above 2000 ng/L AMI very likely. Above all grades, Grade III is considered to be high while compare with grade I, II, and IV.

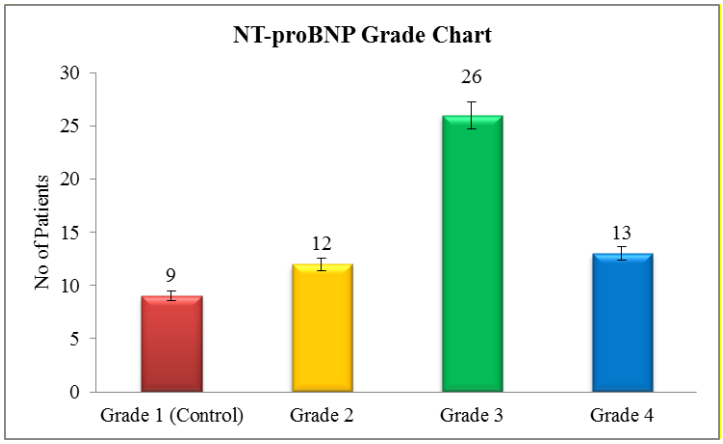

Figure 4: Evaluation and grading of NT-pro BNP levels in a random analysis of Cardiac risk patients

Fig. 4: represents the grading of NT-pro BNP as Grade I consider as < 125 pg/ml Exclusion of non- acute heart failure, Grade II consider as < 300 pg/ml Exclusion of acute heart failure, Grade III and Grade IV are classified based on consideration of age-stratified cut-points for diagnosis that is (< 50 y: >450 pg/ml, 50 - 75 y: >900 pg/ml, >75 y: >1800 pg/ml). Above all the grades, Grade III is considering to be high while compare with grade I, grade II and grade IV.

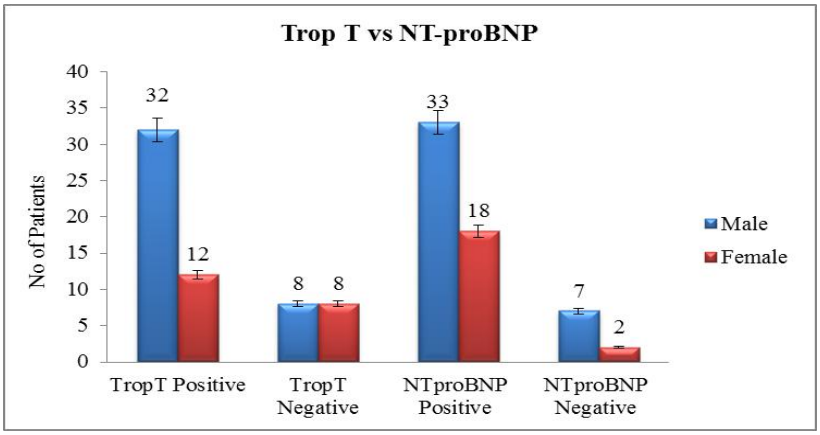

Figure 5: Gender based risk assessment of Troponin-T and NT-pro BNP

Fig. 5: represents the gender biased risk assessment of Troponin-T and NT-pro BNP. Set one indicates the Troponin-T positive of male and female and set three indicates the NT-proBNPpositive of male and female. While compare with positive cases of Troponin-T versus NT-pro BNP. There is no significance difference. Since cases of higher incidence and high values of Troponin-T patients shows increased value of NT-pro BNP. As in the negative case shows the significant difference.

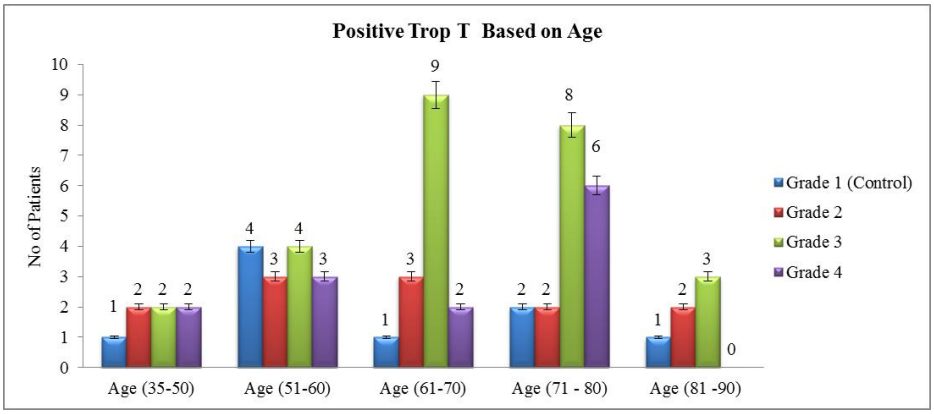

Figure 6: Age wise cardiac risk assessment based on Troponin-T

Fig.6: Each bar represents the number of patients of cardiac risk assessment by using Troponin T positive based on age criteria.

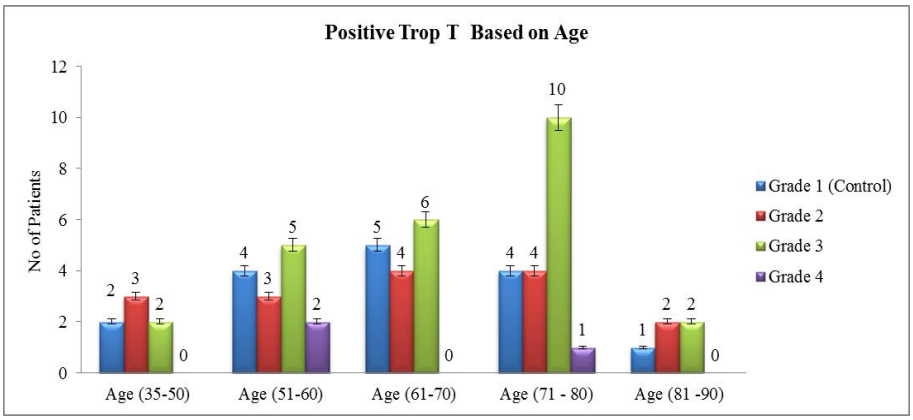

Figure 7: Age wise cardiac risk assessment based on NT-pro BNP

Fig.7: Each bar represents the number of patients of cardiac risk assessment by using NT-pro BNP positive based on age criteria.

Table 1: Positive renal marker values:

S.No	AGE	GENDER	UREA(mg/dl)	CREATININE(mg/dl)
1.	74y	Male	77	1.84
2.	65y	Male	67	2.14
3.	67y	Female	53	1.23
4.	72y	Male	90	3.15
5.	81y	Female	60	1.92
6.	77y	Male	134	3.1
7.	74y	Male	87	2.93
8.	76y	Male	71	1.55
9.	59y	Male	106	1.72
10.	62y	Male	68	1.7
11.	60y	Female	52	1.13
12.	78y	Male	148	2.32
13.	61y	Male	60	2.59
14.	52y	Male	174	2.74
15.	78y	Female	47	2.31
16.	61y	Female	75	2.15
17.	74y	Male	55	1.54
18.	51y	Male	71	1.4
19.	67y	Male	73	1.27
20.	85y	Female	57	0.74
21.	63y	Female	86	1.24

22.	77y	Female	122	3.21
23.	57y	Female	48	1.43
24.	56y	Male	51	1.84
25.	42y	Male	87	2.52

Based on the deviation (or) values exceeds the biological reference (urea: 14-40 mg/dl), (Creatinine: 0.5-1.2 mg/dl) is considered as positive for Renal failure. The value within the reference value is considered as negative for renal failure. Out of 60 patients 25 patients we considered as positive for renal injury.

Table 2. Correlation of cardiac marker (Troponin-T) with renal markers

TROP T	RENAL MARKER(urea, creatinine)		TOTAL
	Positive	Negative	
Positive	19	25	44
Negative	06	10	16

Table 2 : It represents 19 patients (31%) were tested positive for Troponin-T and 25 patients (41%) were tested negative for troponin-T and renal markers (urea, Creatinine). Second column it represents 6 patients (10%) were tested negative for troponin-T and tested positive for renal markers (urea, Creatinine), and 10 patients (16%) were tested negative for troponin-T and renal markers (urea, Creatinine).

Table 3: Correlation of cardiac marker (NT-pro BNP) with renal markers

NT-Pro BNP	RENAL MARKER		TOTAL
	Positive	Negative	
Positive	25	26	51
Negative	0	09	09

Table 3: It represents 25 patients (41%) were tested positive for NT-ro BNP and renal markers (urea, creatinine) and 26 patients (43%) were tested positive for NT-pro BNP and negative for renal markers (urea, creatinine) negative. Second column represents no one having NT-pro BNP negative and renal markers (urea, creatinine) positive and 9 patients (15%) were tested negative for NT-pro BNP and renal markers (urea, creatinine).

5. DISCUSSION:

In this study to identify the role of cardiac biomarkers (Troponin T, NT-pro BNP) and renal markers (urea, Creatinine and potassium) for diagnosis of myocardial infarction. Myocardial infarction (MI) is a major cause of death and disability in worldwide. The minor event in undetected state of MI which shows a lifelong chronic disease and major catastrophic event of MI leading to sudden death or severe hemodynamic deterioration (Thygesen *et al*., 2018). Myocardial cell death can be identified by the appearance of different proteins in the circulation which is released from damaged myocytes, myoglobin, cardiac troponin T and I, CK, LDH, as well as many others(Baker *et al*., 2019). Biochemical markers of myocardial damage play a key role in the diagnosis and risk stratification of acute coronary syndromes. mainly cardiac troponins (cTn) are the most specific and sensitive indicators of myocardial damage (Katus *et al*., 2018). An increased blood level of troponins particularly cTnT, also predicts a less favorable outcome in patients with acute coronary syndromes (Ibanez *et al*., 2018). Obling *et al*.,(2018) described that patients hospitalized for ST segment elevation of MI are subjective to several complications and interventional procedures associated with AKI, such as cardiogenic shock, heart failure, cardiac catheterization, and coronary artery bypass surgery. Natriuretic peptides are mainly formed inside the heart and released into circulation in response to increased stress in the wall. In comparison to the atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) is not only secreted from the atria but also from the ventricles, particularly in heart failure patients (Yasue *et al*., 1994). Circulating concentrations of several cardiac natriuretic peptides including ANP, BNP, and their N-terminal pro-hormones are raised in both symptomatic and asymptomatic patients with left ventricular dysfunction(Brunner-La *et al*., 2019). Recent studies in the detection of left ventricular dysfunction propose that BNP and NT-pro BNP may be superior to ANP and NT-pro ANP(Shah *et al*., 2019).

Acute renal failure (ARF) is seen commonly in the perioperative period and in the Intensive Care Unit (ICU). It is associated with a high morbidity and mortality (oliguric 50- 80% and non-oliguric 10-40%) (Peregrín*et al.*, 2019; Rangaswami *etal.*, 2019).Therefore, it is important to either avoid or acknowledge its presence and handle it as soon as possible and as efficiently as possible. Urea and Creatinine are good indicators of a normal functioning of the kidney and increase of the substances in the serum are indications kidney dysfunction, although several factors such as excessive protein intake, shock, gastrointestinal hemorrhage etc., (Aroesty *et al*., 2019). Blood urea levels are quite sensitive indicators of renal disease, becoming elevated when renal function drops to around 25-50% of normal

(Cardenas-Gonzalez *et al*., 2018; Qian *et al*., 2019). Creatinine levels slightly increased due to damage to the kidney and with this; there was reduced glomerular filtration rate due to inflammation of the kidney (Chevalier., 2016). When gender wise compared for both male and female, male showed slightly higher Creatinine level than the female. This result is supported by various researchers who showed that high serum Creatinine level was seen in males than females, which could be because of storage of Creatinine as a waste product in muscle mass and the presence of high muscle mass in males (Roshanravan *et al*., 2017). Development of Acute Kidney Injury (AKI) after ST-segment Elevation Myocardial Infarction (STEMI) has been regarded as an important issue in patients with STEMI because of the increased in-hospital and long-term mortality and subsequent risk of End Stage Renal Disease (ESRD) (Chalikias *et al*., 2019) observed that the associated risk factors of AKI in these settings, including use of contrast agents, diabetes, previous kidney disease, hemodynamic instability, low cardiac output, and volume depletion. Deterioration of renal function following acute alterations in cardiac function due to Acute Decompensated Heart Failure (ADHF) or acute coronary syndrome (ACS) is classified as type 1 CRS (Ronco et al., 2019), it has been proposed that cardiac dysfunction and hemodynamic perturbations could result in systemic under filling and renal hypo perfusion, leading to further renal injury. The present study is also reflected the result that the MI patients are more prone to the renal injury (Ronco *et al*., 2019), however, there is increasing evidence that it may be venous congestion rather than arterial under filling that is associated decreasing renal blood flow and worsening renal function. (Zile *et al*., 2016), given its association with capillary wedge pressure and venous congestion, BNP has been demonstrated to be an indirect marker for worsening renal function in ADHF (Rangaswami *et al*., 2019).

In addition to the hemodynamic effects of myocardial injury, the activation of the immune and the sympathetic nervous system as well as hormonal factors have been suggested as underlying mechanisms of cardio-renal syndrome(Tung et al., 2015)189 STEMI patients were sequentially enrolled and serum samples were collected at presentation for B-type Natriuretic peptide, soluble ST2, Neutrophil Gelatinase Associated Lipocalin and cystatin C analysis. Thirty-seven patients (19.6 per cent) developed AKI of varying severity within 48 hours. Hypertension, white blood cell counts, hemoglobin, estimated glomerular filtration rate, blood urea nitrogen, creatinine, and all four biomarkers were AKI predictive. Serum levels of the biomarkers were correlated with risk of AKI and the Acute Kidney Injury Network (AKIN) stage and all significantly discriminated AKI. In this study also25 patients developed AKI out of 60 patients after affecting the myocardial infarction similar to previous studies. That reveals 41% of people affected with acute renal injury out of 100% among 25 patients 16 male patients (26%) and 9 females patients (15%) were affected with acute renal injury(Qian *et al*., 2019).

6. CONCLUSION:

In this study to assess the ability of troponin-T and NT-pro BNP in primary detection of acute myocardial infarction and to assess the role of urea, creatinine and potassium to find out the incidence and risk factors of acute kidney injury in acute myocardial infarction. Randomly 60myocardial infarction patients (40 male: 20female) samples were used for this study. The severity of MI compared the age between (50y-70y) found to be increased then the other age categories. We can conclude that severity of myocardial infarction is based on the age but not gender biased. Definite possibility to develop acute kidney injury in acute myocardial infarction patients is high whereas it also includes the life style, social habits, comorbidity diseases, stress and treatment and procedures followed in the hospital during and post treatment of myocardial infarction.

CONFLICT OF INTEREST: Nil

REFERENCES

1. Baker P., Leckie T., Harrington D., Richardson A, (2019): Exercise-induced cardiac troponin elevation: An update on the evidence, mechanism and implications. *IJC Heart & Vasculature*, *22*, 181-186.
2. Brunner-La Rocca H. P., and Sanders-van Wijk S. (2019): Natriuretic peptides in chronic heart failure. *Cardiac failure review*, *5*(1), 44.
3. Cardenas-Gonzalez M., Pavkovic M., Vaidya V.S, (2018): Biomarkers of acute kidney injury.
4. Chalikias G., Serif L., Kikas P., Thomaidis A., Stakos D., Makrygiannis D., Chatzikyriakou S, Papoulidis N., Voudris V., Lantzouraki A., Müller M., Arampatzis S., Konstantinides S., Tziakas D (2019): Long-term impact of acute kidney injury on prognosis in patients with acute myocardial infarction. *International journal of cardiology*, *283*, 48-54.
5. Chevalier R. L, (2016): The proximal tubule is the primary target of injury and progression of kidney disease: role of the glomerulotubular junction. *American Journal of Physiology-Renal Physiology*, *311*(1), F145-F161.
6. Eggers K. M, and Lindahl B, (2017): Prognostic biomarkers in acute coronary syndromes: risk stratification beyond cardiac troponins. *Current cardiology reports*, *19*(4), 29.
7. Ibane, B., James S., Agewall S., Antunes M. J., Bucciarelli-Ducci, C., Bueno H., Hindricks G, (2018) : 2017 ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment

elevation: The Task Force for the management of acute myocardial infarction in patients presenting with ST-segment elevation of the European Society of Cardiology (ESC). *European heart journal*, *39*(2), 119-177.

8. Katus H. A., and Giannitsis, E, (2018): Prognostic Value of Serum Troponin T in Unstable Angina. *Clinical chemistry*, *64*(2), 396-397.
9. Khan M. H, (2018): TCTAP A-128 Raised Level of Cardiac Troponin I (50 Folds Upper Limit of Normal) Is a Sensitive and Specific Marker for Extent of Coronary Artery Disease in First Attack of Non-ST Segment Elevation Myocardial Infarction in Bangladeshi Population.
10. Khan M. H, (2019). Raised Level of Cardiac Troponin I (50 Folds Upper Limit of Normal) is a Sensitive and Specific Marker for Extent of Coronary Artery Disease in First Attack of Non-ST Segment Elevation Myocardial Infarction in Bangladeshi Population. *EC Cardiology*, *6*, 754-760.
11. Klüser L., Maier E. T., Wess G. (2019): Evaluation of a high-sensitivity cardiac troponin I assay compared to a first-generation cardiac troponin I assay in Doberman Pinschers with and without dilated cardiomyopathy. *Journal of veterinary internal medicine*, *33*(1), 54-63.
12. Kochar A., Chen A. Y., Sharma P. P., Pagidipati N. J., Fonarow G. C., Cowper P. A., Wang T. Y, (2018): Long-term mortality of older patients with acute myocardial infarction treated in US clinical practice. *Journal of the American Heart Association*, *7*(13), e007230.
13. Leppert M. H., Poisson S. N., Sillau S. H., Campbell J. D., Ho P. M., and Burke J. F, (2019): Is Prevalence of Atherosclerotic Risk Factors Increasing Among Young Adults? It Depends on How You Ask. *Journal of the American Heart Association*, *8*(6), e010883.
14. Aroesty M., Julian S., Simons M., Breall JA., (2019): "Overview Of The Acute Management Of Non-ST Elevation Acute Coronary Syndromes." *UpToDate*.
15. McLellan J., Heneghan C. J., Perera R., Clements A. M., Glasziou P. P., Kearley K. E., Bankhead C, (2016): B-type natriuretic peptide-guided treatment for heart failure. *Cochrane database of systematic reviews*, (12).
16. Mongraw-Chaffin M., Gujral U. P., Kanaya A. M., Kandula N. R., Carr J. J., Anderson C. A, (2018): Relation of Ectopic Fat with Atherosclerotic Cardiovascular Disease Risk Score in South Asians Living in the United States (from the Mediators of Atherosclerosis in South Asians Living in America [MASALA] Study). *The American journal of cardiology*, *121*(3), 315-321.
17. Narang U., Gupta A., Gupta S., Gupta N., Joshi S., Sharma S, (2018): Risk factors and demographic profile in acute myocardial infarction: a prospective study from tertiary care rural hospital in North India. *International Journal of Contemporary Medical Research*, *5*(6), F14-F21.
18. Obling L., Frydland M., Hansen R., Møller-Helgestad O. K., Lindholm M. G., Holmvang L., Kjærgaard J, (2018). Risk factors of late cardiogenic shock and mortality in ST-segment elevation myocardial infarction patients. *European Heart Journal: Acute Cardiovascular Care*, *7*(1), 7-15.
19. Olivier A., Girerd N., Michel J. B., Ketelslegers J. M., Fay R., Vincent J., EPHESUS Investigators. (2017): Combined baseline and one-month changes in big endothelin-1 and brain natriuretic peptide plasma concentrations predict clinical outcomes in patients with left ventricular dysfunction after acute myocardial infarction: Insights from the Eplerenone Post-Acute Myocardial Infarction Heart Failure Efficacy and Survival Study (EPHESUS) study. *International journal of cardiology*, *241*, 344-350.
20. Pandey K. N, (2019): Genetic Ablation and Guanylyl Cyclase/Natriuretic Peptide Receptor-A: Impact on the Pathophysiology of Cardiovascular Dysfunction. *International journal of molecular sciences*, *20*(16), 3946.
21. Peregrín C. M, (2019): "Acute Renal Failure (I)." *Medicine (Spain)*.
22. Qian H., Tang C., Yan G, (2019): Predictive value of blood urea nitrogen/creatinine ratio in the long-term prognosis of patients with acute myocardial infarction complicated with acute heart failure. *Medicine*, *98*(11).
23. Rangaswami J., Bhalla V., Blair J. E., Chang T. I., Costa S., Lentine K. L., Ronco C, (2019): Cardiorenal syndrome: classification, pathophysiology, diagnosis, and treatment strategies: a scientific statement from the American Heart Association. *Circulation*, *139*(16), e840-e878.
24. Ronco C., Bellasi A., Di Lullo L, (2019): Implication of Acute Kidney Injury in Heart Failure. *Heart failure clinics*, *15*(4), 463-476.
25. Roshanravan B., Gamboa J., Wilund K, (2017): Exercise and CKD: skeletal muscle dysfunction and practical application of exercise to prevent and treat physical impairments in CKD. *American Journal of Kidney Diseases*, *69*(6), 837-852.
26. Safi M., Serati A., Emami S., Movahed M. R, (2020). Coronary dissection with ST elevation myocardial infarction responding to thrombolytic and conservative therapy alone. *Future Cardiology*, Mar 31. doi: 10.2217/fca-2018-0071.
27. Shah A. M., Cikes M., Prasad N., Li G., Getchevski S., Claggett B., Rizkala A., Lukashevich I., O'Meara E., Ryan J.J., Shah S.J., Mullens W., Zile M.R., Lam C.S.P., McMurray J.J.V., Solomon S.D. PARAGON-HF Investigators. (2019): Echocardiographic features of patients with heart failure and preserved left ventricular ejection fraction. *Journal of the American College of Cardiology*, *74*(23), 2858-2873.

28. Shiraishi Y., Kohsaka S., Abe T., Mizuno A., Goda A., Izumi Y., Yagawa M, Akita K, Sawano M., Inohara T., Takei M., Kohno T., Higuchi S., Yamazoe M., Mahara K., Fukuda K., Yoshikawa T., West Tokyo Heart Failure Registry Investigators. (2016): Validation of the Get with the Guideline–Heart Failure risk score in Japanese patients and the potential improvement of its discrimination ability by the inclusion of B-type natriuretic peptide level. *American heart journal*, *171*(1), 33-39.
29. Shridhar K., Satija A., Dhillon P. K., Agrawal S., Gupta R., Bowen L., Kinra S, Bharathi A.V., Prabhakaran D., Srinath Reddy K., Ebrahim S., Indian Migration Study group. (2018): Association between empirically derived dietary patterns with blood lipids, fasting blood glucose and blood pressure in adults-the India migration study. *Nutrition journal*, *17*(1), 15.
30. Singh R., Bhalla K., Nanda S., Gupta A., Mehra S, (2019): Correlation of spot urinary protein: Creatinine ratio and quantitative proteinuria in pediatric patients with nephrotic syndrome. *Journal of family medicine and primary care*, *8*(7), 2343.
31. Sorbets E., and Steg P. G, (2020): Direct-acting Anticoagulants in Chronic Coronary Syndromes. *European Cardiology Review*, *15*, 1.
32. Tamis-Holland J. E., Jneid H., Reynolds H. R., Agewall S., Brilakis E. S., Brown T. M., Lerman A., Cushman M., Kumbhani D.J., Arslanian-Engoren C., Bolger A.F., Beltrame J.F.; American Heart Association Interventional Cardiovascular Care Committee of the Council on Clinical Cardiology; Council on Cardiovascular and Stroke Nursing; Council on Epidemiology and Prevention; and Council on Quality of Care and Outcomes Research. (2019): Contemporary diagnosis and management of patients with myocardial infarction in the absence of obstructive coronary artery disease: a scientific statement from the American Heart Association. *Circulation*, *139*(18), e891-e908.
33. Thiele H., Zeymer U., Thelemann N., Neumann F. J., Hausleiter J., Abdel-Wahab M., Meyer-Saraei R, Fuernau G., Eitel I., Hambrecht R., Böhm M., Werdan K., Felix S.B., Hennersdorf M., Schneider S., Ouarrak T., Desch S., de Waha-Thiele S.; IABPSHOCK II Trial (Intraaortic Balloon Pump in Cardiogenic Shock II) Investigators. (2019).Intraaortic balloon pump in cardiogenic shock complicating acute myocardial infarction: long-term 6-year outcome of the randomized IABP-SHOCK II trial. *Circulation*, *139*(3), 395-403.
34. Thygesen K., Alpert J. S., Jaffe A. S., Chaitman B. R., Bax J. J., Morrow D. A., Bucciarelli-Ducci C, (2018): Fourth universal definition of myocardial infarction. *European heart journal*, *40*(3), 237-269
35. Tung Y. C., Chang C. H., Chen Y. C., Chu, P. H, (2015): Combined biomarker analysis for risk of acute kidney injury in patients with ST-segment elevation myocardial infarction. *PloS one*, *10*(4).
36. Vaideeswar P., Tyagi S., Singaravel S, (2019): Pathology of atherosclerotic coronary artery disease in the young Indian population. *Forensic sciences research*, *4*(3), 241-246.
37. Volgman A. S., Palaniappan L. S., Aggarwal N. T., Gupta M., Khandelwal A., Krishnan A. V., Shah S. H, (2018): Atherosclerotic cardiovascular disease in South Asians in the United States: epidemiology, risk factors, and treatments: a scientific statement from the American Heart Association. *Circulation*, *138*(1), e1-e34.
38. Wang J., Fang Y., Li P., Lin H., Jin H., Gao L., Zhang Z. Y, (2018): Evaluation of a newly developed chemiluminescence immunoassay for detecting cardiac troponin T. *Journal of clinical laboratory analysis*, *32*(3), e22311.
39. Wang X. Y., Zhang F., Zhang C., Zheng L. R., Yang J. (2020): The Biomarkers for Acute Myocardial Infarction and Heart Failure. *BioMed Research International*, *2020*.
40. Yadav N., and Khanagavi J, (2017): Non–ST-Segment Acute Coronary Syndromes. *Emergency Cardiology: From ED to CCU, An Issue of Cardiology Clinics, E-Book*, *36*(1), 37-52.
41. Zhang Z. Q., Ding J. W., Wang X. A., Luo C. Y., Yu B., Zheng X. X., Zhang, J. (2019): Abnormal circadian rhythms are associated with plaque instability in acute coronary syndrome patients. *International Journal of Clinical and Experimental Pathology*, *12*(10), 3761.
42. Zile M. R., Claggett B. L., Prescott M. F., McMurray J. J., Packer M., Rouleau J. L., Solomon S. D, (2016): Prognostic implications of changes in N-terminal pro-B-type natriuretic peptide in patients with heart failure. *Journal of the American College of Cardiology*, *68*(22), 2425-2436.