Evaluation of B-Type Natriuretic Peptide as a Diagnostic Marker in Patients of Myocardial Infarction

Dr. Rupak Das¹, Dr. Sangeeta Naorem¹, Dr. Sneha Saha¹, Dr. Tina Das¹, Dr. M. Amuba Singh¹, Dr. Victoria Laishram¹, Dr. Racheal Sweet Marbaniang¹, Dr. Ursula Khwairakpam¹
¹(Department of Biochemistry, RIMS, India)

Abstract: Myocardial infarction (MI), commonly known as heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. About 30% of people have atypical symptoms. MI may cause heart failure, an irregular heartbeat, cardiogenic shock or cardiac arrest. A case-control study was conducted in Dept. of Biochemistry in collaboration with Dept. of Medicine, Regional Institute of Medical Sciences (RIMS), Imphal (Manipur) from June 2016 to May 2019. Blood samples were collected from 40 diagnosed patients of myocardial infarction within 12 hours of onset of symptoms and 40 healthy individuals. Samples were analyzed for serum BNP, Trop I, CK-MB, alkaline phosphatase levels. BNP was measured by ELISA, Trop I by rapid card test, alkaline phosphatase by colorimetric method and CK-MB by UV method with help of autoanalyser. Alkaline phosphatase was found to be higher in 12.5% whereas 85% have shown values in the normal range. Trop I was positive in 87.5% cases whereas in rest of the patients it was negative. 65% patients have shown higher CK-MB value, rest had values within normal range. BNP values of 100-500 pg/ml were seen in 37.5% patients and 62.5% patients have shown the range >500 pg/ml. BNP was found to be more sensitive as compared to traditional biomarkers for MI. The current study aims to diagnose MI with better sensitivity by comparing serum BNP levels in ST elevated myocardial infarction (STEMI) patients and normal healthy individuals.

Keywords: alkaline phosphatase, Trop I, CK-MB, BNP, myocardial infarction

Date of Submission: 22-08-2019
Date of acceptance: 07-09-2019

I. Introduction

Myocardial infarction (MI), commonly known as heart attack, occurs when blood flow decreases or stops to a part of the heart, causing damage to the heart muscle. The most common symptom is chest pain or discomfort which may travel into the shoulder, arm, back, neck, or jaw. Often it is in the centre or left side of the chest and lasts for more than a few minutes. About 30% of people have atypical symptoms. MI may cause heart failure, an irregular heartbeat, cardiogenic shock, or cardiac arrest. Women more often have atypical symptoms than men. Risk factors include high blood pressure, smoking, diabetes, lack of exercise, obesity, high blood cholesterol, poor diet, and excessive alcohol intake, among others. Heart failure (HF) is a common complication of myocardial infarction (MI), which may develop early or late and persist, resolve or recur. Older patients are at greater risk of developing HF and have a poorer prognosis. B-type Natriuretic Peptide (BNP) is a cardiac neurohormone secreted from membrane granules in the cardiac ventricles as a response to ventricular volume expansion and pressure overload. The natriuretic peptide system allows the heart to participate in the regulation of vascular tone and extracellular volume status. The measurement of BNP has been shown to be useful in detecting left ventricular (LV) dysfunction, particularly after AMI. Elevated levels of BNP and N-terminal pro-BNP may indicate the extent or severity of the ischaemic insult correlating with adverse outcomes. Many of the studies have concentrated on the role of BNP levels in predicting the long term morbidity and mortality of AMI. This study intends to determine the relationship between BNP levels and outcome in patients with AMI.

II. Materials and Methods

A case control study was conducted in Department of Biochemistry in collaboration with Department of Medicine, Regional Institute of Medical Sciences, Imphal, Manipur from June 2016 to May 2019. A total 80 participants were included in this study.

Study Design: Case-control study

DOI: 10.9790/264X-0505010107 www.iosrjournals.org
Study location: This was a tertiary care teaching hospital based study done in Department of Biochemistry in collaboration with Department of Medicine, RIMS, Imphal.

Study duration: June 2016 to May 2019.

Sample size: 80

Sample size calculation: The sample size was estimated on the basis of a single proportion design. We assumed confidence interval = 95%, type 1 error = 5% and precision of 5 on either side, \( Z = 1.96 \), specificity=98 and prevalence of 24%,

\[
\frac{1.96^2 \times 98 \times (100-98)}{(0.5)^2(100-24)} = 40
\]

So, No. of cases = 40 No. of controls =40 Total = 80

Subjects and selection method: The study population was drawn from 80 participants. Samples were collected for estimation of BNP, Trop I, CK-MB, alkaline phosphatase.

Inclusion criteria:
1. 40 diagnosed patients of myocardial infarction within 12 hours of onset of symptoms (cases)
2. 40 healthy individuals (controls)

Exclusion criteria:
1. Chronic heart failure
2. Hepatic disease
3. Renal disease
4. Malignancy
5. Diabetes mellitus
6. Anaemia

Procedure methodology:
Written informed consent was obtained from all the participants. A brief clinical history was taken from all cases.

Blood samples for estimation of serum BNP, CK-MB, trop T, alkaline phosphatase were taken within 12 hours of onset of symptoms of cases as well as from controls. BNP levels were estimated by ELISA. Trop I by rapid card test, alkaline phosphatase by colorimetric method and CK-MB by UV method with help of autoanalyser

Statistical analysis:
Data was analysed using SPSS version 20 (SPSS Inc., Chicago, IL). Analysis was performed by using t-test. For comparison of the mean values ANOVA test was used. \( P<0.05 \) was considered significant.

III. Results

Fig. 1 shows that maximum no. i.e. 13(32.5%) of cases are in the age group of 71 and above years. Among controls most of them i.e. 15 (37.5%) belong to 61-70 years age group.

Fig. 1: Age distribution between case and control groups
Fig. 2 shows that numbers of males are more in both the groups. Among cases 28(70%) are males as compared to 12(30%) females. Among controls number of males and females are 23 (57.5%) and 17(42.5%) respectively.

**Fig. 2: Distribution of the respondents by sex in cases and controls**

![Bar chart showing sex distribution in cases and controls](image)

Figure 3 shows that serum alkaline phosphatase levels were normal in most of the cases (85%). In 5(12.5%) cases it was high and in 1 case it was lower than normal.

**Fig. 3: Distribution of cases by serum alkaline phosphatase level**

![Graph showing serum alkaline phosphatase levels](image)

Figure 4 shows that creatinine kinase MB was high in 26(65%) of the cases. In 14(35%) cases it was found to be normal.
Figure 5 shows that in most of the cases, 35 (87.5%) cardiac troponin I was found to be positive whereas in 5 (12.5%) trop I level was below the detection range.

Figure 6 shows that majority of the patients had high BNP level in 25 (62.5%) of cases. Mean BNP level was 754.82 ± 531.54 pg/ml. None of the cases had normal BNP levels. Among controls mean BNP was 135±79.39 pg/ml.
Evaluation of B-Type Natriuretic Peptide as a Diagnostic Marker in Patients of myocardial Infarction

Figure 7 shows that among those who had high BNP 84% of them had high/positive CKMB level. Among those who had midrange BNP value, 33.3% of them had high CKMB level. And this finding was statistically significant (p<0.05).

Fig. 7: Relation of BNP and CKMB among cases

IV. Discussion

This study was conducted to estimate serum BNP in patients with ST elevated myocardial infarction and normal individuals. And also to compare the findings with other established parameters such as CKMB, Trop I, alkaline phosphatase. Maximum number of myocardial infarction patients were in the age group of 71 years and above. This finding was supported by the study conducted by Canto JG et al. According to sex also it was seen that males comprised of more in numbers as compared to females among the myocardial infarction patients. In a study done by Bazzino O et al., it was seen that MI was more common in males. Infact 63.6% cases were males as compared to females. Serum alkaline phosphatase levels, as observed in this study, were high in 12.5% cases followed by normal levels seen in 85% of the cases. Low value was seen in 5% cases. Kunutsor SK et al. opined that there was a non-linear association between serum alkaline phosphatase and cardiovascular disease. Troponin I was found positive in 35(87.5%) patients among the cases and negative in 5(12.5%) patients. BNP can be produced in both atria and ventricles, and is upregulated in failing ventricular myocardium. In response to increased myocardial stretch and wall stress, ventricular myocytes secrete the pro-hormone pro-BNP, which is then cleaved into biologically active BNP and the inactive bi-product N-terminal-proBNP (NT-proBNP). The biological actions of natriuretic peptides are mediated through membrane-bound natriuretic peptide receptors (NPR) that are linked to a cyclic guanosine monophosphate-dependent signalling cascade, including NPR-A, which preferentially binds ANP and BNP, and NPR-B, which preferentially binds CNP. Elevated BNP levels have been demonstrated to respond to increased angiotensin-dependent and sympathetic tones. The predominant path-physiological process underlying increased circulating levels of BNP and NT-pro-BNP is regional or global impairment of left ventricular systolic or diastolic function leading to left ventricular wall stretch. In addition, their increased levels may also result directly from cardiac ischaemia. It appears that ischaemic or injured myocardial tissue releases extra BNP irrespective of haemodynamic factors. Serum BNP levels were estimated among the cases and controls. Serum BNP levels were divided into three ranges. 0-100 pg/ml was accepted as normal range. 100-500 pg/ml as the mid range or the gray zone and values more than 500 pg/ml were considered high. In this study 25(62.5%) patients had high BNP values and 15(37.5%) patients had values in the mid range or gray zone. None of the cases had values in the normal range. In the study done by Brenden CK et al. 33% cases had BNP in the gray zone. The gray zone as defined in the study as the range in which arriving at a definitive conclusion regarding condition of the patient was not possible. According to the study done by Strunk A et al. they also opined that there remains some ambiguity in the interpretation of results in the medium range (100-500 pg/ml). The mean BNP level among the cases was 754.82 pg/ml and standard deviation was 531.54 pg/ml. Fazlinezhad A et al. reported that the mean BNP level measured in the case group was 3784.57 pg/ml and standard deviation was 6344.97 pg/ml. The mean

DOI: 10.9790/264X-0505010107  www.iosrjournals.org
BNP level in controls was 68.35 pg/ml and standard deviation was 69.66 pg/ml. CKMB was seen to be high in 65% patients among the case group. It was also seen that among those patients who had high BNP level 84% of them had high CKMB level also. Among those who had BNP level in the mid range 33% had high CKMB level. This finding was statistically significant (p<0.05). It was seen that BNP and CKMB were positively correlated (P<0.01) & R=0.538. Similar correlation was also seen in the study by Nalbantic AD et al.\textsuperscript{11} Bassan R et al\textsuperscript{11} opined that sensitivity of admission BNP for MI (cut off value of 100pg/ml) was significantly higher than CKMB and Trop I. They also advocated that BNP can be a useful co-marker along with the standard cardiac markers like CKMB and Trop I.

V. Conclusion

The results of this study shows BNP level was more than the normal range i.e. 0-100 pg/ml in all the cases and most of the patients had BNP levels in the high range. When compared with CKMB values among the cases along with BNP values, the correlation is found to be significant. In fact it was observed that BNP levels had better sensitivity then CKMB and Trop I. As the study pattern is a case control study, so the future pattern of BNP levels among the patients in the follow-up period could not be ascertained. If follow ups could be done, this could have helped to understand how long the BNP levels remain high in the post hospitalization period. Also the patients were selected as diagnosed cases of MI depending upon their ST segment elevation. So those patients with MI who did not show ST segment elevation in their ECG were left out. The efficiency of BNP in diagnosing such cases could be a matter of interest for future researchers. Nevertheless it may be concluded that serum BNP can be used as a diagnostic marker in addition to conventional biomarkers like CKMB and Trop I.

References

[4]. American heart association. Heart attack or sudden cardiac arrest: are they different? Available at: http://www.heart.org/HEARTORG/Conditions/More/My%20HeartandStroke/Heart-Attack-or-Sudden-Cardiac-Arrest-How-Are-They-Different_UCM_440804_Article.jsp#.Wd-JhmxCzIW. Accessed August 30, 2017.

DOI: 10.9790/264X-0505010107 www.iosrjournals.org