

Research Article

# Evaluation of the Efficiency of N-terminal Pro-B-type Natriuretic Peptide for Diagnosis of Acute Myocardial Infarction

Abuagla M. Dafalla<sup>1</sup>, Leena A. Dafalla<sup>1</sup>, ShamsEldein M. Ahmed<sup>1</sup>, Yousif A. Mohammed<sup>2</sup>, Adam D. Abakar<sup>3</sup>, Wed elbahar H.Aballah<sup>4</sup>, Elhadi A. Ahmed<sup>5</sup>, and GadAllah Modawe<sup>6</sup>

<sup>1</sup>Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, University of Gezira, Sudan

<sup>2</sup>National Cancer Institute, University of Gezira, Sudan

<sup>3</sup>Department of Medical Parasitology, Faculty of Medical Laboratory Sciences, University of Gezira, Sudan

<sup>4</sup>Department of hematology and immunohematology Faculty of Medical Laboratory Sciences, Managil University of Science and Technology Sudan

<sup>5</sup>Department of Medical Microbiology, Faculty of Medical Laboratory Sciences, University of Gezira, Sudan

<sup>6</sup>Department of Biochemistry, Faculty of Medicine and Health Sciences, Omdurman Islamic University, Omdurman, Sudan

Corresponding Author:

GadAllah Modawe;

email:

gadobio77@hotmail.com

Received 20 June 2020

Accepted 15 August 2020

Published

30 September 2020

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Editor-in-Chief:

Prof. Mohammad A. M. Ibnouf

## Abstract

**Background:** Cardiac diseases are one of the major causes of death worldwide with increasing incidence rate per year, particularly in developing countries such as Sudan owing to urbanization and changing lifestyle. Myocardial infarction is a consequence of the imbalance between the heart blood supply and the required heart cell; this disorder leads to necrosis of myocardium and may cause death. It could be diagnosed by at least two of the following criteria: chest pain, electrocardiography (ECG) elevation, and levels on cardiac biomarkers. This study aimed to evaluate the efficiency of N-terminal pro-B-type natriuretic peptide (NTproBNP) for the diagnosis of acute myocardial infarction (AMI).

**Methods:** This analytical case-control hospital-based study was conducted on total of 70 individuals, of which 40 participants were suspected of or diagnosed with AMI, while 30 healthy subjects were included as a control group. Three ml of venous blood were collected in lithium heparin containers. Troponin I (TnI) as a cardiac biomarker was measured by TOSOH AIA-360, while the NTproBNP level was detected using I-Chroma II. Personal and clinical data were collected directly from each participant using a predesigned questionnaire.

**Results:** A significant increase in the TnI level (mean:  $13.13 \pm 18.9$  ng/ml) and NTproBNP (mean:  $5756.5 \pm 8378.2$  pg/mL) in AMI patients were detected when compared with control mean ( $0.02 \pm 0.00$  ng/ml and  $57.8 \pm 42.32$  pg/mL, respectively).

**Conclusions:** NTproBNP gave a high sensitivity (87.5%), specificity (100%), positive predictive value (100%), and negative predictive value (85.7%) in the diagnosis of AMI when compared with another cardiac biomarker such as TnI.

**Keywords:** acute myocardial infarction, NTproBNP, troponin I, Medani Heart Center, Sudan

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## 1. Introduction

A cardiac disease refers to any disorder that affects the heart function by either minimizing or eliminating the heart output [1]. Cardiac diseases are caused either by structural heart disorder or myocardium abnormalities such as myocardial infarction (MI) [2]. An acute myocardial infarction (AMI) is a consequence of the imbalance between the heart blood supply and the required heart cell. This disorder leads to necrosis of the myocardium and may even cause death [1]. MI is the most common cause of death worldwide [3, 4]. The frequency of MI has increased over the last few decades throughout several states of Sudan, which may be due to the increase in the prevalence of risk factors such as underlying diseases and habits [5]. The symptoms of a cardiac disease include chest pain and dyspnea due to the reduction of oxygen in myocardial cells, which is considered as a cardinal indication of AMI [6], and palpitations due to the increase in oxygen demand. Other symptoms include headache and limb weakness [7]. The diagnosis of cardiac diseases depends on the history, risk factor, clinical examination, symptoms, laboratory investigation, chest radiology, electrocardiography (ECG), and echocardiography (Echo) [8].

Moreover, AMI can be diagnosed by at least two of the following three criteria; first, typical symptoms such as a history of chest pain; second, changes on the ECG, and third, elevation on cardiac biomarkers [9]. The latter are specific elements produced by the cardiac cells and increase in cardiac disorders. Cardiac biomarkers include troponin, creatine kinase (CK), myoglobin [10, 11], and brain natriuretic peptides (BNPs) [12]. Cardiac troponin is a muscle-regulatory protein produced by a muscular cell present in skeletal and heart muscles. Troponins are generally categorized into three types; troponin T, troponin I (TnI), and troponin C [13]. For cardiac biomarkers, TnI is more sensitive and specific than others troponins [14]. In AMI, the TnI rises in plasma after 4–8 hr of the onset of the symptoms, reaches the peak at 12–24 hr, and then returns to normal within 7–10 days of AMI [15]. CK, on the other hand, is an enzyme consisting of two protein subunits: muscle protein (M) and brain protein (B), and depending on the constituent, CK has three isoenzymes; CKBB, CKMM, and CKMB [16]. While CKBB is more abundant in the brain cells, CKMM is more abundant in the muscular cells and CKMB in the cardiac muscles [17]. CKMB is more sensitive and specific for the diagnosis of cardiac disease than CKMM and CKBB [15]. CKMB level in plasma increases after 4–8 hours of MI and reaches the peak at 12 – 24 hours then return to the normal level within 2 – 3 days [16]. BNPs are polypeptides produced by myocardium in response to the increased wall stress due to an increase in volume or pressure of blood, to reduce intravascular volume

by diuretics, vasopressin, and suppression the sense of thirst (16). BNP's are secreted as pro-hormone then activated by reacting with protease enzyme to cleave it into active form BNP and inactive form NTproBNP(18). In the case of cardiac disease, both BNP's are elevated, thus, measurement of plasma BNP and /or NTproBNP is a useful indicator for cardiac diseases (16). The objective of the present study was to evaluate the efficiency of N-terminal pro-B-type natriuretic peptide (NTproBNP) for the diagnosis of AMI.

## 2. Materials and Methods

This analytical case-control hospital-based study aimed to evaluate the efficiency of NTproBNP for the diagnosis of AMI.

The study was conducted in Medani Heart Center, Sudan. A purposive sample was collected from patients with AMI attending Medani Heart Center from April 2018 to June 2019. A total of 70 individuals participated in this study, 40 were AMI cases and 30 were healthy individual as a control group. AMI cases were included according to the final diagnoses by Medani Heart Center physicians. AMI patients with renal failure or Biotin treatment were excluded. The control group was non-smokers, non-obese, normotensive, non-diabetic and have no history of renal or cardiac diseases. The demographic data were collected from each participant after final diagnosis using a questionnaire included clinical remarks such as AMI symptoms, ECG, Echo and risk factors.

### 2.1. Ethical consideration

Permission to carry out the study was obtained from the College of Graduate Studies, Faculty of Medical Laboratory Sciences, University of Gezira and Ministry of Health, Sudan. All enrolled patients were informed about the purpose of the study before collection of specimens and consents for participation were taken.

### 2.2. Data variable, collection and criteria

Sex, age (Year) - Tnl (ng/ml) - NTProBNP (pg/ml) – Risk factors - Clinical Diagnosis - Echocardiogram – Electrocardiogram were the variables used and also the data were collected using laboratory analysis, doctor's report, other findings and data collection form. Restricted criteria for eligibility of case and control (inclusion and exclusion criteria)

was followed to reduce sources of bias. A purposive sample was used to determine the sample size because there is no previous prevalence for AMI in Sudan.

### 2.3. Measurement of cardiac biomarkers

Three ml of blood specimen from each participant were collected in lithium heparin anticoagulant tubes for laboratory analysis; plasma was separated into two new plain containers and examined within 2 hrs. The laboratory work was done in Medani Heart Center and Department of Clinical Chemistry, Faculty of Medical Laboratory Sciences, University of Gezira. TOSOH AIA-360 automated machine (Germany) was used to measure TnI levels while I-Chroma II immunofluorescence system (Korea) was used to measure NTproBNP levels.

## 3. Data analysis

Collected data were analyzed by using suitable statistic software including SPSS computer version 22 and Medical calculator program version 16. Calculation of sensitivity, specificity, positive predictive value and the negative predictive value was done by these equations:

$$\text{Sensitivity} = \text{TP}/\text{TP}+\text{FN} \times 100.$$

$$\text{Specificity} = \text{TN}/\text{TN}+\text{FP} \times 100.$$

$$\text{Positive predictive value} = \text{TP}/\text{TP}+\text{FP} \times 100.$$

$$\text{Negative predictive value} = \text{TN}/\text{TN}+\text{FN} \times 100.$$

TP: true positive - FP: false positive - TN: true negative -FN: false negative.

## 4. Results

### 4.1. Demographics of AMI subjects

This study enrolled 40 patients with AMI, among whom 62.5% were male, 45% diabetic, 40% hypertensive, 25% smokers, 25% obese, 97.5% has no history of cardiac diseases. Patients with age group above 59 years constituted 50% as shown in Table (1).

## 4.2. Performance of NTproBNP and Tnl

Total positive results of NTproBNP and Tnl were 35/40 and 32/40, respectively. Sensitivity, specificity, positive and negative predictive values of NTproBNP and Tnl of AMI patients and control were shown in Table 2.

## 4.3. Biomarkers levels

Plasma levels of NTproBNP and Tnl were significantly detected among AMI patients; the level of NTproBNP ranged from 15 to 30000 with mean of 5756.5 pg/ml while Tnl recorded from 0.015 to 50 with mean of 13.1 ng/ml (Table 3).

## 4.4. Biomarkers results related to ECG and Echo

Positive ECG was recorded with 26 patients of 32 Tnl positive and with 27 patients of 35 NTproBNP positive. While, less sensitively positive Echo were obtained with 20 patients of 32 Tnl positive, and with 21 patients of 35 NTproBNP positive Table 4. Measuring of NTproBNP and Tnl results using Area Under the Curve AUC according to ECG as the gold standard method shown in Table 5, Figure (1).

TABLE 1: Characteristics of acute myocardial infarction patients.

		<b>N</b>	<b>%</b>
<b>Sex</b>	Male	25	62.5
	Female	15	37.5
<b>Age/year</b>	<59	20	50
	>59	20	50
<b>Diabetes</b>	Diabetic	18	45
	Non-diabetic	22	55
<b>Chest pain</b>	Yes	40	100
	No	0	0
<b>Hypertension</b>	Yes	16	40
	No	24	60
<b>Smoking</b>	Yes	10	25
	No	30	75
<b>History of cardiac disease</b>	Yes	1	2.5
	No	39	97.5
<b>ECG</b>	STEMI	32	80
	Non-STEMI	8	20
<b>Obesity</b>	Obese	10	25
	Non-Obese	30	75

TABLE 2: Performances of NTproBNP and TroponinI among cases and control.

Biomarker		Case	Control	Sensitivity %	Specificity %	Positive predictive Value%	Negative predictive Value%
NTproBNP	Positive	35	0	87.5	100	100	85.7
	Negative	5	30				
Tnl	Positive	32	0	80	100	100	78.9
	Negative	8	30				

TABLE 3: Levels of NTproBNP (pg/ml) and Troponin I (ng/ml) among 40 cases of AMI patients and 30 control subjects

		NO	Mean	SD	p.value
NTproBNP	Case	40	5756.5	8378.2	0.00
	Control	30	57.8	42.3	
Tnl	Case	40	13.1	18.9	0.00
	Control	30	0.02	0.000	

TABLE 4: Relationship between the results of Troponin I and NTproBNP with ECG and Echo

Tnl / NTproBNP		ECG		Total
		Positive	Negative	
NTproBNP	Positive	27	8	35
	Negative	5	0	5
Tnl	Positive	26	6	32
	Negative	6	2	8
		Echo		
		Positive	Negative	
NTproBNP	Positive	21	14	35
	Negative	3	2	5
Tnl	Positive	20	12	32
	Negative	4	4	8

TABLE 5: Therea under ROC curve for NTproBNP and Tnl according to ECG as a gold standard method.

Variable 1	Tnl
Variable 2	NTproBNP
Classification variable	ECG
Sample size	70
Positive group <sup>a</sup>	32 (45.71%)
Negative group <sup>b</sup>	38 (54.29%)
Area under the ROC curve for Tnl	0.827
Area under the ROC curve for NTproBNP	0.817

## 5. Discussion

MI is a consequence of the imbalance between heart blood supply and the heart cell needs; this disorder leads to necrosis of the myocardium and may cause death (1). It is diagnosed by at least two of three of the following criteria; firstly, chest pain, secondly changes on the ECG, and thirdly elevation on cardiac biomarkers (9).

From this study, chest pain was recorded with all AMI patients, male patients more frequently than females with a percentage of 62%. On the other hand, the age group above and below 59 years were equally stated, these findings were in agreement with a study done by Ahmed in Sudan(19). Diabetes mellitus and hypertension as risk factors in the current study were observed in 45 % and 40% from AMI cases, this threat could be decreased by routine follow up of patients and establishment of specialized centers for care.

From the results, smokers were less than non-smokers; this was in concord with a similar study(20) and in contrast with Elkhader *et al*(21). According to the clinical diagnosis, 80% of AMI patients were ST-Elevation Myocardial Infarction (STEMI), this result was near to the percentage concluded by Abdallah in Sudan(22). In the current study, each of TnI and NTproBNP had significant values in the diagnosis of AMI in studied patients, same findings were reported in the UK(23) and USA(24), however, in our study 12.5% (5/40) and 20% (8/40) of suspected cases gave insignificant concentrations for NTproBNP and TnI, respectively. NTproBNP values were highly sensitive when compared with TnI according to ECG and Echo, this result differs with those done by Dimiati *et al.* in Indonesia who found TnI was more sensitive(25). The area under ROC curve for NTproBNP was (0.817) and for TnI equal (0.827) according to ECG as a gold standard method, this indicates that each of the studied biomarkers had a good performance in the diagnosis of AMI.

## 6. Conclusions

The NTproBNP had high sensitivity, specificity, positive predictive value and negative predictive value when compared with TnI in the diagnosis of AMI.

## Funding

This research has been fully financed by the German Academic Exchange Service (DAAD) In-Country Scholarship Program Sudan, 2016 (57298697).

## Acknowledgments

I am grateful to the help and support offered by the staff of Wad Medani Cardiac Center for helping me in my practical (lab and Archive department) and staff of laboratory of Professor BakryYousif. Especial thanks to laboratory specialist Mohamed Snhory. I owe a deep debt of gratitude to Dr. Mohamed Hamza and laboratory specialist (Sidig Said and Omer ELtigani) for helping me to obtain NTproBNP reagents.

I am very grateful to the patients and healthy peoples who participated in the study from Gezira state.

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