IJBPAS, March, 2021, 10(3): 1058-1078

ISSN: 2277–4998

International Journal of Biology, Pharmacy and Allied Sciences (IJBPAS)

'A Bridge Between Laboratory and Reader'

www.ijbpas.com

ASSESSMENT OF CIRCULATING BIOCHEMICAL MARKERS OF PROGNOSTIC IMPORTANCE HAVING ROLE IN THE DEVELOPMENT OF ACUTE MYOCARDIAL INFARCTION

HAFEEZ Z[3], KHOKHAR MAS[2], ANWAR MZ[2], KHALID A[1], RASOOL R[1] AND MALIK A[1]

1: Institute of Molecular Biology and Biotechnology (IMBB), The University of Lahore-Pakistan

2: Major Shabbir Sharif Shaheed Hospital, Kunjah-Gujrat Pakistan

3: University College of Medicine and Dentistry, The University of Lahore-Pakistan

***Corresponding Author: Dr. Arif Malik (Ph.D): E Mail: arifuaf@yahoo.com; Cell: 0321-8448196; Tel: +92 42-7515460-7, Fax: +92-42-7515519**

Received 11th May 2020; Revised 6th June 2020; Accepted 12th July 2020; Available online 1st March 2021

https://doi.org/10.31032/IJBPAS/2021/10.3.5421

ABSTRACT

BACKGROUND: Acute myocardial infarction is characterized by a significant hemodynamic insult leading to epicardial coronary arteries atherosclerosis. As thyroid hormone is important regulator of the cardiac gene expression, many of the cardiac expressions of thyroid dysfunction are linked with the alterations in the T3-mediated gene expression that changes in the cardiac contractility, cardiac output, vascular resistance, rhythm disturbances and blood pressure.

METHODOLOGY: We have selected fifty AMI patients from Gulab Devi Chest Hospital, Lahore to evaluate thyroid biomarkers, oxidative stress and lipid peroxidation markers from their blood samples. Variables include antioxidant (CAT, SOD, GPX, GRx, GSH, Vitamins (A, C, E, B6, B9, B12), stress markers (NO, AOPPs, MDA), and thyroid biomarkers (T3, T4, TSH, TPOAb, TgAb) are determined by different lab tests and ELISA kits. Independent t-test was applied for analysis.

RESULTS: The mean MDA level in AMI patients was 2.16 ± 0.0015µmol/L while in control group was 0.951±0.001µmol/L. Nitric oxide in diseased patients 35.26±3.26µmol/L is remarkably increased as compared to normal subjects' 23.26±4.26µmol/L. The AOPPs shows

significant increased levels in AMI group 127.06±7.26µmol/L in comparison with normal subjects 99.26±4.23µmol/L. AMI disease patients shows a decreased level of T3 3.05±0.16µg/dl, T4 16.35±4.26pmol/L, TSH 5.26±2.16IU/L, TPO9.66±2.66 IU/L and TBG 51.26±4.41 IU/L as compared to healthy controls. The mean SOD (0.36±0.0016U/ml vs. 0.625±.0011U/ml), CAT serum levels in AMI group were 2.16±0.47 U/L, whereas in the control group was 4.26±0.016 U/L. The mean serum level of GSH and GRx, and GPx in acute myocardial infarct disease patient was recorded as 6.23±1.99 µmol/L, 3.08±0.06 µmol/L and 7.23±1.66 µmol/L respectively. Levels of IL-6 and TNF-α in blood serum of AMI patients reported 6.28±1.23pg/ml and 37.09±2.09pg/ml respectively. Vitamin A, C, E, B_6, B_9, and vitamin B_{12} in blood serum of AMI group are 4.26±1.08nmol/L, 0.415±0.014nmol/L, 0.326±0.0014nmol/L, 66.35±4.29nmol/L, 2.16±0.016nmol/L, and 201.11±6.35pmol/L respectively compared to healthy controls group.

CONCLUSION: The present work signifies that dysfunction of thyroid along with the oxidative stress and decreased antioxidant capacity might be associated with the progression of acute myocardial infarction by induction of endothelial dysfunction followed by atherosclerosis.

Keywords: Acute myocardial infarction, Thyroid Hormones, Oxidative Stress, Lipid Peroxidation, antioxidants, vitamins

INTRODUCTION

Chronic heart disease is manifested by the Myocardial infarction (MI) and is sufficient to cause sudden death of patient. The disease in which patient is affected extremely in a stressful way is AMI. It reported as a threat to life and mainly for couples it is a high value family stress **[1]**. Even though, mainly there is occurrence of myocardial infarction in the patients with age 45 or more, young women or men can suffer with MI. The transmularity and reversibility of myocardial injury due to insufficient supply of blood and oxygen depends mostly on duration of the blockage of coronary artery; there may also be influence of many other factors that intensify the damage, like IPC (Ischemic preconditioning) or the collateral circulation to the affected area of the myocardium. The nuclear loss and the shrinking nucleus are first microscopic signs of reduced blood flow towards heart preventing it from receiving enough oxygen and it is observed about after 6-hours from the emergence of the occlusion of coronary artery. The leukocyte infiltration of polymorphonuclear nature, the swelling of the myocyte and the necrosis of the contraction band are also the characterization

of acute MI **[2]**. Cardiovascular diseases (CVD) are the foremost case of death in western countries. According to the report of WHO, 14 million of the people die per year due to MI (WHO 2011). For the year 2008, the data of mortality shows that in 2008 the total 32.8% (811,940) was accounted for CVD of all 2,471,984 deaths **[3]**. Risk factors for coronary artery disease (CAD) includes high BP, raised cholesterol levels in serum, smoking, abdominal obesity, high-risk diet, moderate alcohol consumption, physical inactivity, psychological stress and diabetes mellitus **[4,5,6,52]**. The symptoms that are reported at the time of myocardial infarction commonly include, crushing pain in the chest, feeling of discomfort or heaviness, nausea, palpitation, vomiting, feeling faint, weak or dizzy, indigestion like feeling, symptoms of flu, shortness of breath, pain in shoulder/jaw/back/head, or panic feelings and collapse (American Heart Association, 2007).

Cardiovascular system is known to be affected in no. of ways by the hypothyroidism or hyperthyroidism. Although, the effects of thyroid dysfunction on cardiovascular system are readily detectable, especially in the case of hyperthyroidism. The evidences of the long-term thyroid dysfunction on cardiovascular outcomes are less clear **[7]**. However, the Rotterdam Study concludes that the patients having a subclinical hypothyroidism have a notable increased aortic atherosclerosis prevalence and MI **[8]**. Receptors for the thyroid hormone are present on vascular endothelial and myocardial tissues and are sensitized to the changes in concentration of thyroid hormone in circulation. Cardiovascular system is influenced adversely even if there is a subtle change in the thyroid hormone i.e. hypothyroidism or hyperthyroidism. There are some mechanisms that link two conditions and that are dyslipidaemia, changes in the BP, endothelial dysfunction and the effects of thyroid hormone directly on myocardium. Various interventional trials have showed that when subclinical thyroid diseases are treated, it improved the cardiovascular risk factors. Over a period of last twenty years, evidences support the association between AMI and abnormal functioning of thyroid following the unfavourable cardiovascular outcomes. Experimental studies have shown that after AMI thyroid hormone has an important role to play in reducing the size of infarct and improve the myocardial function **[9]**. Vascular and cardiac effects was shown by thyroid hormone **[7]** and in most of the tissues, biochemical reactions are also

regulated by thyroid hormones. Some of the patients having AMI have been reported with low levels of biologically active T3 (triiodothyronine) which shows the metabolism of the thyroid hormone is altered **[10]**. These patients with low T3 had AMI with congestive heart failure **[11]**, after the heart surgery **[12, 53]**, and in addition, in patients with variant serious systemic diseases **[13]**.

In serious chronic failure of heart, acute myocardial infarction **[14, 15, 54]**, and the surgery of heart **[16],** low T3 levels are common **[17]**. High mortality rate is associated with the low TH levels in plasma, in both the patients with AMI and heart failure **[10]**. Recently this hypothesis has been addressed in the ischemia-reperfusion experimental models and MI in animals, and interestingly, evidences shows for the proper response of myocardium to the stress of ischemia TH has a critical role, and TH also possess properties of cytoprotective nature that in healthy tissues are silent, hence manifesting during stress only **[18,19,20]**. So, evaluation of relationship between the thyroid hormones, oxidative stress markers and acute myocardial infarction is designated.

MATERIALS AND METHODS

Fifty AMI patients were screened at Gulab Devi Chest Hospital, Lahore for assessing thyroid biomarkers, oxidative stress and lipid peroxidation markers. Informed consent was obtained before being included in this study. Twenty clinically apparently healthy individuals were included as controls. Five ml of venous blood sample were taken from the anti-cubital vein of each participant. The sample bottles were centrifuged within one hour of collection, after which the serum were separated and stored at -70°C until assayed**.** Following variables were performed: GSH **[21]**, CATALASE **[22]**, SOD **[23]**, MDA **[24]**, GPX **[25]**, GR **[25]**, NO **[26**], AOPPs **[27]**, IL-6 (BioVendor Human IL-6 ELIZA Kit), TNF-α (BioVendor Human TNF-α ELIZA Kit), VIT-A **[28]**, VIT-C **[29]**, VIT-E **[30]** , T3, T4, TSH, TPO Anti-bodies, TBG Anti-bodies (human Bio Vendor ELIZA kits) is determined by Commercial Human Diagnostics Kits.

STATISTICAL ANALYSIS

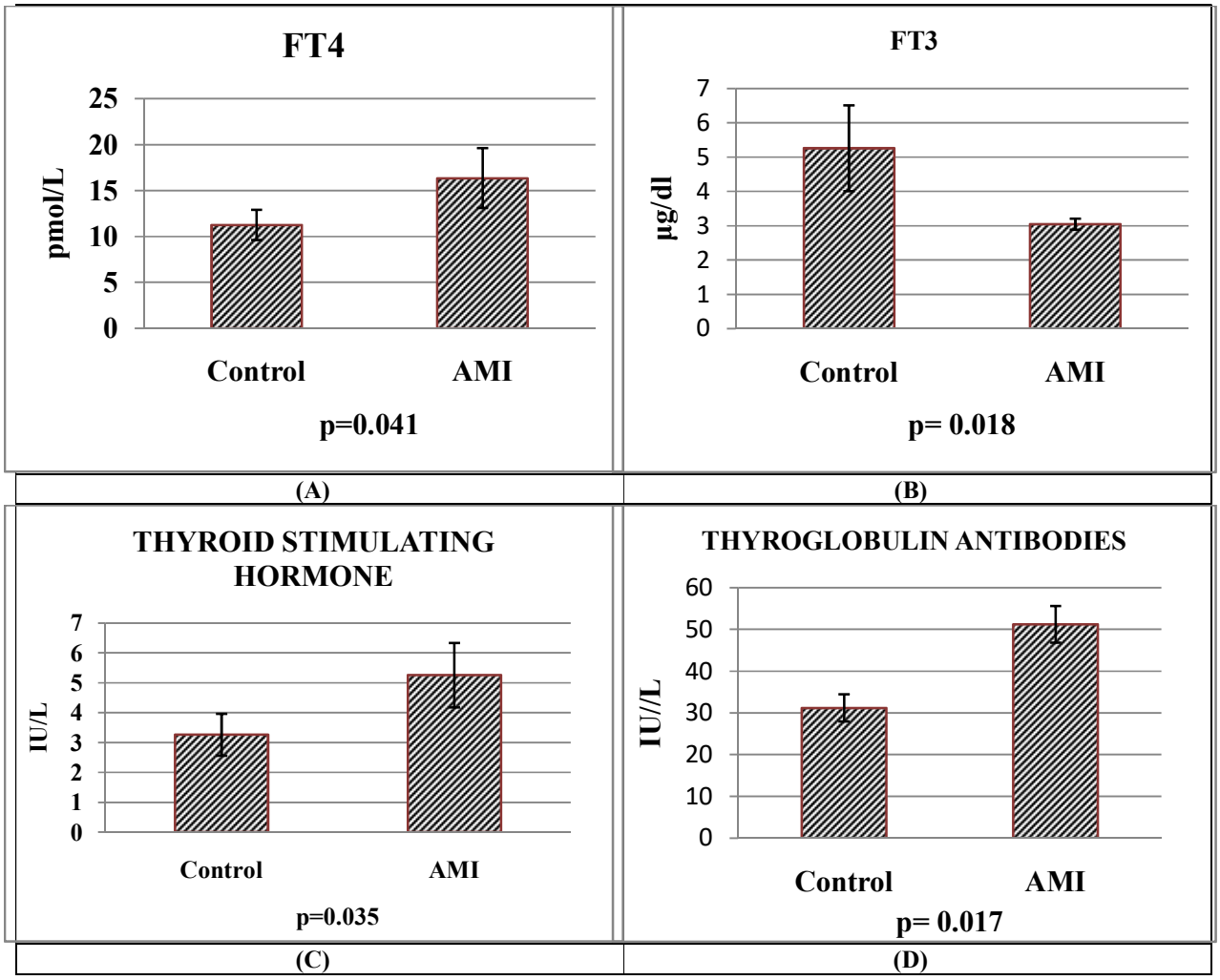
The study was prospective case control and the data was scrutinized statistically by independent T-test and articulated as mean±SD. $P \leq 0.05$ is cut point to be statistically significant.

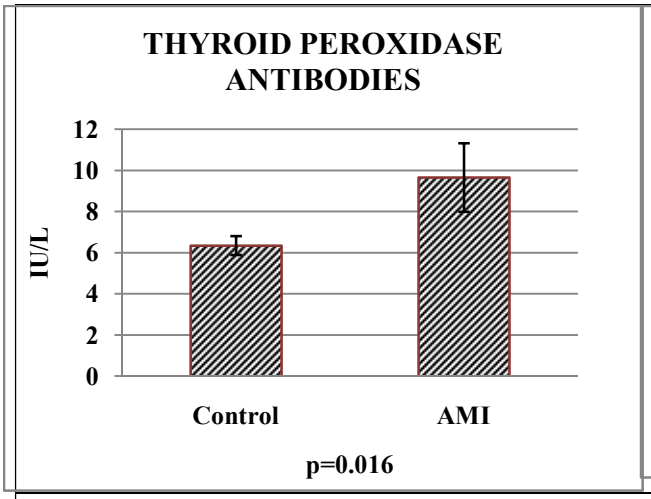
RESULTS

The results depicted in table 1 reflect that thyroid profile (T3, T4, TSH, Tg Ab, and TPOAb) of acute myocardial infarction

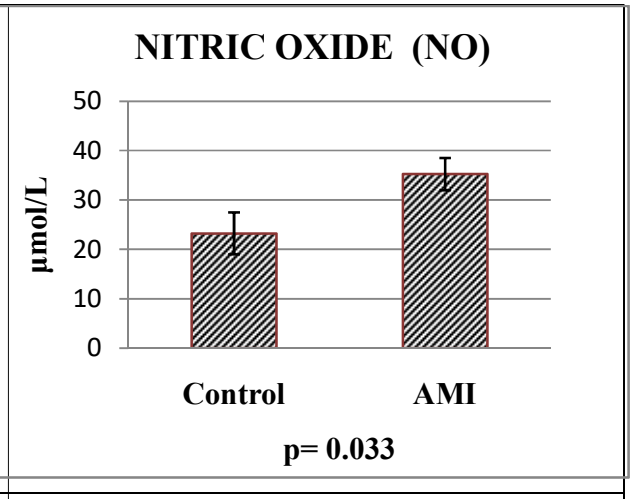
disease patients were statistically highly significant ($p \leq 0.05$). An increased level of T4 in AMI patients (16.35±4.26pmol/L) were recorded as compare to normal individuals (11.25±2.25pmol/L). The mean value of TSH in both normal and AMI patients were 3.26±1.005IU/L and 5.26±2.16IU/L respectively. Similarly, TgAb and TPOAb, thyroid associated auto antibodies levels in acute MI patients (51.26±4.41IU/L and 9.66±2.66IU/L) were significantly increased as compare to healthy individuals (31.25±3.26IU/L and 6.35±1.05IU/L) respectively. While in the case of FT3, high values were recorded in control group (5.26µg/dl) as compared to diseased group (3.05µg/dl). Levels of HDL in CVD patients decreased significantly ($p=0.018$). The mean value of MDA in AMI patients was 2.16µmol/L while in control group was 0.951µmol/L. This shows that MDA level increases in cardiovascular patients as compared to healthy individuals and also found to be statistically significant ($p=0.000$). The nitrosative stress biomarker, NO in diseased patients (35.26±3.26µmol/L) is remarkably increased as compared to normal subjects (23.26±4.26µmol/L). The data interpretation of AOPPs shows statistically significant increased levels in AMI group (127.06±7.26µmol/L) in comparison with normal subjects (99.26±4.23µmol/L). The mean serum level of IL-6 in acute myocardial disease patients and normal individuals was recorded as 6.28±1.23pg/ml and 3.73±2.76pg/ml respectively showing the increased levels of IL-6 in AMI patients as compared to normal and statistically significant. The data interpretation of TNF- α shows statistically significant increased levels in AMI group 37.09pg/ml in comparison with normal subjects' 21.26pg/ml. This entails the higher value in acute myocardial infarction patients as compared to normal subjects. So, the results concluded that increasing trends of oxidative stress biomarkers observed in AMI patients than normal subjects give a picture of their importance in the pathogenicity of myocardial infarction. Data interpretation of AMI disease patients demonstrated that decrease levels of enzymatic antioxidants SOD (0.36±0.0016U/ml vs. 0.625±.0011U/ml), CAT (2.16±0.47 U/L vs. 4.26±0.016 U/L), glutathione (6.23±1.99 µmol/L vs. 8.06±1.26µmol/L), and glutathione reductase (3.08±0.06µmol/L vs. 4.26±0.0015µmol/L) except GPx (7.23±1.66µmol/L Vs. 6.26±1.22µmol/L) which is raised in case of acute myocardial infarction. Non-enzymatic antioxidant biomarkers reported that Vitamin A level in

AMI patient decreases as compared to controlled persons and are found highly significant. An overall decreasing trend in vitamin C was seen between both AMI (0.415±0.014nmol/l) as compared to normal subjects (0.65±0.0016nmol/L). The low levels of vitamin B6 (66.35±4.29nmol/L), vitamin B9 (2.16±0.016nmol/L) and vitamin B12 (201.11±6.35pmol/L) were observed in AMI patients as compared to vitamin B6 (77.26±6.25nmol/L), vitamin B9 (3.26±0.0018nmol/L) and vitamin B12 (226.25±8.26pmol/L) respectively.

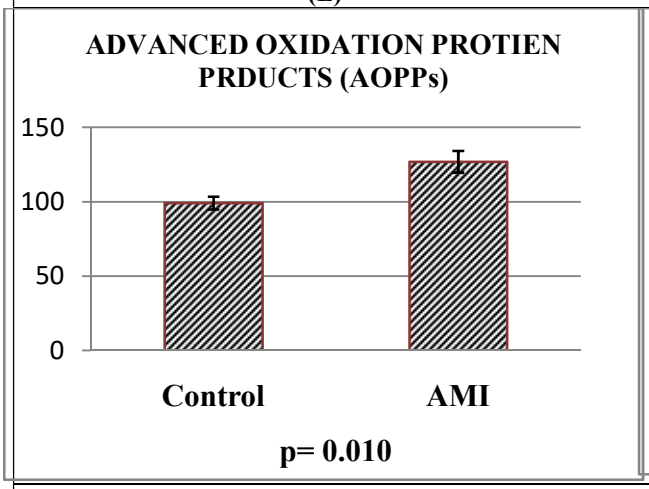



THYROID PEROXIDASE ANTIBODIES
IU/L
12
10
8
6
4
2
0
Control
AMI
p=0.016

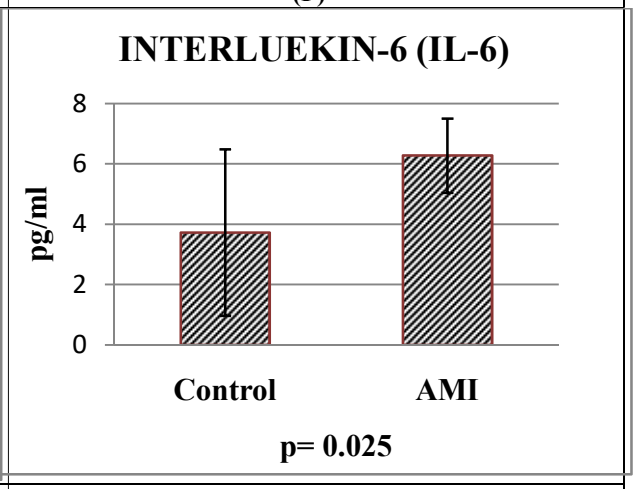
(E)


NITRIC OXIDE (NO)
µmol/L
50
40
30
20
10
0
Control
AMI
p= 0.033

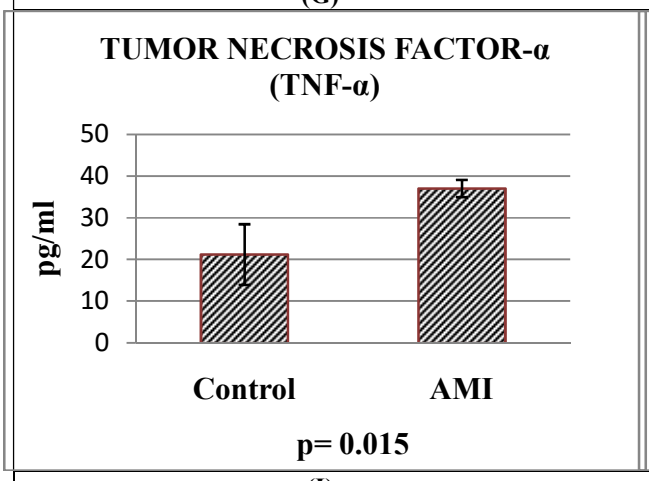
(F)


ADVANCED OXIDATION PROTIEN PRDUCTS (AOPPs)
150
100
50
0
Control
AMI
p= 0.010

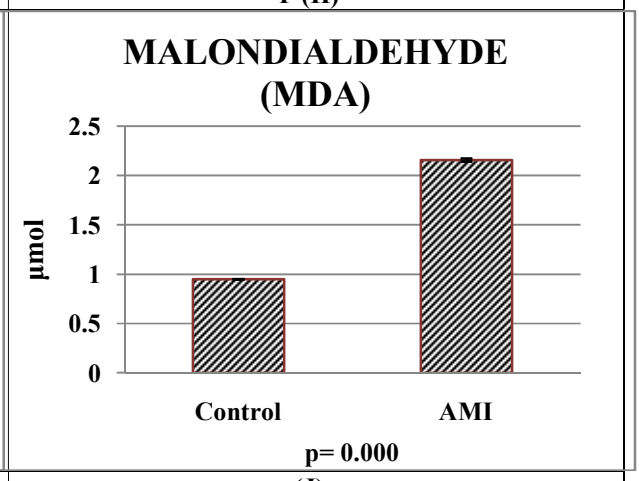
(G)


INTERLUEKIN-6 (IL-6)
pg/ml
8
6
4
2
0
Control
AMI
p= 0.025

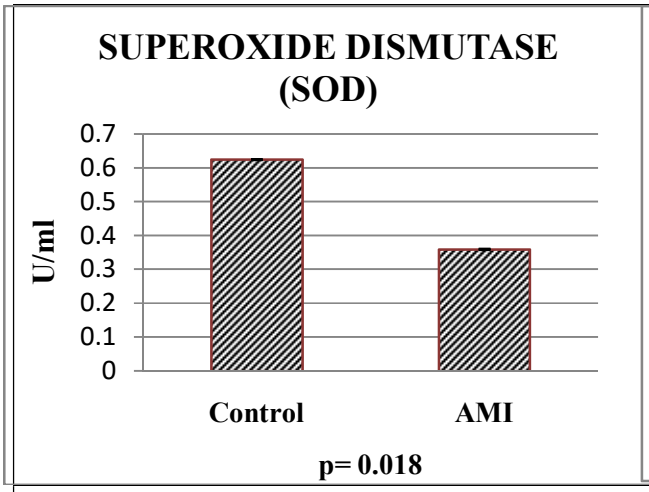
F (H)


TUMOR NECROSIS FACTOR-α (TNF-α)
pg/ml
50
40
30
20
10
0
Control
AMI
p= 0.015

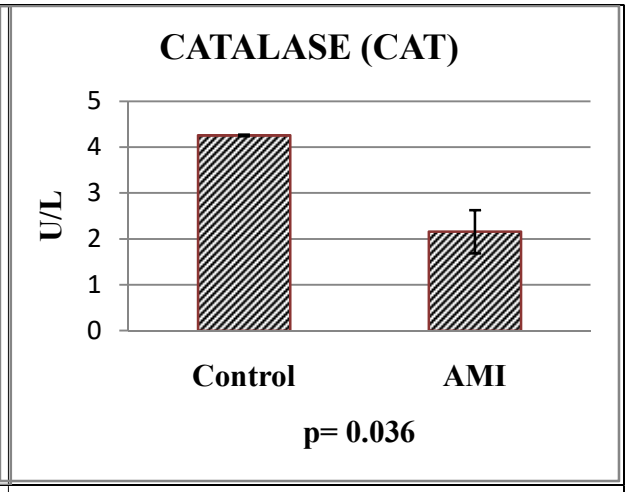
(I)


MALONDIALDEHYDE (MDA)
µmol
2.5
2
1.5
1
0.5
0
Control
AMI
p= 0.000

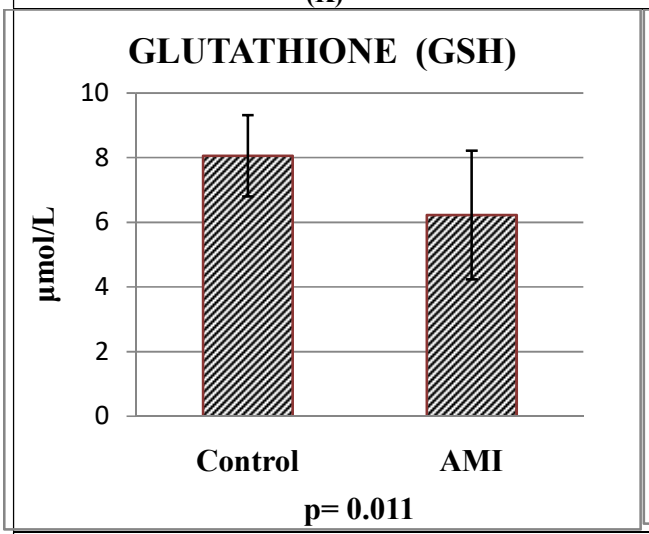
(J)


SUPEROXIDE DISMUTASE (SOD)
U/ml
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
Control
AMI
p= 0.018

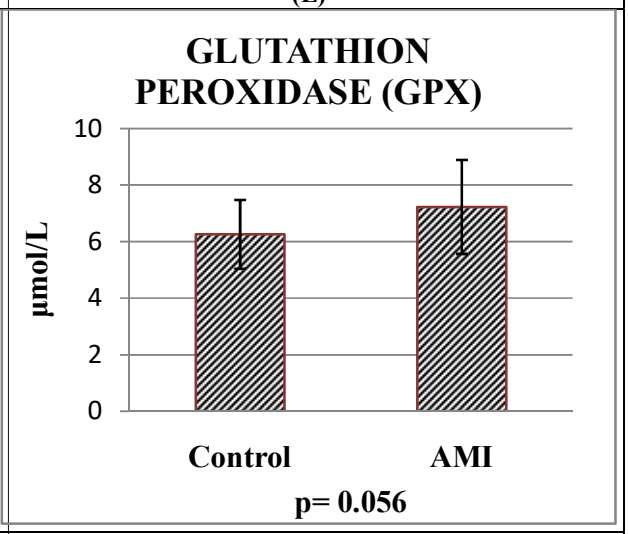
(K)


CATALASE (CAT)
U/L
5
4
3
2
1
0
Control
AMI
p= 0.036

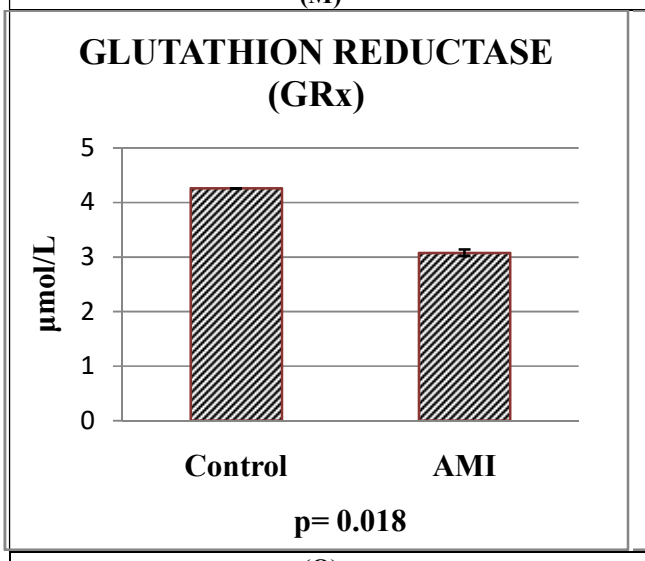
(L)


GLUTATHIONE (GSH)
µmol/L
10
8
6
4
2
0
Control
AMI
p= 0.011

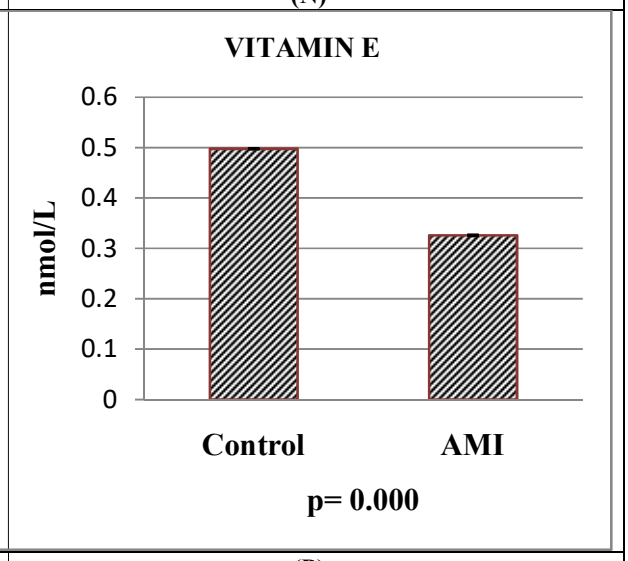
(M)


GLUTATHION PEROXIDASE (GPX)
µmol/L
10
8
6
4
2
0
Control
AMI
p= 0.056

(N)


GLUTATHION REDUCTASE (GRx)
µmol/L
5
4
3
2
1
0
Control
AMI
p= 0.018

(O)


VITAMIN E
nmol/L
0.6
0.5
0.4
0.3
0.2
0.1
0
Control
AMI
p= 0.000

(P)

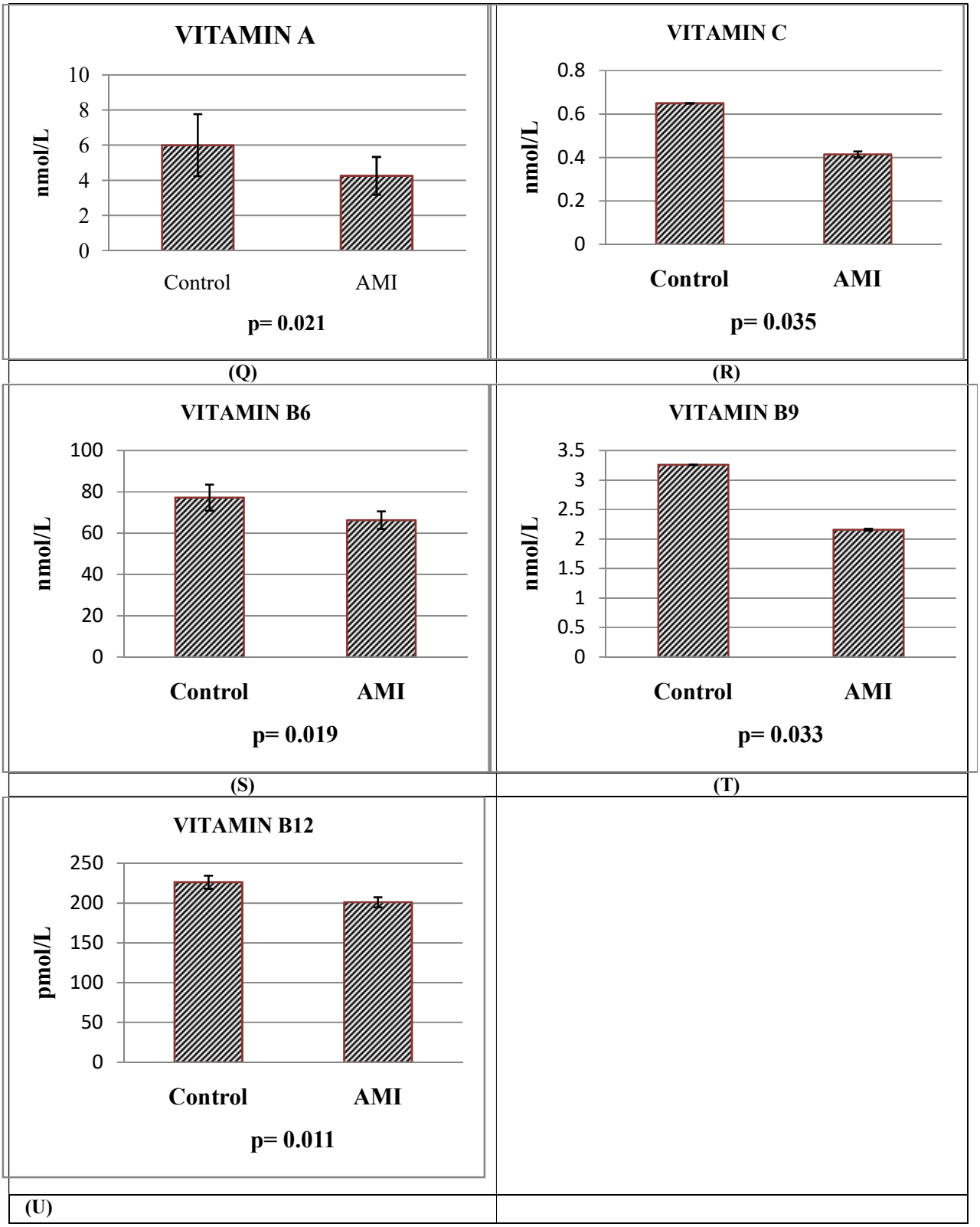


Figure 1: Graphical Presentation of Prophetic Variable of Medical Importance In Patients of Acute Myocardial Infarction (AMI)

DISCUSSION

The myocardial ischemia is known to be induced by the spasm in the coronary artery, thrombosis or atherosclerosis, which causes a decrease in the supply of blood to the heart. The supply of oxygen may be restored by reperfusion of the ischemic myocardium. However, abrupt massive increase in the supply of oxygen causes a burst of consumption of oxygen with consequent production of ROS (reactive oxygen species). An increased production of ROS causes the inhibition of activity of antioxidant, which may cause alteration of the cellular lipids, DNA and proteins of the myocardium and it results in the formation of atherosclerotic lesions. Atherosclerosis, which is the root cause of the acute myocardial infarction, appears to be an inflammatory condition of chronic nature that has converted to an acute clinical event by the initiation of the rupture of the plaque, which leads to the thrombosis. Also, a very important and central position is occupied by inflammation in all the phases of atherosclerosis, which is the latent cause of AMI, even though inflammation must smolder for many years before resulting a clinical event, like myocardial infarction **[31]**.

Molecular pathways of the angiogenesis; myocyte regeneration and differentiation are regulated by TH, and it finally improve the shape of myocyte and function of left ventricle, that ultimately leads to the improved cardiac performance. It is associated closely with various other cardiac diseases like arterial hypertension, dyslipidaemia, heart failure, AMI, atherosclerosis **[32,33]**. Heat shock proteins (HSP) are also regulated by TH, which by nature is cardio protective. Hence it can control the response to stress. When TRα (thyroid hormone receptor alfa) are inhibited, it causes the down regulation of thyroid hormone in the post ischemic myocardium. MI is elevated in ST segment has found to have TH dysfunction **[34]**. The beta myosin heavy chain (MCH) expression was decreased after the administration of TH, which promotes ultimately the wall thickening of ventricle and preventing a state of hypothyroidism **[35]**. Kalofoutis C *et al* **[36]** found that in diabetic rats, AMI caused by the TH receptors down regulation. Some believes that TH starts this down regulation much before the start of the process of infarction. In our study, the total serum T3 levels were observed to be reduced remarkably in AMI patients after 12 to 24 hours of the onset of symptoms possibly

considering a state like hypothyroid in AMI. Mechanism for the impermanent low T3 levels in the acute cases may be due to the reduced peripheral and hepatic conversion of T4 to T3, as of the 5' monodeiodinase enzyme level activity is low. Level of the TSH will be increased from pituitary by low T3 levels that leads to an increase in the T4 and T3 level in the serum. Our study is in accordance with friberg *et al* **[37]** and Chan-hee *et al* **[38]** that reports low fT3 levels with increment in FT4 in the first few days of AMI. The low levels of fT3 are a powerful predictor of long- and short term poor prognosis in the condition of AMI. Wang *et al* **[39]** reports a lower level of fT3 correlates with elevated levels of cardiac markers and a lower LVEF (left ventricular ejection fraction). Therefore, in AMI lower levels of T3 may be the predictor for myocardial injury.

To the injury, the immuno-inflammatory response that results from reperfusion and ischaemia of the infarcted myocardium is associated with the initiation of various cytokines including TNF-α and IL-6 **[40]**. A pleiotropic cytokine IL-6 has a cellular and humoral immune effect and are related to inflammation in response to TNF-α, IL-1, and is involved in the recruitment and activation of inflammatory cell, also stimulate liver to produce CRP and it may also have negative inotropic effect that is mediated through the myocardial nitric oxide synthase **[41]**. Raised levels of IL-6 increase the instability in the mechanism of the formation of unstable plaque **[42]**. An inverse co-relation has shown by IL-6 with T3 in AMI **[43]**. In the present study, there has been observed a notable increase in the levels of IL-6 in the AMI patients as compared to the normal individuals. Our results resemble with the study of Chen *et al* **[38]** that exhibit the raised levels of IL-6 caused damage in tissues and aggravation of disease in MI. In Myocardial infarction, there is an involvement of TNF-α in the inflammation by stimulating the apoptosis of cardiac cells. Various studies, including in vitro and in vivo have proclaimed that an elevated amount of TNF-α is produced by heart cells when mechanical stress is present. During the excess pressure, TNF-α contribute to the adverse remodelling of LV, which results in ventricular impairment. The reports of Cesari *et al* **[44]** and Tuomisto *et al* **[45]** shows a positive association of cardiovascular diseases and TNF-α in their prospective studies, which are also confirmed by our study. In our research, raised TNF-α levels were recorded in the diseases patients as

compared to the control group that is also parallel with the study of Ridker *et al* **[46]**.

Particularly the chlorinated oxidants, chlorinated amines and hypochlorous acid, are products of MPO (myeloperoxidase) system which cause the damage of protein that results in the generation of modified proteins called AOPPs. Our results are concurrent with the study of Skvarilova, *et al* **[47]** that demonstrated notably raised AOPPs level in the patients with non-ST elevated myocardial infarction and acute coronary syndrome. This indicates that myeloperoxidase system in patients is contributing relatively to the genesis of enormous amount of hypochlorous acid. Immoderate accumulation of this particular ROS, causes it to react with most abundant protein, which is albumin, it oxidizes it and form AOPPs, which then further triggers the NADPH oxidase and hence contributes to inflammation as well as oxidative stress.

This study demonstrated that the increase in the levels of NO in AMI patients as compared to the normal individuals which is concurrent with the study of Sanchez de Miguel *et al* **[48]**, that the amount of nitric oxide (NO) that is generated by neutrophils from the AMI patients was notably higher than that was generated by the neutrophils from UA patients. Many studies on the individuals of cardiovascular disease have been reported an elevated lipid hydro peroxides (LHP) and MDA level in serum and blood samples. Our study reported notably high levels of MDA in AMI patients in comparison with the healthy individuals. These results provide verification that a major fraction of generated free radicals are contributed by the atherosclerosis, which then leads to raised levels of lipid peroxidation. Therefore, oxidative stress leads to the lipid peroxidation. Our results are in accordance with Walter *et al* **[49]**, and showed that the TBARS serum elevated levels in CAD has been found to predict the major cardiovascular events.

Up to date evidences proposes that in each sub-cellular location, S0D catalyse the conversion of O_2- to H_2O_2, which participate in the signalling of cell. Additionally, a critical role played by SOD in inhibiting the oxidative inactivation of NO (nitric oxide), thereby preventing the formation of peroxynitrite and mitochondrial and endothelial dysfunction **[50]**. Our study showed a notably reduced level in patients of AMI in comparison to the normal individuals, which are coincident with Seema *et al* **[51]** indicated a notable reduced SOD levels in many groups of CVD. Reduced levels may be due to production of very large

amounts of endogenous superoxide ions in body of the patients, which then led to the increased reaction of SOD with NO and it forms peroxynitrite ions instead of converting superoxide to H_2O_2. Also the diminished levels of SOD led to further production of SOD ions and H_2O_2. An increment in the lipid per oxidation also contributed in the reduced levels of SOD. In the catalysis of reduction of the fatty acids into hydrogen peroxide (H_2O_2) and hydroperoxides, GPx is involved. In the present study the levels of GPx were raised in diseased group when compared with the normal. The raised level of GPx proposes that the activity of GPx enhances due to the reduction in SOD and CAT to fight the oxidative stress and reduced H_2O_2. It may also be due to the elevated concentration of lipo-peroxides, which incite the GPx production. The catalase level was decreased notably in AMI patients compared to the controls. Our findings are in accord with the findings of Kumar *et al* **[52]** and Gunasekara *et al* **[53]**. Experimental studies have showed that diminished glutathione (GSH) is involved in cellular defence from detrimental effects of the oxygen free radicals in reperfusion and ischemia. In our study, GSH along with its diminished form, levels of glutathione reductase are reduced in patients of AMI as compared to the controls which display the condition of increased oxidative stress in myocardial cell. Our study in concurrent with Kharb **[54]** and Bashar *et al* **[55]** reported depletion in both the anti-oxidant biomarkers. Low concentrations of vitamin C in plasma are reported frequently in the elderly people, a group with high-risk of sub-clinical inflammation. Our study described significantly low vitamin C levels in the patients of AMI in accordance with the normal group. Which is supported by study, which concludes that visible risk of AMI that is associated with the low ascorbic acid levels in plasma was disfigured by APR (acute phase response) **[56]**. Various studies have discerned the raised levels of homocysteine as risk factor for the atherothrombosis. Patients having acquired vitamin B12 deficiency for folate had a very high risk of thrombus because of hyperhomocysteinemia **[57]**. Melhem *et al* **[58]** studied that in young men AMI and the pulmonary embolism with anemia of pernicious nature induced hyperhomocysteinemia. A case-control study of 224 Pakistani patients suffering with the AMI has displayed that there was a notable correlation between the vitamin B12, B6 and folic acid deficiency and the mild hyperhomocysteinemia in patients with AMI

[59] and that is in the accordance with results of our study, which was showing vitamin B9, B6 and vitamin B12 deficiency in AMI. A fat-soluble antioxidant with the alpha tocopherol is vitamin E. it is involved in the CVD prevention through the oxidation of LDL that stimulates inflammatory markers that are involved in the formation of foam cells **[60-71]**. On the endothelial cells, it has cytotoxic effects, limits the tissue macrophages mortality thus inhibiting the vasodilation induced by NO that leads to the atherosclerotic plaque formation. Our study described vitamin E decreased levels in AMI patients as compared to the healthy individuals.

CONCLUSION

Cardiovascular signs and symptoms of the thyroid disease are some of the most acute and clinically relevant findings that supplement both hypothyroidism and hyperthyroidism. On the premise of understanding of cellular mechanism of the action of thyroid hormone on heart and cardiovascular system, it is probable to explain alterations in the cardiac output, blood pressure, rhythm disturbances, cardiac contractility and vascular resistance that results from the thyroid dysfunction. The condition of oxidative stress is generated by it along with the depletion in antioxidant capacity to conquest over this stress and leading that induce endothelial dysfunction leading to atherosclerosis and eventually AMI. The significance of the identification of the effects of thyroid disease on acute myocardial infarction also extract an observation that the restoration of normal thyroid function repeatedly reverses the abnormal cardiovascular hemodynamic.

ACKNOWLEDGEMENTS

Authors are highly thankful and pay their gratitude to Mr. Awais Raoof, Chairman BOG, The University of Lahore for supporting and providing financial assistance for the current project.

CONFLICT OF INTEREST

Authors declare no conflict of interests.

REFERENCES

[1] Eriksson M, Asplund K, Svedlund M. Couples' thoughts about and expectations of their future life after the patient's hospital discharge following acute myocardial infarction. Journal of Clinical Nursing. 2010;19(23-24):3485-93.

[2] Burke AP, Virmani R. Pathophysiology of acute myocardial infarction. Med Clin North Am. 2007;91:553-572.

[3] Roger VL, Go AS, Lloyd-Jones DM, Benjamin EJ, Berry JD, Borden WB, Bravata DM, Dai S, Ford ES, Fox CS, Fullerton HJ, Gillespie C, Hailpern SM, Heit JA, Howard VJ, Kissela BM, Kittner SJ, Lackland DT, Lichtman JH, Lisabeth LD, Makuc DM, Marcus GM, Marelli A, Matchar DB, Moy CS, Mozaffarian D, Mussolino ME, Nichol G, Paynter NP, Soliman EZ, Sorlie PD, Sotoodehnia N, Turan TN, Virani SS, Wong ND, Woo D, Turner MB. Heart disease and stroke statistics--2012 update: a report from the American Heart Association. Circulation. 2012;125:e2-e220.

[4] Welin L, Eriksson H, Larsson B, Svardsudd K, Wilhelmsen L, Tibblin G. Risk factors for coronary heart disease during 25 years of follow-up. The study of men born in 1913. Cardiology 1993;82(2-3):223-228.

[5] Njolstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996; 93(3):450-456.

[6] Hansson L. The Hypertension Optimal Treatment study and the importance of lowering blood pressure. J Hypertens Suppl 1999;17(1):S9-13.

[7] Klein I, Ojamaa K. Thyroid hormone and the cardiovascular system. N Engl J Med. 2001; 344: 501–509.

[8] Hak AE, Pols HA, Visser TJ, Drexhage HA, Hofman A, Witteman JC. Subclinical hypothyroidism is an independent risk factor for atherosclerosis and myocardial infarction in elderly women: The rotterdam study. Ann Intern Med. 2000;132:270-278.

[9] Jabbar A, Alessandro Pingitore, Simon H. S. Pearce, Azfar Zaman, Giorgio Iervasi & Salman Razvi. Thyroid hormones and cardiovascular disease. Nature Reviews Cardiology. 2017; 14:39–55.

[10] Friberg L, Werner S, Eggertsen G, Ahnve S. Rapid down-regulation of thyroid hormones in acute myocardial infarction: is it cardioprotective in patients with angina? Arch Intern Med 2002;162(12):1388-94.

[11] Hamilton MA, Stevenson LW, Lu M, et al. Altered thyroid hormone metabolism in advanced heart failure. J Am Coll Cardiol. 1990;16: 91–95.

[12] Holland FW, Brown PS Jr, Weintraub BD, et al. Cardiopulmonary bypass

and thyroid function: a "euthyroid sick syndrome". Ann Thorac Surg. 1991; 52:46-50.

[13] Camacho PM, Dwarkanathan AA. Sick euthyroid syndrome. What to do when thyroid function tests are abnormal in critically ill patients. Postgrad Med. 1999; 105:215-219.

[14] Franklyn JA, Gammage MD, Ramsden DB & Sheppard MC. Thyroid status in patients after acute myocardial infarction. Clinical Science 1984; 67 585–590.

[15] Eber B, Schumacher M, Langsteger W, Zweiker R, Fruhwald FM, Pokan R, Gasser R, Eber O & Klein W. Changes in thyroid hormone parameters after acute myocardial infarction. Cardiology 1995; 86 152–156.

[16] Cerillo AG, Storti S, Clerico A & Iervasi G. Thyroid function and cardiac surgery: what should we measure, and when? Annals of Thoracic Surgery 2010, 89:1010–1011.

[17] Pingitore A, Chen Y, Gerdes AM, Iervasi G. Acute myocardial infarction and thyroid function: new pathophysiological and therapeutic perspectives. Ann Med 2012;44(8):745-57.

[18] Kalofoutis C, Mourouzis I, Galanopoulos G, Dimopoulos A, Perimenis P, Spanou D Cokkinos DV, Singh J, Pantos C. Thyroid hormone can favorably remodel the diabetic myocardium after acute myocardial infarction. Mol Cell Biochem 2010;345(1-2):161-9.

[19] Pantos C, Mourouzis I & Cokkinos DV. Rebuilding the postinfarcted myocardium by activating physiologic hypertrophic signaling pathways: the thyroid hormone paradigm. Heart Failure Reviews, 2010, 15 143–154.

[20] Pantos C, Mourouzis I, and Cokkinos DV. New insights into the role of thyroid hormone in cardiac remodeling: time to reconsider? Heart Fail Rev ,2011,16, 79-96.

[21] Moron MS, Depierre JW, Mannervik, B. Levels of glutathione reductase and glutathione S-transferase in rat lung and liver. Biochem Biophysic Acta, 1979;582, pp. 67-68.

[22] Aebi H. Catalase: In: Bergmeyer. Methods In Enzymatic Analysis Academic Press Inc., New York,1974; Pp.673-686.

[23] Kakkar, PB, Das P, Viswanathan PN. A Modified Spectrophotometer Assay Of Superoxide Dismutase. Ind J Biochem Bio. 1984; 21, Pp.130-132.

[24] Ohkawa H, Ohishi N, Yagi KK. Assay for lipid peroxides in animal tissues by thiobarbituric acid reaction. J Anal Biochem,1979, 95; pp. 351-358.

[25] David, M And Richard, JS. Glutathione Reductase. Methods Of Enzymatic Analysis,1983,3; pp.258-265.

[26] Moshage H, Kok B, Huizenga JR, Jansen PL. Nitrite and nitrate determinations in plasma: a critical evaluation. Clin Chem,1995,41; pp. 892-896.

[27] Kalousova M, Skrha J, Zima T. Advanced glycation end-products and advanced oxidation protein products in patients with diabetes mellitus. Physiol Res, 2002, 51(6);pp. 597-604.

[28] Rutkowski M, Grzegorczyk K, Gendek E, Kedziora J. Laboratory convenient modification of Bessey method for vitamin A determination in blood plasma J. Physiol. Pharm. 2006;57:221.

[29] Roe J, Kuether C. Estimation of ascorbic acid. J Biol Chem. 1943;147:3999.

[30] Rosenberg IH, Miller JW. Nutritional factors in physical and cognitive functions of elderly people. The American journal of clinical nutrition. 1992 Jun 1;55(6):1237S-43S.

[31] Libby P. Vascular biology of atherosclerosis: Overview and state of art. Am J Cardiol 2003; 91(suppl): 3A-6A.

[32] Pantos C, Mourouzis I, Tsagoulis N, Markakis K, Galanopoulos G, Roukounakis N, Perimenis P, Liappas A, Cokkinos DV. Thyroid hormone at supra-physiological dose optimizes cardiac geometry and improves cardiac function in rats with old myocardial infarction. J Physiol Pharmacol 2009;60(3):49-56.

[33] Pingitore A, Chen Y, Gerdes AM, Iervasi G. Acute myocardial infarction and thyroid function: new pathophysiological and therapeutic perspectives. Ann Med 2012;44(8):745-57.

[34] Ozcan KS, Osmonov D, Toprak E, Gungor B, Tatlısu A, Ekmekçi A, Kaya A, Tayyareci G, Erdinler I. Sick euthyroid syndrome is associated with poor prognosis in patients with ST segment elevation myocardial infarction undergoing primary

percutaneous intervention. Cardiol J 2014;21(3):238-44.

[35] Cokkinos DV, Pantos C. Type 1 diabetes impairs compensatory response after myocardial infarction; role of tissue hypothyroidism and effects of thyroid hormone administration. Bull Acad Natl Med 2011;195(1):151-64.

[36] Kalofoutis C, Mourouzis I, Galanopoulos G, Dimopoulos A, Perimenis P, Spanou D, Cokkinos DV, Singh J & Pantos C. Thyroid hormone can favorably remodel the diabetic myocardium after acute myocardial infarction. Molecular and Cellular Biochemistry .2010 345:161-169.

[37] Friberg L, Werner S, Eggertsen G, Ahnve S. Rapid down-regulation of thyroid hormones in acute myocardial infarction: is it cardioprotective in patients with angina? Arch Intern Med 2002;162(12):1388-94.

[38] Chen, Y. F., Kobayashi, S., Chen, J., Redetzke, R. A., Said, S., and Liang, Q., et al. (2008). Short term triiodo-l-thyronine treatment inhibits cardiac myocyte apoptosis in border area after myocardial infarction in rats. J Mol Cell Cardiol, 44(1): 180-187.

[39] Wang WY, Tang YD, Yang M, Cui C, Mu M, Qian J, Yang YJ. Free triiodothyronine level indicates the degree of myocardial injury in patients with acute ST-elevation myocardial infarction. Chin Med J (Engl), 2013;126(20):3926-9.

[40] Chen T, Huang Z, Wang L, Wang Y, Wu F, Meng S, Wang C. MicroRNA-125a-5p partly regulates the inflammatory response, lipid uptake, and ORP9 expression in oxLDL-stimulated monocyte/macrophages. Cardiovascular research, 2009, 1;83(1):131-9.

[41] Bodi V, Sanchis J, Lopez-Lereu MP, Losada A, Nunez J, et al. Usefulness of a comprehensive cardiovascular magnetic resonance imaging assessment for predicting recovery of left ventricular wall motion in the setting of myocardial stunning. J Am Coll Cardiol,2005,46; 1747-175.

[42] Liuzzo G, Buffon A, Biasucci LM, Gallimore JR, Caligiuri G, Vitelli A, Altamura S, ciliberto G, Rebuzzi AG, Crea F, Pepys MB. Enhanced inflammatory response to coronary angioplasty in patients with severe unstable angina. Circulation. 1998,98(22):2370-6.

[43] Nishino M, Kimura T, Kanda T, Kotajima N, Yoshida A, Kuwabara A, Tamama K, Fukumura Y, Kobayashi I. Circulating interleukin-6 significantly correlates to thyroid hormone in acute myocardial infarction but not in chronic heart failure. Journal of endocrinological investigation. 2000 Sep 1;23(8):509-14.

[44] Cesari M. Inflammatory markers and onset of cardiovascular events: results from the Health ABC study. Circulation,2003,108(19):2317-2322.

[45] Tuomisto K. C-reactive protein, interleukin-6 and tumor necrosis factor alpha as predictors of incident coronary and cardiovascular events and total mortality. A population-based, prospective study. Thromb Haemost,2006, 95(3):511-518.

[46] Ridker PM. Elevation of tumor necrosis factor-alpha and increased risk of recurrent coronary events after myocardial infarction. Circulation,2000, 101(18): 2149-53.

[47] Skvarilova M, A Bulava, D Stejskal, S Adamovská and J Bartek. Increased level of advanced oxidation products (AOPP) as a marker of oxidative stress in patients with acute coronary syndrome. Biomed papers,2005,149(1):83-7.

[48] de Miguel LS, aMar Arriero M, Montón M, López-Farré A, Farré J, Cabestrero F, Martín E, Romero J, Jiménez P, García-Méndez A, de Frutos T. Nitric oxide production by neutrophils obtained from patients during acute coronary syndromes: expression of the nitric oxide synthase isoforms. Journal of the American College of Cardiology. 2002 Mar 6;39(5):818-25.

[49] Walter MF, RF Jacob, B Jeffers, MM Ghadanfar, GM Preston, J Buch and RP Mason (2004). Serum levels of thiobarbituric acid reactive substances predict cardiovascular events in patients with stable coronary artery disease: a longitudinal analysis of the PREVENT study. Journal of the American College of Cardiology, **44(10):1996-2002**.

[50] Fukai Tand Ushio-Fukai M (2011). Superoxide Dismutases: Role in Redox Signaling, Vascular Function, and Diseases. Antioxidants & Redox Signaling.**15(6); 1583-1606.**

[51] Seema LJ, JK Ujjwala, TS Vasant and YA Deshmukh. Role of Oxidants and Anti Oxidants in Patients with

Cardiovascular Diseases. Asian Journal of Medical Sciences,2010,2(4):181-184.

[52] Kumar A, Sivakanesan R, Singh S. Oxidative stress, endogenous antioxidant and ischemia-modified albumin in normolipidemic acute myocardial infarction patients. Journal of health science. 2008;54(4):482-7.

[53] Kumar A, Sivakanesan R, Gunasekera S. Oxidative stress and antioxidant status in normolipidemic AMI patients. Indian Journal of Clinical Biochemistry. 2008 Jul 1;23(3):296-8.

[54] Kharb, S. Low blood glutathione levels in acute myocardial infarction,2003.

[55] Bashar T, Sultan A, Zeba-un-nisa, Afree M. Erythrocyte glutathione level in patients of Acute Myocardial Infarction. J. Uni. Heart,2011, 7(2):63-66.

[56] Riemersma RA, Carruthers KF, Elton RA, Fox KA. Vitamin C and the risk of acute myocardial infarction. The American journal of clinical nutrition, 2000,1;71(5):1181-6.

[57] Lange H, Suryapranata H, De Luca G, Börner C, Dille J, Kallmayer K, Pasalary MN, Scherer E, Dambrink JH. Folate therapy and in-stent restenosis after coronary stenting. New England Journal of Medicine, 2004, 24;350(26):2673-81.

[58] Melhem A, Desai A, Hofmann MA. Acute myocardial infarction and pulmonary embolism in a young man with pernicious anemia induced severe hyperhomocyteinemia. Thrmb J 2009; 7: 5.

[59] Iqbal MP, Ishaq M, Kazmi KA, Yousuf FA, Mehboobali N, Ali SA *et al*. Role of vitamins B6, B12 and folic acid on hyperhomocysteinemia in a Pakistani population of patients with acute myocardial infarction. Nutr Metab Cardiovasc Dis. 2005; 15: 100-8.

[60] Carr AC, MR McCall and B Frei. Oxidation of LDL by myeloperoxidase and reactive nitrogen species: reaction pathways and antioxidant protection, Arteriosclerosis, Thrombosis and Vascular Biology,2000, 1716-1723.

[61] Hafeez M, Yasin T, Safdar U, Waquar S, Rana M, Malik A. An evidence based assessment of most common risk factors of myocardial infraction: analysis from a local population. Biol Clin Sci Res J 2020(1):e044.

[62] Khalil R, Ali Q, Hafeez M, Malik A. Phenolic acid profiling by rp-hplc:

evaluation of antibacterial and anticancer activities of *Conocarpus erectus* plant extracts. Biol Clin Sci Res J 2020(1):e010.

[63] Hameed B, Ali Q, Hafeez MM, Malik A. Antibacterial and antifungal activity of fruit, seed and root extracts of Citrullus colocynthis plant. Biol Clin Sci Res J. 2020;33.

[64] Ali J, Ali Q, Hafeez MM, Malik A. Clinical features, diagnosis and treatment of COVID-19. Biol Clin Sci Res J. 2020;2020:e032.

[65] Siddique A, Fateh A, Idrees N, Hafeez MM, Ali Q, Malik A. The epidemics of COVID-19. Biol Clin Sci Res J. 2020:e030.

[66] Rashid M, Kari M, Rashid R, Rana M, Amjad A, Hafeez M. Uterine artery doppler indices as predictive measures for the pre-eclampsia and intrauterine growth restriction. Biol Clin Sci Res J; 2020(1):e023.

[67] Omer M, Malik S, Anjum M, Riaz A, Ali R. Diagnostic accuracy of ultrasound in detecting meniscal tears taking magnetic resonance imaging as gold standard. Biol Clin Sci Res J 2020(1):e040.

[68] Ali Q, Khalil R, Nadeem M, Hafeez, MM, Malik, A. Antibacterial, antioxidant activities and association among plant growth related traits of *Lepidium draba*. Biol Clin Sci Res J. 2020:011.

[69] Khalid A, Anjum M, Daraaz U, Hussain K, Omer M. Predictive accuracy of cervical length in mid trimester on transabdominal ultrasound for cesarean section. Biol Clin Sci Res J 2020(1):e043.

[70] Chudhary H, Amin A, Malik M, Hafeez M, Rana M, Malik A. Risk assessment of non-conventional contributory factors in onset of diabetes mellitus type II. Biol Clin Sci Res J 2020(1):e036.

[71] Ali S, Gillani S, Afzal M, Parveen K. Assessment of nurses management skills for critically ill patients. Biol Clin Sci Res J 2020(1):e013.