Evaluation of Fractalkine and Migration Inhibitory in the Patient with Atherosclerosis

Huda W.A. AL-Nazal[1], Ali M.A. Al-Kufaishi[2*], Khalid M. Dakhel[3]

Abstract

Atherosclerosis (AS) a is the major underlying clinical mechanism of CVD. Cardiovascular diseases (CVD) are the leading cause of death globally, many factors such as MIF, CX3CL1, GSH and MDA were isociated with atherosclerosis. **Materials and method:** Sixty back to back patients with conclusion of atherosclerosis along with 30 sound control subjects were enlisted. Venous blood tests were gathered not long before the coronary atheterization methodology (in examination patients). MIF, CX3CL1, GSH and MDA fixation was resolved utilizing financially accessible colorimetric kits. **Results:** The most elevated value of MIF, MDA, FKN in patient group while decline of GSH in serum level patients. (0.482, 0.512 (ng\ml), 7.28 (µmole/L), respectively; p<0.05). **Conclusion:** The new data MIF, CX3CL1, GSH and MDA demonstrate a significant job for these components being developed of atherosclerosis, simultaneously these elements information were reveals insight into their job in tweak the safe reaction and irritation in the aortic divider.

Key Words: Atherosclerosis, MIF, CX3CL1, GSH and MDA.

DOI Number: 10.14704/nq.2021.19.6.NQ21061 **NeuroQuantology 2021; 19(6):15-19**

Introduction

Atherosclerosis (AS) a is the major underlying clinical mechanism of CVD. Cardiovascular diseases (CVD) are the leading cause of death globally, with 30 million deaths expected each year by 2030 (Alwan *et al.*, 2011). In plaques, macrophages are the most common cells. and are essential in the progression of atherosclerosis (Wang *et al.*, 2019). Both circulating monocytes that bind to activated endothelial cells and enter the intimal layer and locally proliferating plaque macrophages are sources of plaque macrophages (Robbins *et al.*, 2013).

Fractalkine (or CX3CL1) is a unique chemokine that is found on actuated endothelium, dendritic cells, and VSMC as a layer bound and solvent chemokine (Lucas et al., 2003). It capacities as a bond particle for leukocytes and is bound to vascular divider cells by an extended mucin tail associated with a transmembrane space (Stolla et al., 2012). At the leukocyte–endothelial cell interface, CX3CL1 and its receptor (CX3CR1) control leukocyte grip and extravasation. More specifically, mounting data shows that FKN plays a part in atherosclerosis pathogenesis, is strongly expressed in early atherosclerotic lesions, and is expressed after arterial injury (Lee *et al.*, 2006).

Human macrophage movement hindrance factor (MIF) is a cytokine and chemokine-like protein that controls an assortment of physiological capacities connected to natural invulnerability and aggravation and cardiovascular illnesses (Illescas *et al.*, 2020; El-Mahdy *et al.*, 2021).

Corresponding author: Ali M.A. Al-Kufaishi

Address: [1]Southern Technical University, College of Health and Medical Techniques, Department of Medical Laboratory Techniques, Basrha, Iraq; [2*]Al-Furat Al-Awsat Technical University, College of Health and Medical Techniques, Department of Medical Laboratory Techniques, Kufa, Iraq; [3]Southern Technical University – Nassriah Technical Institute, Iraq.

[2*]E-mail: Kuh.ali@atu.edu.iq

Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

Received: 21 March 2021 **Accepted:** 10 May 2021

Glutamine (GS) is the most abundant non-essential amino acid in human blood, with a wide range of physiological effects (Chen *et al.*, 2020). Atherosclerosis (As) is the leading cause of CAD (Chen *et al.*, 2020). It describes the loss of artery elasticity and the buildup of lipid and fibrous material in the arterial wall, as well as the narrowing of arteries that allows atherosclerotic plaques to develop (Chen *et al.*, 2020). Malondialdehyde (MDA) is a well-known secondary product of lipid peroxidation that can be used as a biomarker for cell membrane damage. Conjugated dienes, isoprostanes, ethane, and pentane gases are other lipid peroxidation products that are used to test lipid membrane peroxidation. 4-Hydroxynonenal and 11-Hydroxynonenal (Al-Kufaishi, Al-Mashhedy and Al-Rubaie, 2020 , Frei *et al.*, 1995). This study was aimed to investigate the effect of fractalkine, migration Inhibitory factor and some biochemical parameters in the patients with atherosclerosis.

Abbreviations: AS, Atherosclerosis, CVD, Cardiovascular diseases, FKN, Fractalkine, MIF, human macrophage migration inhibition factor, GS, Glutamine, CAD, coronary artery disease, MDA, Malondialdehyde, MI, myocardial Infraction.

Material and Methods

Study Design and Population

A case-control research was performed on 60 heart failure patients and 30 stable controls. This research was carried out on Hilla patients. In Babylon province, there is a hospital named Mirjan Medical City / Shahid Al- Mihrab Base. Both samples were obtained between October, 2020 and November, 2020. The study's functional side was carried out at the University Al-Furat Al-Awsat Technical's Biochemistry laboratory.

Exclusion criteria: Diabetes**,** Obesity**,** Women and Children, Kidney disease.

Specimen Collection: Blood is extracted from each person using a sterile syringe (5 mL). Every subject gave five mL of blood, which was slowly forced into a Gel tube and centrifuged at 3000 r.p.m. for 10-15 minutes, after which the serum was separated into three sections and processed at -20 ºC before examination.

Determination of Human CX3C-chemokine\Fractalkine

Fractalkine was measured using enzyme linked immunosorbent assay (ELISA) kits by Bioassay Technology.

Determination of Human Macrophage Migration Inhibitory Factor

Migration Inhibitory Factor MIF was measured using enzyme linked immunosorbent assay (ELISA) kits by Bioassay Technology.

Determination of Serum Malondialdehyde (MDA)

The technique depended on the spectrophotometric estimation of the shading, happened during the response between thiobarbituric corrosive (TBA) and MDA, (Al-Kufaishi, Al-Mashhedy and Al-Rubaie, 2020).

Determination of Reduced Glutathione (GSH)

Technique was utilized to decide serum glutathione (GSH) contingent upon the activity of sulfhydryl gatherings. Accordingly strategies incorporate photometric, enzymatic, flourometric and HPLC are utilized (Al-Kufaishi, Al-Mashhedy and Al-Rubaie, 2020).

Statistical Analysis

For information examination, SPSS rendition 22 was utilized. The outcomes were addressed as mean ± SD for consistent information or frequencies and percent for clear cut factors. autonomous understudy t-test were utilized for correlation between the two inspected gatherings, We considered a two-followed P-worth of under 0.05 measurably critical.

Results and Discussion

In this study, results showed that expression of Macrophage gone inhibitor factor (MIF) is significantly more in patient group (0.482ng/ml) compared with healthy group (0.379ng/ml) Table 1. This effect may arise from risk factors that have been contributed the incidence of atherosclerosis. such as formation of serious atherosclerotic lesions, plaque formation, increment levels of monocyte and macrophage enlistment, bond and created different chemokines that basically add to frequency of atherosclerosis. This result was consistent with Zernecke et al., (2008). They referred MIF is a chemical-like protein and thus

possesses many chemical-like features related to the recruitment and chemotaxis of inflammatory cells and the development of atherosclerotic lesions.

The worth of MIF in patients isociated with well known more seasoned, had all the more regularly blood vessel hypertension, hyperlipidemia, Those with high MIF ranges showed eminently higher quantities of monocytes in the fringe blood (Müller et al., 2012).

Due to the important of Macrophage movement as inhibitor factor (MIF) is engaged with the advancement of atherosclerosis and plaque destabilization and assumes a vital part in the improvement of heart illnesses. Little is known today about the clinical effect of MIF in patients with suggestive occurrence of atherosclerosis incidence of atherosclerosis (Ouertatani-Sakouhi et al., (2010); Müller et al.,2012).

Table 1. Showed the expression of Macrophage migration inhibitory factor (MIF) and fractalkine (FKN) in patient group and healthy group isociated with atherosclerosis.

Parameters	*Type of Group*	*Mean ±SD*	*S.E*	*P-Value*
MIF(ng\ml)	Patient	0.482±0.148	0.019	0.001
	Healthy	0.379±0.098	0.017	
FKN (ng\ml)	Patient	0.512±0.163	0.021	0.012
	Healthy	0.424±0.128	0.023	

*The significance related when P- Value < 0.05

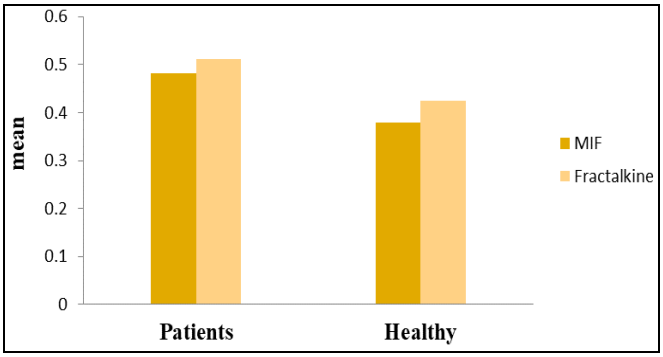

Fig. 1. The mean difference in (MIF, Frectlkine) between patients of atherosclerosis and healthy atherosclerosis group

Roger *et al.*, 2001 referred to that MIF is a fundamental part of the host antimicrobial caution framework and stress reaction that advances the favorable to incendiary elements of insusceptible cells. A developing group of writing proposes that MIF is engaged with patho-mechanisms of sepsis, provocative and immune system illnesses and atherosclerosis.

Ultimately, winning realities highlight the need to portray the job of MIF for hazard marker examination and its prescient capacity in patients with side effects of atherosclerosis. We show that MIF articulation relates with calming reaction and scope of markers for cardiovascular putrefaction. Therefore, assurance of MIF yield can aid hazard separation in atherosclerosis various marker methods.

The Table 1 summarized the values of fractalkine (FKN), this factor shown high in patient group (0.512 ng/ml). Compared with healthy group (0424ng/ml**.** based on considerd fractalkine (or CX3CL1) is a basically and practically interesting chemokine with a very much recorded part in atherosclerosis. In light of the explination of Apostolakis and Spandidos (2013). In its layer bound structure it advances the firm attachment of moving leucocytes onto the vessel divider, while in its dissolvable structure it fills in as a strong chemo-attractant for CX3CR1-communicating cells.

These markers or helpful focuses of atherosclerotic cardiovascular sickness. Furthermore, CX3CL1 applies cytotoxic consequences for the endothelium just as against apoptotic and proliferative impacts on vascular cells, influencing the unique circumstance and steadiness of the atherosclerotic plaque. The risk of Fractalkine arised from it considerd exceptional chemokine which has both cement and chemoattractant capacities. With the expanding accentuation on the significance of aggravation in atherosclerosis, more consideration has been centered around the part of chemokines in atherosclerosis (Apostolakis and Spandidos, 2013).

The *glutathione* (*GSH*) values was detected in this result shown elevation of GSH in healthy group (27.94), while decline it value in patient group (21.90), this result was consistant with role of *GSH function as antioxidant,* glutathione-related cancer prevention agent guards (which assume a vital part in tissue cell reinforcement insurance) in carotid atherosclerotic plaques in human. This outcome was concur with Lapenna et al., (1998), when they inferred that a frail glutathione-related enzymatic cell reinforcement safeguard is available in human atherosclerotic injuries. Albeit the reason for this marvel stays to be resolved, the current information recommend that a particular cancer prevention agent/prooxidant lopsidedness usable in the vascular divider might be associated with atherogenic measures in people. And they have never observed the absence of GSH-Px activity in normal human vessels obtainable in vivo. Also, our result was consistant with Zuzak E. et al., (2017).

The results shown that the statistical evaluation of GSH showed that just glutathione reductase action was fundamentally higher in serum acquired from myocardial localized necrosis patients, The raised action of glutathione reductase in serum of patients with temperamental angina pectoris and myocardial dead tissue recommends the part of cell reinforcement framework intense coronary disorder.

The outcome shown that the mean serum MDA levels were essentially raised in patients with predominant cardiovascular infection (7.28 µmole/L) contrasted and those without (3.44 µmole/L). In univariate examination of serum MDA levels in HD patients, pretreatment serum MDA levels (MDA1) were discovered to be altogether emphatically connected with predominant CVD.Based on letreture the MDA consider as a risk factor correlated with many human disease (Jung et al.,2004), serum or plasma MDA is raised in different illness states, including the period promptly following an intense myocardial localized necrosis (MI)(Kanitz et al.,1996) . Serum MDA levels have likewise been demonstrated to be raised in upkeep hemodialysis (HD) patients, a populace with a sped up cardiovascular dreariness and heart death rate (Jung *et al*., 2004).

Table 2. Showed the expression of *glutathione* (*GSH*) factor and malondialdehyde (MDA) in patient group and healthy group isociated with atherosclerosis.

Biochemical Parameters	Type of Group	Mean ±SD	S.E	P-Value
GSH (µmol/L)	Patient	21.90±6.001	0.775	0.001
	Healthy	27.94±5.341	0.992	
MDA (µmole/L)	Patient	7.28±7.615	0.983	0.009
	Healthy	3.44±0.636	0.120	

*The significance related when P- Value < 0.05

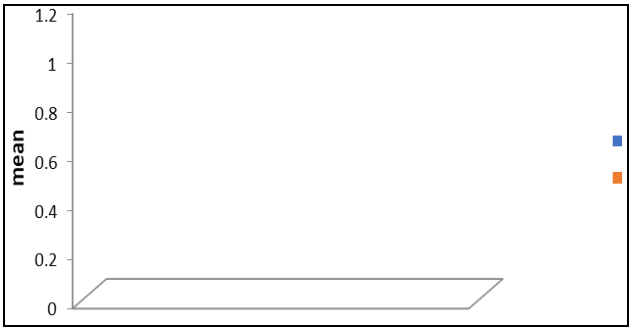

Fig. 2. The mean difference in (GSH, MDA) between patients of atherosclerosis and healthy atherosclerosis group

The MDA levels expanded ($p < 0.05$) with expanding atherosclerosis. The degrees of MDA in Patients in the most elevated level contrasted and the sound gathering were more than four times as prone to have extreme coronary supply route infection, and the most elevated tertile of MDA was a free indicator of serious coronary course illness, alongside a past cardiovascular occasion. End: An expanded degree of MDA, which was related with fiery markers, was a predictive factor for severe coronary artery disease patients (Jung et al., 2004).

Conclusion

An important conclusion is our understanding of atherosclerosis significantly isociated many factors like MIF, CX3CL1, GSH and MDA.

This opened up new points of view on thier part of aggravation and insusceptible reactions in atherosclerosis. The new data MIF, CX3CL1, GSH and CX3CL1 indicate an important role for these factors in development of atherosclerosis, at the same time these factors data were reveals insight into their job in adjust the safe reaction and irritation in the aortic divider.

Mounting proof proposes that parts of the invulnerable framework may change lipid digestion and along these lines influence atherosclerosis in another manner. More work is expected to comprehend the impact of statins on aggravation and the insusceptible framework. The entirety of this information will help characterize potential treatment objectives for forestalling and treating atherosclerosis and other cardiovascular illnesses.

Conflict of Interest

For publishers, there is no conflict of interest.

Funding: Personal funding.

Compliance with Ethical Standards

This study was approved by the science committee at my university and the Iraqi Ministry of Health.

References

Al-Kufaishi AMA, Al-Mashhedy LAM, Al-Rubaie BJ. 'A Modified Method to Determine Lipids Peroxidation in patients with HPV16 Cervicitis'. *Research Journal of Pharmacy and Technology* 2020; 13(9): 4087–4091.

Al-Kufaishi AMA. Evaluation of the Oxidative Stress Status in the Girls with Hyperprolactinemia Through Some Biochemical Parameters. *Indian Journal of Public Health Research & Development* 2020; *11*(4).

Alwan A, Armstrong T, Bettcher D, Branca F, Chisholm D, Ezzati M, Wild, C. World Health Organization 2010 global status report on noncommunicable diseases 2011.

Apostolakis S, Spandidos D. Chemokines and atherosclerosis: focus on the CX3CL1/CX3CR1 pathway Acta *Pharmacologica Sinica* 2013; 34(10): 1251-1256.

Chen J, Zhang S, Wu J, Wu S, Xu G, Wei D. Essential Role of Nonessential Amino Acid Glutamine in Atherosclerotic Cardiovascular Disease. *DNA and Cell Biology* 2020; 39(1): 8–15.

El-Mahdy RI, Saleem TH, Essam OM, Algowhary M. 'Functional variants in the promoter region of macrophage migration inhibitory factor rs755622 gene (MIF G173C) among patients with heart failure: Association with echocardiographic indices and disease severity. *Heart & Lung* 2021; 50(1): 92–100.

Morrow JD, Frei B, Longmire AW, Gaziano JM, Lynch SM, Shyr Y, Roberts LJ. Increase in circulating products of lipid peroxidation (F2-isoprostanes) in smokers—smoking as a cause of oxidative damage. *New England Journal of Medicine* 1995; 332(18): 1198–1203.

Freitas RWJF, Araújo MFM, Lima ACS, Pereira DCR, Alencar AMPG, Damasceno MMC. Study of Lipid profile in a population of university students. *Revista latino-americana de enfermagem* 2013; 21(5):1151-1158.

Illescas O, Pacheco-Fernández T, Laclette JP, Rodriguez T, Rodriguez-Sosa M. Immune modulation by the macrophage migration inhibitory factor (MIF) family: D-dopachrome tautomerase (DDT) is not (always) a backup system. *Cytokine* 2020; 133: 155121.

Jain RB, Ducatman A. Associations between smoking and lipid/lipoprotein concentrations among US adults aged ≥20 years. *Journal of circulating biomarkers* 2018; 7:1-10.

Jung HH, Choi DH, Lee SH. Serum malondialdehyde and coronary artery disease in hemodialysis patients. *American journal of nephrology* 2004; 24(5): 537-542.

Kanitz MG, Giovannucci SJ, Jones JS, Mott M. Myocardial infarction in young adults: risk factors and clinical features. *The Journal of emergency medicine* 1996; 14(2): 139-145.

Lapenna D, De Gioia S, Ciofani G, Mezzetti A, Ucchino S, Calafiore AM, Cuccurullo F. Glutathione-related antioxidant defenses in human atherosclerotic plaques. *Circulation* 1998; 97(19): 1930-1934.

Lee KM, Park KG, Kim YD, Lee HJ, Kim HT, Cho WH, Lee IK. lpha-lipoic acid inhibits fractalkine expression and prevents neointimal hyperplasia after balloon injury in rat carotid artery. *Atherosclerosis* 2006; 189(1): 106-114.

Lucas AD, Bursill C, Guzik TJ, Sadowski J, Channon KM, Greaves DR. Smooth muscle cells in human atherosclerotic plaques express the fractalkine receptor CX3CR1 and undergo chemotaxis to the CX3C chemokine fractalkine (CX3CL1). *Circulation* 2003; 108(20): 2498-2504.

Müller II, Müller KA, Schönleber H, Karathanos A, Schneider M, Jorbenadze R, Geisler T. Macrophage migration inhibitory factor is enhanced in acute coronary syndromes and is associated with the inflammatory response. *PloS one* 2012; 7(6): e38376.

Ouertatani-Sakouhi H, El-Turk F, Fauvet B, Cho MK, Karpinar DP, Le Roy D, Lashuel HA. Identification and characterization of novel classes of macrophage migration inhibitory factor (MIF) inhibitors with distinct mechanisms of action. *Journal of Biological Chemistry* 2010; 285(34): 26581-26598.

Robbins CS, Hilgendorf I, Weber GF, Theurl I, Iwamoto Y, Figueiredo JL, Swirski FK. Local proliferation dominates lesional macrophage accumulation in atherosclerosis. *Nature medicine* 2013; 19(9): 1166-1172.

Roger T, David J, Glauser MP, Calandra T. MIF regulates innate immune responses through modulation of Toll-like receptor 4. *Nature* 2001; 414(6866): 920-924.

Stolla M, Pelisek J, Von Brühl ML, Schäfer A, Barocke V, Heider P, Schulz C. Fractalkine is expressed in early and advanced atherosclerotic lesions and supports monocyte recruitment via CX3CR1. *PloS one* 2012; 7(8): e43572.

Wang Y, Xie AY, Zhang AO, Wang M, Fang Z. Exosomes: An emerging factor in atherosclerosis. *Biomedicine & Pharmacotherapy* 2019; 13(9): 4087-4091.

Zernecke A, Shagdarsuren E, Weber C. Chemokines in atherosclerosis: an update. *Arteriosclerosis, thrombosis, and vascular biology* 2008; 28(11): 1897–908.

Zuzak E, Horecka A, Kiełczykowska M, Dudek A, Musik I, Kurzepa J, Kurzepa J. Glutathione level and glutathione reductase activity in serum of coronary heart disease patients. *Journal of Pre-Clinical and Clinical Research* 2017; 11(2): 103-105.

Aysa NH. Elastic properties of undegradable nanocomposites at human body temperature using as prosthetics. *NeuroQuantology* 2020; 18(1): 32-36