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ASSESSMENT OF PPARγ LEVEL IN PATIENTS WOMEN WITH CARDIOVASCULAR DISEASE AFTER MENOPAUSE

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ABSTRACT : The aim of this study is to measure Peroxisome proliferator-activated receptor gamma (PPARγ) in menopausal women with cardiovascular disease (CVD) as indicators for the prediction and diagnosis of cardiovascular disease. Ninety patients with cardiovascular disease (Unstable angina and myocardial infarction). Participated in this study, their age arranges between (34-70) years. And as a control group forty-five volunteers participated, Fasting blood samples were taken. Some biomarkers like lipid profile and PPAR was estimated for both CVD women and healthy group. There is study a significant increase (P< 0.05) in lipid profile criteria Triglycerides (TG), Low density lipoproteins -cholesterol (LDL) and Total cholesterol (TC) in patients women compared to healthy group, but the high density lipoproteins-cholesterol (HDL) exposed a significant decrease (P < 0.05) for the same group of patients compared to healthy group, also significantly increase (P < 0.05) between the age of premenopausal women and postmenopausal period in CVD women patients. The strongest predictor of cardiovascular risk is relation with age in women after the menopause. Biomarker PPARγ as well show a significantly increase (P<0.05) in patients women compared to healthy women's group. We conclude from this study that the PPARγ is important in identification and follow up of cardiovascular diseases as well as it is PPARγ important indicator for myocardial infarction in patients women.

Key words : PPARγ, women, cardiovascular disease, menopause.

INTRODUCTION

Cardiovascular disease is the leading cause of morbidity and mortality in Western countries. Previous studies have emphasized the useful effects of PPARγ activators on cardiovascular disease (Castrillo and Tontonoz, 2004). PPARγ is playing an important role in CVD, known risk factors associated with cardiovascular disease (Chandra ***et al***, 2017). Recent research has implicated PPAR-γ in macrophage biology, cell cycle regulation, cellular differentiation and atherosclerosis. Because the PP-AR-γ gene is expressed in mononuclear phagocytes, which respond to hypoxia or ischemia with an exuberant early growth response-1 (Egr-1)-dependent inflammatory response, physiological, PPAR-γ expression might serves as mechanism of endogenous to reduce this pathological response to ischemia trigger via zinc finger transcription factor (Egr-1) induction. Activation of PPAR-γ provides protection against ischemic injury (Ketsawatsomkron and Sigmund, 2015).

There are many studies which demonstrate the beneficial role of PPARγ in limiting the progression of atherosclerosis as well as the acceleration of atherosclerosis with the knockout of PPARγ in macrophages (Huang ***et al***, 2012).

PPARγ ligands are expressed inthe atherosclerotic plaques (Marx ***et al***, 1998) and have an effect on both these cells (Chandra ***et al,*** 2017). PPAR-γ is expression by macrophages and monocytes during atherogenesis, First, attracting of monocytes to the wallof vascular to large arteries via adhering to them by integrins-endothelial cell activation and integrins-l. By a chemokine gradient, such as IL-8, Monocytes are in filtrated to the sub-endothelial space, this originate fromthe infection source, where they would be differentiated into macrophages. This is the first step already changed in response to PPAR-γ activation (Hamblin ***et al***, 2009).

In macrophages oxidized LDL induces macrophage proinflammatory gene expression. Activation of PPARγ is upregulates expression of CD36, result of the increase uptake of oxidized LDL. Increased level of oxidized LDL further stimulate expression of PPARγ, which are leading to increased expression of CD36 which illustrates the

PPAR γ role as pro-inflammatory transcription factor (Hobson ***et al,*** 2011).

MATERIAL AND METHODS

One hundred thirty five women divided as (90) patients and (45) control. The patient group was subdivided into two study groups: unstable angina patient group (included 40 subjects aged 34-70 years) and myocardial infarction patient group (included 50 subjects aged 34-70 years). The diagnosis of patients was based on clinical presentation, such as chest pain, electrocardiogram (ECG) changes and troponin I. The samples of blood are taken from all patients and then the criteria were measured.

Lipid profile criteria

Measurements of total cholesterol (TC)

Determined by using a total human cholesterol kit (cypress diagnostic, Langdrop-Belgium. Cat. No. HB006)

Measurements of Triglycerides (TG)

Determinedthe Triglycerides by Triglycerides kit supplied by (cypress diagnostic, Langdrop - Belgium. Cat. No. HB021).

Measurements of HDL-Cholesterol (HDL-C)

Determined the Serum HDL-Cholesterol level by HDL-Cholesterol phosphotungstic acid (PTA) precipitant kit,supplied from (cypress diagnostics, Langdrop – Belgium. Cat. No. HB007).

Calculation of low density lipoprotein by Lee *et al* (2008)

Determination of PPARγ Serum

The measure PPARγ by ELISA Kit, supplied by according to the industrial company Ray Biotech, Inc.. U.S.A. (Catalog #: ELH- PPARγ, GA 027382).

Statistical analysis

The data were statistically analyzed through SPSS package (SPSS, Version 24). These tests are: mean ± SE, the independent-sample t-test, one way ANOVA test, Significance was assumed for P values ≤ 0.05. And the figure construction by using excel program of Microsoft office 2010.

RESULTS

The biochemical parameters of study group

Comparison serum level of pparγ in CVD women and healthy group. The result showed significantly increased (P<0.05) in pparγ level in CVD women patients compared to control group, as shown in Fig. 1.

Comparison serum level of PPAR γ between healthy group, unstable angina and acute myocardial infraction in women's groups. The result showed significantly increased (P<0.05) in pparγ level in Acute myocardial infraction women patients compared to control and unstable angina group, as shown in Fig. 2.

Comparisonthe risk factors of Cardiovascular between CVD women patients and healthy group. The present results shown a significantly increase (P < 0.05) in lipid profile criteria TC, TG and LDL in women patients compared to healthy women's group, but the high density lipoproteins-cholesterol (HDL) revealed a significant decrease (P < 0.05) in the same group of patients compare to healthy group, as shown in Table l.

Comparison the risk factors of cardiovascular between premenopausal and postmenopausal group of women patients

The postmenopausal women had a significantly increase (p<0.05) in lipid profile criteria TC, TG and LDLcomparison to the premenopausal women's group, but the high density lipoproteins-cholesterol (HDL) appearance a significantly decrease (P < 0.05) revealed in Table 2.

DISCUSSION

In the current study, the result revealeda significant increase in PPAR-γ level in, unstable anginaand Acute myocardial infractionin women (UA, MI) patients as compared to controls (p value<0.05), which is in agreement with Abdelrahman ***et al*** (2005), Ivanova ***et al*** (2015), Wakino ***et al*** (2002) and Takano ***et al*** (2002), who reported that the ischemia–reperfusion injury of the heart associated with tissue injury, results in the activation some factors of transcription, includingEgr-1, NF-κB, AP-1, NFAT and STAT, which results in the up-regulation of the genes for some primary pro-inflammatory chemokines, cytokines and adhesion molecules, all of the action in concerted to coordinate an inflammatory response.

As the inflammatory gene transcription is the primary stage of any inflammatory cascade, anti-inflammatory mechanism curtailsoxidative stress and inflammatory gene expression at the very beginning of the signaling process. But, PPAR-gamma activation was thought to play a pro-atherogenic role, through stimulating the uptake of oxidized LDL by macrophages and the expression of scavenger receptor CD36, leading to the fact that the activation of transcription can be viewed as a two-edged sword since the transcriptional factors of individual con induce cardio-toxic or cardio-protective events.

Ye ***et al*** (2010) and Cabrero ***et al*** (2002), mention the protective effect of PPARγ on the Cardiac function

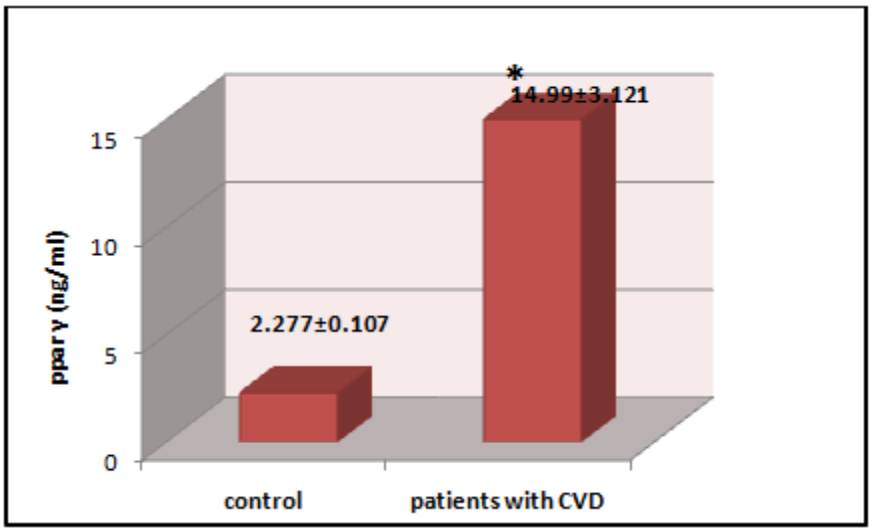

Fig. 1 : Serum PPAR γ level in cardiovascular disease and healthy women group.

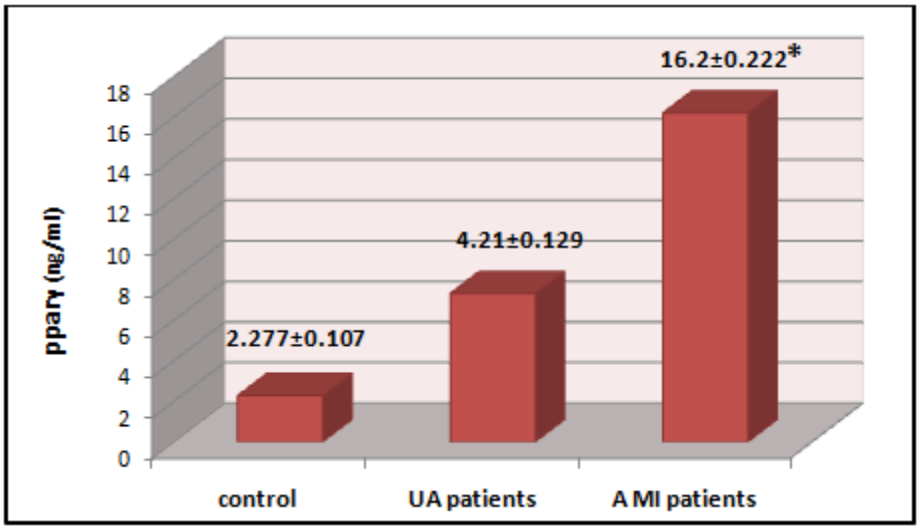

Fig. 2 : Comparison, serum level of ppar γ between healthy group,unstable angina and Acute myocardial infarction in women.

may be related to suppression of the excessive inflammatory process and inhibitor of apoptosis.

Also, Wojtkowska ***et al*** (2017) shows higher PPARγ expression in the myocardium of patients, who are developing heart failure.

In macrophage, PPRAγ suppresses the inducible nitric oxide synthase (iNos) upregulation and reactive oxygen species (ROS) production. These roles serve to benefit against many diseases which are risk factors for cardiovascular disorders such as atherosclerosis, hypertension, dyslipidemia and diabetes (Chandra ***et al***, 2017).

The present study has shown significantly increase ($p<0.05$) in (TCLDL and TG, while significantly decrease in HDL in women with CVD).

LDL cholesterol levels continue to correlate with ischemic rates in the elderly. Aging is too related to changes in the structural and mechanical a properties tothe wall of vascular, which leads to reduced arterial compliance and the loss of arterial elasticity then might subsequently lead to coronary artery disease (Erbel ***et al***, 2010).

The postmenopausal women had a significantly increase ($p<0.05$) in (TC, TG, LDL) while decreasing the HDL comparison to the premenopausal women group.

The change in lipid metabolism may be due to decreases of estrogen production. Whereas premenopausal women less liable to be at risk of ACS as they are in the cardio protective period of endogenous estrogen, which provide a high level of HDL cholesterol. This finding is in agreement with Rocca ***et al*** (2012), who reported that the reduction of estrogen happens naturally, the risk of developing hypertension, myocardial infarction, ischemic heart disease and stroke increases in women next the onset of menopause. According to one hypothesis, estrogens have protective effects on

Table 1 : Compare of cardiovascular risk factors between women patients with cardiovascular disease and healthy women.

Variables	Patients				P. value
	Premenopausal Women No.	Percent (%)	Postmenopausal Women No.	Percent (%)	
HDL< 50 mg/dl	24	21.6	59	53.1	.001**
TG > 150 mg/dl	22	19.8	54	48.6	.001**
TC > 200 mg/dl	27	24.3	57	51.3	.001**
LDL > 150 mg/dl	28	25.2	52	46.8	.001**
SBP > 120mm Hg	25	16.2	41	36.9	.005*
DBP> 80 mm Hg	15	13.5	29	26.1	.005*
Total number of patients	32	28.8	58	52.2	.001**
Age (years)	38±5.21	34.2	56±7.322	50.4	.001*

* (P < 0.05) is significant , ** (P < 0.05) is significant

Table 2 : The cardiovascular risk factors of patients in premenopausal and Postmenopausal group.

Variables	Healthy women group n = 45	Std. Error Mean	Women patient with cardiovascular disease n = 90	Std. Error Mean	P. value
HDLmg/dl	41.333	±2.510	30.184	±.582	.000 *
TG mg/dl	87.233	±1.956	209.802	± 4.066	.043*
TC mg/dl	132.772	± 3.202	282.252	± 4.835	.005*
LDL mg/dl	107.302	± 2.976	188.682	± 2.514	.005*
SBP mm Hg	119	± 3.132	180	± 5.023	.004*
DBP 0mm Hg	78	± 2.214	97	± 2.98	.015*
Age (mean)	45.69	±6.101	48.3	±7.04	.100

* (P < 0.05) is significant.

atherosclerosis. The mortality rate of CVD in women prior after menopause is rapidly increasing. One underlying cause might be the presence of estrogens, which have a protective impact on women before menopause; though, this factor is not existing after menopause (Alexander and Clearfield, 2006; Matthews ***et al,*** 2006; Menon and Vongpatanasin, 2006).

CONCLUSION

They conclude from this study that the dyslipidimia and pressure with old age are risk factors for cardiovascular disease. Also PPARγ is important in identification and follow up of cardiovascular diseases as well as it is PPARγ important indicator for myocardial infarction in patients.

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