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Assessment of Marker of Systemic Inflammation, Oxidative Stress and Plasma Lipid Profile in Psoriasis Patients

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ABSTRACT
There is a close link between systemic inflammation, oxidative stress and dyslipidemia in increasing the frequency of CVD risk in psoriasis patients. Inspite of improvement in our knowledge on psoriasis from pathologic point of view the intimate mechanisms involving systemic inflammation, oxidative stress and dyslipidemia in psoriasis patients making them more susceptible to develop future CVD are complex and not yet fully understood. In the present study, 32 psoriasis patients were screened for active psoriasis (having more than 10% body area covered with severe psoriasis lesion) and 25 patients with active psoriasis (18 males and 7 females of 30-50 years age group) were recruited (Group B). Age and sex matched 25 normal healthy volunteers do not have skin disorder were recruited as controls (Group A). $P<0.05$ and <0.001 were considered as significant and highly significant respectively. Plasma CRP and erythrocyte MDA levels were found to be significantly high ($p<0.001$, 41.02% and $p<0.05$, 29.4% high) in patient group as compared to healthy controls which reflect the role of inflammation and oxidative stress in disease process. Plasma lipid profile along with apolipoproteins levels, as depicted in Table 2 revealed that Plasma total cholesterol, triglycerides and LDL cholesterol levels were significantly high ($p<0.05$, 33.3%, 27.2% and 31.2% high) in patient group as compared to healthy controls. Life style modification, regular exercise and antioxidant rich diet should be incorporated along with prescribed drug for psoriasis treatment so that two important goal of CVD prevention i.e. maintenance of healthy lipid profile and regulation of inflammation along with oxidative stress can be easily achieved.

INTRODUCTION

Amusingly, the concentrations of apolipoprotein B (ApoB) and apolipoprotein A1 (Apo A1) as well as the ratio of Apo-B/ Apo A1 have received much attention in prediction of CVD risk[1]. Psoriasis is one of the chronic and recurrent inflammatory skin disorders that have been associated with oxidative stress, abnormal plasma lipid metabolism[2]. The clinically active psoriasis lesions reveal infiltration of WBC, and several studies report high levels of WBC activation products in the peripheral blood of these patients[3,4]. It has been suggested that C-reactive protein, an acute phase reactants, synthesized in liver and raised by many folds following acute inflammation, is a marker of systemic inflammation in several conditions including psoriasis, rheumatoid arthritis, tuberculosis, cancer, and myocardial infarction[5].

Oxidative stress ensues when large amount of reactive oxygen species are produced in the cells, that can evade or overwhelm the antioxidant protective mechanisms of cells and tissues, and produce major interrelated impaired cell metabolism including DNA strand breakage, rises in intracellular free Ca2+, damage to membrane ion transporters and other specific proteins leading to cell death. Prime target to free radicals attack are the polyunsaturated fatty acids in the membrane lipids, causing lipid peroxidation, has been found to be a major event in the development of various diseases[6,7]. Lipid peroxide (malonaldialdehyde) is the most abundant among the reactive aldehydes derived from lipid peroxidation. It has been suggested that binding to these aldehydes to membrane protein may alter their function, tonicity, permeability, rigidity and integrity and thereby may induce culprit effect[8]. In addition, presence of inflammation further enhances the frequency to develop CVD[9].

It is conceivable that there is a close link between systemic inflammation, oxidative stress and dyslipidemia in increasing the frequency of CVD risk in psoriasis patients. Inspite of improvement in our knowledge on psoriasis from pathologic point of view the intimate mechanisms involving systemic inflammation, oxidative stress and dyslipidemia in psoriasis patients making them more susceptible to develop future CVD are complex and not yet fully understood. In addition, as best of our knowledge, previous studies on psoriasis patients have not included systemic inflammation, oxidative stress and dyslipidemia in a single setting[10-12].

The disease is with obscure aetiology, however, immunological, genetic, infectious and environmental factors may play a role in the development of psoriasis[13-15]. Previous studies indicated that psoriasis started as local skin disease and subsequently associated with systemic inflammatory immunologic and metabolic changes[16,17]. The systemic changes in patients with psoriasis were reported in studies conducted in Iraqi population[18,19] and worldwide. The data presented in the above studies that are from different global communities indicated that psoriasis co-morbidities development are not confined to specific race, developing or developed communities. Previous studies conducted small study population, thus this study was conducted in a large-scale study population in comparison with controls.

MATERIALS AND METHODS

In the present study, 32 psoriasis patients were screened for active psoriasis (having more than 10% body area covered with severe psoriasis lesion) and 25 patients with active psoriasis (18 males and 7 females of 30-50 years age group) were recruited (Group B). Age and sex matched 25 normal healthy volunteers do not have skin disorder were recruited as controls (Group A)[3].

These subjects were recruited only after taking their informed consent and approval of protocol by ethics committee of college. A general information or pre-experimental questionnaire regarding demographic information, family history and limited physical examination including involvement of the body area according to the rule of nine, was completed from all the subjects.

Inclusion Criteria: Subjects, who gave informed consent for study, having no history of cardio vascular disease, don't under any medical treatment (local steroid medication, any phototherapy treatment) or taking antioxidant supplement for at least 1 month prior to blood collection were included.

Exclusion Criteria: Patients with diabetes mellitus, arthritis, hypertension, renal insufficiency, hepatic disease, acute illness such as fever, joint pain, abdominal complaint, malignancy, history of chest pain, deep fungal or disseminated localized gonococcal infection, or under any medicinal were excluded.

Blood samples (approximately 10 mL) were collected in sterile EDTA vials by venous puncture from overnight fasting subjects. Plasma was separated by centrifugation of blood at 1000 g for 15 min at room temperature and stored at-80°C until use. Plasma CRP levels were measured using commercially available ELISA kits (R and D Systems, USA), according to manufacturer's instructions.

Plasma apolipoproteins B, A1 were done using immunoturbidity method (Randox kit) and ApoB/A1 ratio was calculated. Erythrocyte malondialdehyde (MDA) levels were measured as thiobarbituric acid

Table 1: Demographic and clinical profile of study group subjects (Mean±SD)

Particulars	Group A (n = 30)	Group B (n = 30)
Age (years)	39±4	43±6.3
Male/female	18/12	21/09
Height (meter)	2.54±0.32	2.61±0.29
Weight (Kg)	62.3±3.2	59.4±2.7
BMI (Kg/m^2)	25.3±2.1	23.6±1.4*
Systolic blood pressure(mmHg)	109.4±4.1	113.0±4.6*
Diastolic blood pressure(mmHg)	77.6±3.32	78.1±3.47*

Table 2: Marker of systemic inflammation, oxidative stress and plasma lipid profile in study group subjects (Mean±SD)

Particulars	Group A (n = 30)	Group B (n = 30)	Percentage increase	Percentage decrease
CRP (mg/L)	4.31±0.17	6.62±0.16***	41.04	-
Malondialdehyde (µmolMDA/mL)	3.74±0.18	4.49±0.25**	29.4	-
Total cholesterol (mg/dL)	157.61±15.8	209.54±20.1**	33.3	-
Triglycerides (mg/dL)	106.81±13.32	134.6±19.2**	27.2	-
HDL cholesterol (mg/dL)	46.8±4.49	38.81±4.20*	-	18.0
LDL cholesterol (mg/dL)	95.8±13.51	124.22±14.3**	31.2	-
Apo-B (mg/dL)	93.51±19.1	114.4±27.6 **	23.51	-
Apo-A(mg/dL)	144.31±29.3	98.82±20.11**	-	32.21
Apo-B/A1	0.70±0.19	2.21±0.46***	83.34	-

reactive substances, after preparation of hemolysate. The heat induced reaction of MDA with thiobarbituric acid (TBA) in the acid solution formed a trimethine colored substance, which was measured spectrophotometrically at 532 nm[15].

Statistical Analysis: The data collected from study group subjects were entered separately in Microsoft Excel sheet of windows 2007 and values were expressed as Mean±SD. The significance of mean difference between study group subjects was compared by using Student's t-test. The distribution of 't'- probability was calculated depending on 'n' and significance of test was obtained. p<0.05 and <0.001 were considered as significant and highly significant respectively.

RESULTS AND DISCUSSIONS

The demographic indices including mean age and blood pressure of the study group subjects, as observed in present study, are depicted in Table 1. Patients with psoriasis have insignificant variation (p<0.1)

Plasma CRP and erythrocyte MDA levels were found to be significantly high (p<0.001, 41.02% and p<0.05, 29.4% high) in patient group as compared to healthy controls which reflect the role of inflammation and oxidative stress in disease process. Plasma lipid profile along with apolipoproteins levels, as depicted in Table 2 revealed that Plasma total cholesterol, triglycerides and LDL cholesterol levels were significantly high (p<0.05, 33.3%, 27.2-31.2% high) in patient group as compared to healthy controls. However, HDL cholesterol levels were altered insignificantly (p<0.1, 18% low) in patient group. In addition, plasma ApoB/Apo A1 ratio were increased significantly (p<0.01) in patient groups as compared to controls.

It is speculated that occurrence of inflammation in psoriasis is associated with dyslipidemia and oxidative stress with unsolved conundrum and the mechanism behind its complex interplay is responsible for the development of future CVD risk. In the present study plasma CRP levels were found to be significantly high in psoriasis patient along perturb lipid profile and increased apolipoprotein B/A1 ratio as compared to healthy controls. Our findings are in concordance with that of several previous studies conducted separately and involving relatively small patient populations[10,12]. According to them enhanced inflammation induces the development of atherogenic dyslipidemic profile in psoriasis patients by modulating the lipoprotein lipase activity via antilipoprotein lipase antibodies. In addition, atherogenic complexes of autoantibodies to oxidized LDL are generated in response to an oxidative inflammatory effect which enhances the accumulation of LDL in the endothelial wall and thereby enhances the CVD risk in psoriasis patients[20].

Perturbation of systemic oxidative balance, i.e, uncontrolled ROS production plays a crucial role in enhancing the disease complexity in psoriasis[11]. Endothelial cells and vascular smooth cells produce ROS which oxidize low density lipoprotein and thereby initiate atherosclerosis. In addition, involvement of ROS in cell membrane damage via lipid peroxidation and its resultant products such as lipid radicals (L$^\circ$), lipid peroxides (LOO$^\circ$), lipid hydroperoxides and highly reactive aldehydes which play a crucial role in the development and progression of vascular complications in psoriasis[21]. In this context, marked increase in erythrocyte MDA levels (i.e, marker of lipid peroxidation) were observed in group II subjects (p<0.005) as compared to healthy controls which clarify the etio-pathogenic role of ROS via lipid peroxidation, in shaping psoriasis patients more susceptible to develop future incidence of CVD and its related complications. Our findings were in concordance with that of previous study carried out on psoriasis patients having CVD risk.

There was a significant difference when male patients compared to male control, female patients compared to female control, however, there was no

significant differences in comparison between the male psoriatic and female psoriatic. These findings were in consistent with that reported previously for different geographical areas irrespective of race, gender and age. The antioxidant activity as measured by TAC, HDL, and antioxidant index calculation show a significantly low capacity in psoriatic patents than in control. This finding was agreed to that reported for Iraq and other geographical areas,[22-23] however, some studies not confirmed such changes[24]. The genetic predisposition may form the first step in the development of psoriasis, and environmental factors interference possibility may initiate disease specific pathogenicity and disease natural history. In literature the previous studies findings suggest that psoriasis is a multisystem chronic disease with multifactorial aetiology and associated with different comorbidities that were a result of inflammatory, immunologic and infectious sequences. Although psoriasis was characterised by local skin lesions due to inflammatory and immunological responses, however, this study and the previously reported studies indicated that systemic changes were more than dermatologic one[25]. Sing *et al*.[26] in a meta-analysis review reported that from 36 studies, only 1 show odd ratio of 2 were demonstrated as association with metabolic syndrome.

CONCLUSION

On the basis of present findings, it can be inferred that apart from lipid profile, regular assessment of apolipoproteins along with markers of inflammation and oxidative stress should be included to predict CVD complication. Moreover, dietary counseling may help in the control of the primary disorder and enable them to reduce the cardiovascular risks. Furthermore, life style modification, regular exercise and antioxidant rich diet should be incorporated along with prescribed drug for psoriasis treatment so that two important goal of CVD prevention i.e, maintenance of healthy lipid profile and regulation of inflammation along with oxidative stress can be easily achieved.

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