Original Article

Role of Oxidative Stress in various stages of Psoriasis

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Abstract

Introduction: Psoriasis is a chronic inflammatory, immune-mediated, provocative, and challenging skin condition. It is a non-contagious but debilitating disease and a leading cause of socioeconomic burden on the health system.

Objective: To evaluate the role of antioxidant levels, lipid peroxidation status, and lipid profile in the etiology and degree of severity of psoriatic illness among psoriasis patients presenting in the Dermatology Department.

Material and Methods: One hundred and twenty cases (n=130) of already diagnosed psoriasis patients were randomly and fifty healthy matched controls (n=50) of the same age and gender were included from the general population for comparison. Lipid profiles including serum total cholesterol, TG, HDL-c, and LDL-c levels were measured by enzyme colorimetric analysis on Micro Lab 300 (Merck & Germany). Antioxidant status SOD and lipid peroxidation status MDA was measured by the ELISA technique. Statistical analysis was performed using SPSS software Version 16. In this analysis, a "*p*" value of less than 0.05 was considered to be significant.

Results: The study showed significantly elevated levels of MDA, serum TG, total cholesterol, and LDL-c levels in psoriatic patients in comparison with controls, whereas SOD levels and HDL-c levels were found to be significantly lower in psoriatic patients as compared to normal healthy matched controls.

Conclusion: The findings of this study support the hypothesis that an imbalance in the oxidant-antioxidant system may play a role in the etiology of psoriasis and the degree of severity of its presentation. The study also concluded that dyslipidemia was an observed risk factor for the development of cardiovascular diseases in psoriatic patients.

Keywords: Oxidative Stress, Psoriasis, Superoxide Dismutase, Lipid Peroxidation, Malondialdehyde.

Introduction

Psoriasis is a chronic inflammatory, immune-mediated, provocative, and challenging skin condition. It is a non-contagious but debilitating disease and a leading cause of socioeconomic burden on the health system. It is characterized by red patchy lesions with grey, silvery whitish lines. Psoriatic rash classically presents on elbows, scalp, knees, nails, joints, and other parts of the body that may often be painful and pruritic when severe.[1] Skin cells multiply and normally as they get older they shed off and are replaced by new cells; whereas, in psoriasis, skin cell production is increased many folds.[2] Psoriasis can be classified as psoriasis vulgaris, guttate psoriasis, erythrodermic psoriasis, and pustular psoriasis.[3]

Psoriasis affects around 2% population of the world. According to the World Health Organization, about 125 million people around the world suffer from this disease, and among them only about half of the new cases are reported annually.[4] Around 4.6% of the American population is affected by psoriasis, lower figures are found among Indians (0.7%) whereas significantly higher prevalence rates have been reported in Kazakistan.[5]

Psoriasis is an idiopathic clinical syndrome with multi-organ involvement. It has been postulated to be strongly associated with the abnormalities in essential fatty acid metabolism[1], lymphokine secretion, and oxidative stress/oxygen-related stress. New evidence has proposed that elevated reactive oxygen species (ROS) generation and reduced function of the antioxidant system may play a vital role in the pathophysiology of this disease. Dyslipidemia has been detected in the earlier stages of the development of psoriasis.[6] Psoriasis is a multi-factorial illness determined by both genetic and environmental influences; also associated with it are abnormal lipid profile, a rise in oxidative stress, and decreased antioxidant capacity. Scientific evidence strongly suggests an association of psoriasis with risk factors including hypertension, obesity, and diabetes mellitus, etc.[7] Chronic inflammation, which is a characteristic feature of psoriasis, may have a crucial role in the development and progression of dyslipidemia.[8] An increase in ROS production during the inflammatory process in psoriasis may result in a reduction of antioxidant mechanisms that lead to lipid peroxidation.[9,10]

Psoriasis presents with abnormalities in lipid profile, depletion of antioxidants defense mechanism with enhanced lipid peroxidation that in turn promote atherogenesis. Hence we have attempted to evaluate serum lipid profile, serum antioxidant levels, and lipid peroxidation status of psoriasis patients.

Materials and Methods

The present research was carried out as a case-control study, carried out in the Department of Biochemistry, Basic Medical Sciences Institute (BMSI) Jinnah Post Graduate Medical Centre (JPMC) Karachi in collaboration with the Department of Biochemistry, Khyber Medical College, Peshawar. The study duration was 9 months after its approval from concerned authorities. Ethical approval was obtained from the Ethical Review Committee of BMSI, JPMC Karachi.

Informed consent was obtained from all participants taking part in the study. Proposed performa was used to collect the baseline data including age, gender, occupation, the ethnicity of the participants. Detailed medical history and relevant investigations were carried out as part of the methodology. Healthy individuals were matched as controls for comparison.

Inclusion Criteria: Diagnosed psoriatic patients were recruited in the study from the Department of Dermatology JPMC Karachi.

Exclusion Criteria: Those who were found to be alcoholics, smokers, hypothyroid, patients with liver disease or kidney disease, other skin diseases, and those who refused to be a part of the study were excluded.

Laboratory investigations e.g. lipid profile including serum total cholesterol, triglycerides (TG), high-density lipoprotein cholesterol (HDL-c), low-density lipoprotein cholesterol (LDL-c) were tested by enzymatic colorimetric method on Micro Lab 300 (Merck & Germany). Antioxidant status was measured using superoxide dismutase (SOD) and lipid peroxidation status using malondialdehyde (MDA) assay was carried out by ELISA method. Non-probability purposive sampling techniques were used in this study. Blood samples of subjects who fulfilled the criteria were collected after an overnight fast of 10-12 hours. A strictly pre-defined protocol was used for sample collection, storage, and analysis.

Statistical analysis was carried out using SPSS software Version 16. The results of lipid tests, antioxidant, and lipid peroxidation status markers were expressed in Mean ± SD. The collected data was scrutinized with student's *t*-test to evaluate the difference between the patients and controls. p values ≤ 0.05 were considered statistically significant.

Results

There was a statistically significant reduction in the mean serum (SOD) superoxide dismutase levels in moderate and severe psoriasis groups when compared to the control group ($p < 0.004$). Whereas a statistically significant increase was noted in the mean serum malondialdehyde assay (MDA) levels in mild, moderate, and severe psoriasis groups in contrast to controls ($p<0.01$). The same can be seen in Figure 1.

Comparison of Lipid Profile among Psoriatic Patients and Healthy individuals as Controls

The mean ± SD serum total cholesterol level of the severe psoriasis group was found to be significantly elevated when compared with the control group and mild psoriasis and moderate psoriasis groups ($p<0.01$). The mean serum triglyceride levels were markedly raised in the severe psoriasis group as compared with the control group, mild psoriasis group, and moderate psoriasis groups ($p<0.01$). The mean ± HDL-c levels were notably reduced in the severe psoriasis group in comparison with the control group, mild psoriasis, and moderate psoriasis groups ($p<0.005$). The mean ± SD LDL-C levels were significantly raised in the severe psoriasis group when matched with the control group, mild psoriasis group, and moderate psoriasis groups ($p<0.005$).

Table 1: Comparison of Biochemical Variables among the Study Population

Variables	Controls (n=50)	Psoriatic Patients		
		Mild (n=50)	Moderate (n=50)	Severe (n=50)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Serum SOD (U/L)	109.2 ± 32.7	92.4 ± 31.7	89.5 ± 25*	84.8 ± 35.6*
Serum MDA (nmol/mL)	10.6 ± 2.8	11.3 ± 2.3	13.3 ± 2.8	29.8 ± 14.4*□Δ

** Statistically highly significant as compared to Controls p < 0.004*

□ Statistically significant as compared to Mild Psoriasis p < 0.05

Δ Statistically significant as compared Moderate Psoriasis p < 0.05

☼ Statistically significant as compared to Severe Psoriasis p < 0.01

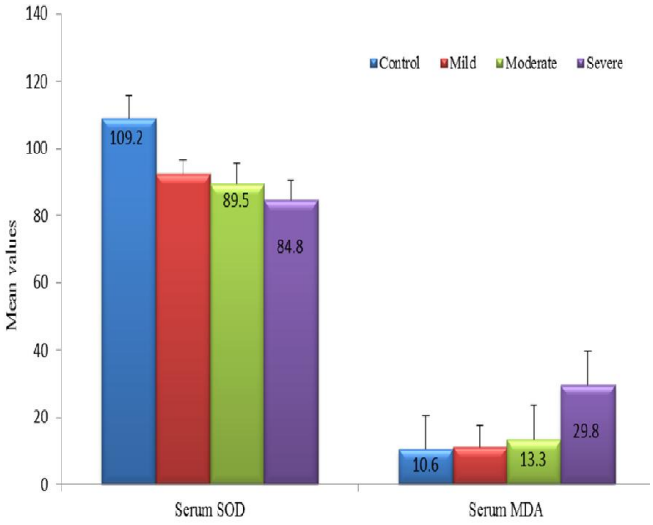

Figure 1: Comparison of Serum SOD, MDA among the Control & Patient Groups

Table 2: Comparison of Lipid Profile among the Study Population

Variable	Controls (n=50)	Psoriatic Patients		
		Mild (n=50)	Moderate (n=50)	Severe (n=50)
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD
Cholesterol	147.5 ± 27.7	151.5± 36	193 ± 42.7	235.1 ± 35*□Δ
Triglyceride	104.4 ± 25	129 ± 19.8	136.8 ± 29.1	160.1± 25.6*□Δ
HDL-c	36.3 ± 4.8	32 ± 8.5	26.6 ± 15.8	21.7 ± 5.9 *□
LDL-c	91.4 ± 30.4	99.7 ± 28.9	104.2 ± 30.4	125 ± 33*□Δ

** Statistically significant as compared to Controls p<0.05*

□ Statistically significant as compared to Mild Psoriasis p<0.005

Δ Statistically significant as compared to Moderate Psoriasis p<0.05

☼ Statistically significant as compared to Severe Psoriasis p<0.01

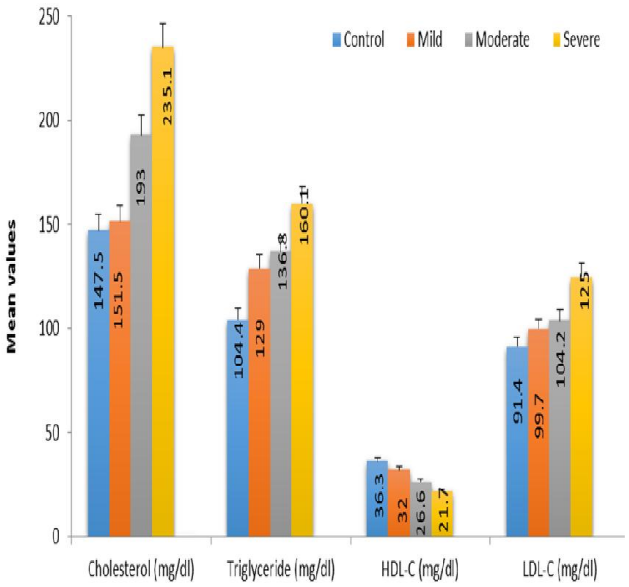

Figure 2: Distribution & Comparison of Lipid Profile among the Study Population

Discussion

Lipid peroxidation can be determined through various methods as ROS provoke oxidation of polyunsaturated fatty acids (PUFA) in the biological system which can be measured with lipid peroxidation markers like MDA, Glutathione, and SOD. In psoriasis, it has been investigated by various researchers and almost all are in agreement that this stress affects all patients irrespective of their age, length, and severity of the disease, diet, and BMI, etc. whereas total antioxidant status in psoriatic patients indicates the aggravation of the disease. In this study, we found a significant increase in mean serum MDA levels in psoriatic patients when compared to controls ($p < 0.05$), mainly because lipid peroxidation, is implicated in the pathogenesis of psoriasis. Similar findings have been suggested by national and international studies e.g. Nast A, *et al*. (2015)[1] elaborated this trend of increased serum MDA levels in psoriatic patients as compared to controls. In another study, Elhaddad and colleagues (2017) observed some disturbances in the serum levels of trace elements and total antioxidant status of patients with psoriasis.[11]

In our study, we have also established a positive correlation between serum MDA levels and the progression of the disease. The possible mechanism of the increased MDA levels in oxidative stress might be due to the increased ROS activity of Phospholipase A_2 causing peroxidation of Arachidonic acid with the help of mediators that lead to increased production of MDA. In contrast to our findings, Augustin *et al*. (2016)[12] reported no remarkable dissimilarity in serum MDA levels among psoriatic cases and controls.

In our study, mean SOD levels were found to be significantly lower in psoriatic patients in contrast to controls ($p<0.05$). These results correlate with the findings of previous studies like (Mawla *et al*. (2013)[13]. Lower levels of antioxidant SOD were observed in psoriatic patients particularly in the severe psoriasis category. The reason for lower levels of antioxidant SOD could be due to its utilization in reducing the inflammatory markers. In contradiction to our study, Menter *et al*., (2008)[14] found no significant variation in serum SOD levels between psoriatic cases and controls.

On evaluating the lipid profile, we found a significant elevation in mean total cholesterol levels in psoriatic patients when compared to controls ($p<0.05$). Similar findings were reported by Latha and Kumar (2014)[15] Bhatia *et al*., (2014)[16] and Khan *et al*., (2017).[17] We also found a significant elevation in the mean triglyceride levels in psoriatic patients when compared to controls ($p<0.05$); Ghafoor *et al*., (2015)[18] reported similar results although Arora *et al*., (2015)[19] found no significant difference in triglyceride levels among psoriatic patients when compared to controls.

Our study also showed a significant reduction in mean HDL-c levels in psoriatic patients when compared to controls ($p<0.05$). This finding has been supported by Arora *et al*., (2015)[19] and Augstin *et al*., (2016)[12], whereas Dsouza and Kuruville (2013)[20] reported no significant difference in HDL-c levels among psoriatic patients and controls. Mean LDL-c levels in psoriatic patients were found to be significantly elevated in our study when compared to controls ($p<0.05$). This finding has been supported by Arora *et al*., (2015)[19], and Bhatia and coworkers (2014)[16] while other studies such as Latha and colleagues (2014)[15] found no significant difference in LDL-c levels between psoriatic patients and controls. And the same was reported in another study.[21]

Conclusion

In conclusion, the results of this study showed that an imbalance in the oxidant/antioxidant status might be implicated in the pathogenesis of psoriasis. In addition, the findings of this study support the previous research studies in concluding that hyperlipidemia is markedly more common in psoriasis patients as compared to their healthy control counterparts in the community. Both these factors may

lead to the development of atherosclerosis with all its complications.

Recommendations

Based on these findings, it is recommended that early detection and management of hyperlipidemia should be considered in psoriasis patients to avoid early or late complications. It will be effective in reducing the morbidity and mortality associated with the disease. Furthermore, based on the findings of this study, antioxidant supplementation is recommended to inactivate free radicals. This could be highly effective in preventing further new epidermal destruction, thereby reducing the severity and progression of the disease.

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