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# A study on status of homocysteine in psoriasis patients

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**Abstract**
Psoriasis is a chronic inflammatory, proliferative skin disease characterized by pathological skin lesions due to various exogenous and endogenous factors. It is associated with a number of biochemical and immunological disturbances. Recently, it has been suggested that increased reactive oxygen species (ROS) production and compromised function of antioxidant system may be involved in the pathogenesis of this disease. This study intends to assess and compare the levels of HCY and MDA amongst the cases and healthy controls. In the present study, total of 100 subjects, among them 25 psoriasis patients were selected. Serum levels of malondialdehyde and Homocysteine levels were increased in psoriasis as compared to controls. We found severity wise significantly increased serum malondialdehyde and HCY status in patients with psoriasis. Our results indicate that, in psoriasis patients with increased oxidative stress there is increased Homocysteine levels. In conclusion, Homocysteine could serve as a biomarker of psoriasis severity but not as a marker of psoriasis.

**Keywords:** Psoriasis, malondialdehyde, homocysteine

## Introduction
Psoriasis is a common chronic inflammatory dermatosis characterized by hyper proliferation of the keratinocytes and inflammatory infiltration in epidermis and dermis with unknown etiology. Psoriasis accounts to 2-3% of the world's population. According to WHO nearly 100 million individuals are affected worldwide. Prevalence studies in India vary from 0% to 2.8%.

Etiopathogenesis of psoriasis is multifactorial, it is provoked by external and internal triggering factors which include mild trauma, sunburn, infections, systemic drugs and stress [1]. About 1.3%to 34.7%individuals with psoriasis develop Psoriatic arthritis that leads to joint deformation and disability [2, 3]. Risk factors such as dyslipidemia, endothelial dysfunction and platelet adhesion are influenced due to the systemic inflammation present in psoriasis [4]. Latest clinical researches have shown an elevated plasma level of the amino acid Homocysteine (HCY) as an independent risk factor for atherosclerosis, including coronary artery disease, cerebrovascular disease, peripheral vascular disease and venous thromboembolism [5].

Skin is the major site of free radical production, oxidative stress is considered as an important factor induced due to tissue damage [6]. Production of ROS can be indirectly assessed by the levels of lipid peroxidation products such as MDA, which is a result of chronic inflammation [7]. Malondialdehyde, which is a product of lipid peroxidation, is considered a marker of oxidative stress and lipid peroxidation. Some previous studies in a North Indian population have shown raised malondialdehyde levels in psoriatic patients with co‐ morbidities like hypertension and diabetes [25, 26].

## Materials and Methods
### Study center
This present study was done at Gandhi Hospital, Secunderabad, after getting approval from Institutional ethics Committee of Gandhi Hospital Secunderabad. Clinically diagnosed psoriasis patients attending dermatology OPD, at Gandhi Hospital Secunderabad were taken into this study.

### Study period
March 2016 – October 2017.

**Study type**
Observational study.

**Sample size:** 100 (25 cases and 75 healthy controls)
1. 25 clinically diagnosed psoriasis cases and 75 controls (healthy individuals without psoriasis) were selected.
2. Samples used for this study- blood samples.

**Selection criteria of patients**
**Inclusion criteria**
1. Clinically diagnosed patients of psoriasis between age group of 20 – 50 years of either sex.

**Exclusion criteria**
1. Patients with hypertension, diabetes mellitus.
2. Patients with hypothyroidism, other skin disorders.
3. Those who are chronic alcoholics and chronic smokers.
4. Patients on corticosteroids, lipid lowering agents.
5. Patients on nephrotoxic and hepatotoxic drugs.

The investigator estimated Plasma Hcy, serum MDA, in the present study in 100 samples by the following methods:-
Homocysteine (Hcy) - Immunoassay
Serum Malondialdehyde (MDA) - spectrophotometry

**Sample collection and storage**
Blood samples were centrifuged – serum and plasma was separated and stored in refrigerator at 2 – 8 $^0$C and were analyzed in batches.
The present study involved 100 subjects, out of which 25 were psoriasis patients who attended skin O.P of Primary care center who fulfilled the inclusion criteria and other 75 were controls without psoriasis.

**Results**
The present study was undertaken to evaluate the plasma Hcy, serum MDA, in psoriasis patients. Results were tabulated in master chart and statistically analyzed using Microsoft excel in 2010, in Department of Community Medicine, Gandhi Medical College, Secunderabad. Results on continuous measurement are presented in mean and SD, and results on categorical measurements are presented in number (%). Significance is assessed at 5% level of significance.

**Demographical profile of the study**
Distribution of study sample according to the gender (N=100)
The distribution of the study samples according to the gender shown in table. In the present study we have evaluated 100 subjects, which includes 75 controls and 25 psoriasis patients as cases. Of these 25 cases, 14 were males and 11 were females and among controls, 41 were males and 34 were females.

**Table 1:** Gender distribution among cases and controls

| Gender | cases | | controls | |
|---|---|---|---|---|
| | No. | % | No. | % |
| Male | 14 | 56 | 41 | 55 |
| Female | 11 | 44 | 34 | 45 |
| Total | 25 | | 75 | |

The distribution of the study samples according to the age shown in table and graphically represented in graph 2. The cases and controls were divided into 3 groups based on age (20-30, 31-40, 41-50 years). There were 5 cases between 20-30 years of age, 6 cases between 31-40 years, and 14 cases between 41-50 years. And there are 17 controls between 20-30years, 28 controls between 31-40 years and 30 controls between 41-50 years.

**Table 2:** The distribution of the study samples according to the age

| Age Group (yrs) | Cases | | Controls | | Total |
|---|---|---|---|---|---|
| | X | % | Y | % | |
| 20-30 | 5 | 20 | 17 | 23 | 22 |
| 31-40 | 6 | 24 | 28 | 37 | 34 |
| 41-50 | 14 | 56 | 30 | 40 | 44 |
| Total | 25 | 100 | 75 | 100 | 100 |

X-Number of cases Y-Number of controls N- Total cohort

The mean age of cases was 39.88 years and mean age of the controls was 37.32 years with Standard Deviation (SD) 8.47 and 7.65 respectively. The p-value obtained on comparing the mean age of cases and controls was not significant (p-value <0.05).

**Comparison of Mean ± SD of age between the two groups, N=100**
All the cases are with psoriasis and all the controls are normal without psoriasis. Mean ± SD for age for cases is 39.88 ± 8.47 and for controls is 37.32 ± 7.65 and the difference of mean of cases and controls is 2.56, with Z-score value being 1.34. Mean ± SD of age and the mean difference is not significant ($p$>0.05).

**Table 3:** The group and mean age

| Group | Mean Age | SD |
|---|---|---|
| Cases(X=25) | 39.88 | 8.47 |
| Controls(Y=75) | 37.32 | 7.65 |

Comparison of plasma HCY between cases and controls is shown in table and graphically represented in graph 4. All the controls were within normal Plasma HCY levels except for 6 controls with increased HCY levels (8%). Among cases 8 were with normal HCY levels (32%). Majority among cases 17 were with increased HCY levels (68%)

**Table 4:** Distribution of Plasma HCY Controls and Cases. N=100

| Plasma HcY | Cases | % | Controls | % |
|---|---|---|---|---|
| Upto 15µ moles/L | 8 | 32 | 69 | 92 |
| >15 | 17 | 68 | 6 | 8 |
| total | 25 | 100 | 75 | 100 |

**Comparison of HCY levels between two Groups**
Mean ±SD of Plasma HCY for cases is 17.11±4.77 and for controls is 8.12 ± 4.21 and difference of means between cases and controls is 8.99 with Z score value being 8.48. Mean ± SD of HCY between the two groups is statistically significant ($p$< 0.01**).

**Table 5:** Comparison of Mean and Standard Deviation of Plasma HCY Between two Groups

| Group | Mean | SD | P-Value |
|---|---|---|---|
| Cases | 17.11 | 4.77 | <0.01 |
| Controls | 8.12 | 4.21 | |

**Comparison of Mean ± SD of MDA levels between the two groups**

All the cases are with psoriasis and all the controls are normal without psoriasis. Mean ± SD for serum MDA levels for cases is 447.11± 82.05 and for controls is 154.35 ± 22.69 and the difference of mean of cases and controls is 292.76, with Z-score value being 17.62. Mean ± SD of MDA is higher in cases than in controls and the mean difference is statistically significant ($p< 0.01$**).

**Table 6:** Comparison of Mean ± SD of MDA levels between the two groups

| Group | Mean | SD | P-Value |
|---|---|---|---|
| Cases(X=25) | 447.11 | 82.05 | <0.01 |
| Controls(Y=75) | 154.35 | 22.69 | |

**Discussion**

Psoriasis is a systemic inflammatory disease with concomitant co-morbidities. It is known that patients with severe forms of psoriasis have a reduced life expectancy which might be due to cardiovascular complications such as myocardial infarction or stroke. In the present study, we found a statistically significant increase ($P< 0.01$) in the malondialdehyde and Homocysteine levels in subjects with psoriasis in comparison with controls, indicating a significantly higher cardiovascular risk. How exactly psoriasis and its co-morbidities are pathophysiologically linked is poorly understood. The disease has been associated with oxidative stress, abnormal lipid metabolism and a high frequency of cardiovascular events resulting in increased morbidity and mortality.

Psoriasis is an autoimmune disease characterized by increasing proliferation of keratinocytes and secretion of inflammatory cells in dermis and epidermis. Psoriasis causes physical, emotional and social burden, with quality of life significantly impaired [8-10].

Many studies have shown increased rates of HTN, dyslipidemia, DM, smoking and excessive alcohol consumption in patients with psoriasis [11]. Neimann *et al.* found psoriasis to be an independent risk factor for mortality as a result of association with atherosclerosis.

In the present study, statistically, there was no difference between the average age of controls and cases. Irrespective of the sex clinically diagnosed cases were selected and controls were without psoriasis.

In the present study we have evaluated 100 subjects, which includes 75 controls and 25 psoriasis patients as cases. Of these 25 cases, 14 were males and 11 were females and among controls, 41 were males and 34 were females.

In the present study, distribution of study population into 3 groups according to their age. There were 5 cases between 20-30years of age, 6 cases between 31-40 years and 14 cases between 41-50 years. And there are 17 controls between 20- 30 years, 28 controls between 31-40 years and 30 controls between 41-50 years and with most of cases and controls in study group coming between age group (41-50 years).

The present study shown demographic characteristics of the study population including the age distribution, with Mean ± SD for cases being 39.88 ± 8.47 and for controls 37.32 ± 7.65. As evident from the table it was not significant with p value > 0.05. These studies also correlate with the above findings showing that age distribution was not significant in the present study.

In the present study showed Plasma HCY levels among cases and controls. Out of 75 controls, 6 controls were with increased HCY levels (8%).

Among 25 cases, 8 cases (32%) were with normal HCY levels and remaining 17 cases (68%) were with increased HCY levels. The statistical analysis of the obtained values showed that the Plasma HCY values are significantly higher in psoriasis cases (17.11 ± 4.77 µmol/L) compared to controls (8.12± 4.21 µmol/L). The mean difference was significant at p- value <0.01**

The above findings were correlate with previous studies, Das *et al.*, studied 50 psoriatic patients and 50 controls and showed significantly high plasma HCY levels in psoriasis group [11]. Kural *et al.* studied 30 psoriatic patients and 30 controls; they found higher homocysteine plasma levels [12].

Malerba *et al.* reported higher homocysteine in 40 psoriatic patients compared to 30 controls [12]. V. Brazelli *et al.*, 2010 also reported significantly high plasma HCY levels in psoriasis patients. Meynadier and Gilhou reported reduced folate levels in psoriasis results from its excessive consumption by the skin [13]. Some earlier studies indicates that Refsum *et al.*, 1989, found that psoriasis patients had low serum folate and high HCY levels than age-matched controls [14].

Tobin AM and Brazelli reported increased HCy levels in patients with psoriasis. Hyperhomocysteinemia in psoriasis patients may be due to genetic or acquired factors [15, 16]. A highly reactive intermediate, Homocysteine lactone, is formed in hyperhomocysteinemia which combines with LDL. The aggregates formed are taken up by the macrophages, incorporated in the foam cells [154] forming atheromatous plaques. Damage to the endothelial cells, stimulation of smooth muscle cell proliferation in the lamina of vessel walls, increase LDL- oxidation, and reduction in blood flow and formation of blood clots are theories postulated for HCY as a causative factor in promotion of atherosclerosis [17].

Accumulation of HcY generates ROS which may be responsible for inhibition of formation of prostacyclin in the endothelium resulting in platelet aggregation [18]. In present study, plasma HCY levels are significantly higher in cases when compared to controls thus correlating with above studies.

In the present study, comparison of Mean ± SD of MDA levels between the two groups where all the cases are with psoriasis and all the controls are without psoriasis. The statistical analysis of the obtained values showed that Mean ± SD for serum MDA levels for cases is 447.11±82.05 and for controls is 154.35±22.69 and difference of means of cases and controls is 292.76, with Z-score value being 17.62 Mean ± SD of MDA is higher in cases than in controls and the p-value being <0.01**

Increased oxidative stress in psoriasis patients is demonstrated by increased levels of MDA with compromised antioxidant defense enzymes [19]. Present findings indicates that Sami A Gabr and Ahmad H Al-Ghadir studied 55 psoriasis cases and 20 controls, they found high serum MDA levels [20].

Vanizer *et al.* reported high MDA levels and lower antioxidant defense enzymes in the keratinocytes of patients with severe psoriasis. Increased production of free radicals or ROS may cause oxidative damage on biological molecules, cell membranes and tissues [21]. It induces oxidation of polyunsaturated fatty acids in biological system, results in the formation of lipid peroxidation

products such as MDA which is used as a biomarker of lipid peroxidation [22, 23].

Previous results showed HCY and MDA levels increase with the disease severity in psoriasis patients, and both are responsible in predisposing cardiovascular events in psoriasis patients [22].

Yildirim *et al.*, reported no difference in serum MDA levels in psoriatic patients compared to controls [24]. Some previous studies found significantly high serum MDA levels in cases of psoriasis with a correlation between severity of psoriasis and serum MDA levels. They also pointed out a decrease in the MDA level after treatment. In present study, MDA levels are significantly higher in cases when compared to controls thus correlating with above studies.

## Conclusion

In conclusion, this study provides an evidence for increased ROS production and decreased antioxidant defenses in psoriasis, reflected by increased lipid peroxidation. Increased MDA end products in these patients may be a result of immunological and inflammatory mechanism which are important in etiopathogenesis of psoriasis. We found that Homocysteine is the important marker for the identification of severity of psoriasis. Finally, of considerable interest is the possibility of using this information to develop novel strategies for diagnosis, prognosis and treatment of psoriasis patients are warranted. Furthermore, these simple indices may be useful in the clinics for cardiovascular risk assessment, thus obviating the need for expensive biomarkers which can be restricted to research settings.

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## Conflict of Interest

The author declare that the, there is no conflict of interest

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