Evaluation of Homocysteine Levels in Patients with Psoriasis Vulgaris – A Case Control Study from Tertiary Care Hospital in North India

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ABSTRACT

Background: Psoriasis is a chronic inflammatory disease that is non-contagious in nature, primarily involving skin and joints. The association of psoriasis with obesity, metabolic syndrome and cardiac problems has been suggested in recent data. Various biochemical markers are of prognostic significance in psoriasis, and out of these, raised homocysteine levels have been reported in various studies. However, some studies have shown no difference in Homocysteine levels in psoriasis patients. Hence, we planned this study to evaluate serum homocysteine levels in psoriasis vulgaris.

Objective: To estimate and compare the serum homocysteine levels in psoriasis vulgaris patients and healthy controls and find any association between the homocysteine levels and severity of the psoriasis vulgaris.

Material and Methods: One hundred clinically diagnosed patients of psoriasis vulgaris along with hundred age and sex-matched healthy controls were enrolled and assessed for serum homocysteine levels.

Results: In this study, there was highly significant difference in the mean homocysteine levels between cases (13.60 ± 11.72) and controls (16.02 ± 11.32) and this difference was statistically highly significant ($p < 0.0001$). We also compared the homocysteine levels in cases and controls based on their demographic profile like age group, gender, occupation, region and in cases based on the disease-specific parameters like duration of disease, family history, nail involvement, joint involvement, age of onset, body surface area and PASI. We observed that homocysteine levels were significantly higher in cases than controls when compared according to gender, region and PASI, and the difference was found to be statistically significant.

Conclusion: Psoriasis has a significant effect on serum homocysteine levels and various studies have reported the risk of cardiovascular diseases with an increase in homocysteine levels. Our study suggests the relationship between psoriasis and serum homocysteine levels and further investigation is required to evaluate the role of serum homocysteine as a cardiac biomarker in patients with psoriasis.

Keywords: Case control study, Exfoliative dermatitis, Homocysteine, Psoriasis.

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INTRODUCTION

Psoriasis is a chronic, inflammatory and proliferative condition of the skin associated with systemic manifestation. Psoriasis is one of the most long-standing skin diseases known to mankind. It is a disorder with a waxing and waning course.

The word psoriasis has Greek origin from "*psora*" meaning itch and "*iasis*" meaning condition. Thus, psoriasis means "itchy condition". Earlier psoriasis was put in a group of skin disorders with leprosy. Psoriasis was differentiated from Leprosy by Hebra based on their clinical features.[1]

The chronic nature of the disease and upcoming cases with cardiovascular diseases in patients with psoriasis and homocysteine is now an independent risk factor for cardiovascular diseases. It is known that keratinocyte turnover is accelerated in patients with psoriasis and increase in the consumption of folate which is used to methylate DNA in actively dividing cells, leads to higher levels of homocysteine.[2]

MATERIALS AND METHODS

Study Area

The study was conducted on patients with psoriasis vulgaris and controlled attending the Dermatology OPD at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala (Haryana).

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Study Design

The study comprised of 200 individuals (100 cases and 100 controls) of either sex attending the dermatology OPD at Maharishi Markandeshwar Institute of Medical Sciences and Research, Mullana, Ambala (Haryana).

Inclusion Criteria

- Patients with clinically diagnosed psoriasis vulgaris.
- Patients of either sex of age 18 years or older.
- Patients willing to participate in study

Exclusion Criteria

- Patients taking any medications known to affect homocysteine level, including vitamin B6 and folic acid.[3]
- Patients with a history of hypertension, diabetes mellitus, obesity, and dyslipidemia.
- Patients who are on methotrexate or have taken methotrexate in the past 3 months.[4]

Controls were patients with other dermatological complaints, who do not have any proven association with derangements of homocysteine levels and attendants of patients visiting the hospital. Controls were age and sex-matched before enrolment into the study.

A detailed medical history was taken, and a thorough dermatological and systemic examination. The severity of psoriasis vulgaris was assessed by using PASI scale and Homocysteine levels were analyzed.

Data Analysis

After all the data has been collected, it was tabulated and analyzed using appropriate statistical tests/methods.

RESULTS

The study was conducted on 100 cases and 100 healthy age and sex-matched controls. The Demographic and clinical data of cases and controls are summarized in Table 1.

The mean age of cases was 31.60 ± 11.72 years. Most of the cases, i.e., 34%, were young adults aged 18 and 28 years. Males outnumbered females in our study, the M: F ratio being 1.7:1.

Twenty-five percent of cases in our study were skilled/semi-skilled workers and Most of the cases, i.e., 56% were from urban backgrounds. The mean duration of disease was 7.05 ± 7.74 years. The mean body surface area was $10 \pm 0.12\%$. Thirty-four percent of cases had nail involvement, and 8% of cases had positive family history. Joint involvement was present in only 16% of cases. Twenty-six percent of cases had age of onset ranging from 11 to 20 years of adolescent young adults. Most of the patients (76%) had PASI score less than 6. The mean homocysteine levels in cases (31.60 ± 11.72) were markedly high as compared to mean homocysteine levels (16.02 ± 11.32) of controls ($p < 0.0001$). Forty-eight percent of the cases had higher levels of homocysteine. The mean homocysteine levels (40.22 μmol/L) were high in cases with PASI more than 12. Serum homocysteine levels showed positive correlation with PASI. Most of the cases were from urban areas (56%) with high mean homocysteine levels of 30.10 compared to controls with mean homocysteine levels of 16.79. The study was observed to be significant. ($p < 0.0001$). Males had relatively higher serum homocysteine levels (33.20 ± 15.96) as compared to females (28.88 ± 8.74). Serum homocysteine levels showed no correlation with disease duration, family history and age of onset. There was no correlation between serum Homocysteine levels with BSA, disease duration, family history, age of onset, positive nail findings, and joint involvement. The difference was statistically not significant in any of them. By correlating the homocysteine levels with patients' clinical data, there was a significant correlation between homocysteine and gender, occupation, region and PASI. (Table 2)

DISCUSSION

100 cases of different age groups and sex diagnosed clinically as psoriasis vulgaris who attended the outpatient department of dermatology, MMIMSR, Mullana were included in the study with 100 age and sex-matched controls.

In our study, most of the patients (34%) affected were between 18 to 28 years of age. Mean age was 39.35 ± 15.96 years. The majority of the controls (32%) were in 18 to 28 years of age group. Mean age of controls was 39.56 ± 14.87 years.

Table 1: Demographic and clinical data of cases and controls

Items	Mean Homocysteine levels (Cases)	Mean Homocysteine levels (Controls)	p-value
Age			
• Mean ± SD	39.35 ± 15.96	39.56 ± 14.87	<0.0001
• 18–28 years(n)	(34)	(32)	
Gender			
• Male (n=63)	33.20 ± 12.96	15.96 ± 11.52	<0.0001
• Female (n=37)	28.88 ± 8.74	16.11 ± 11.12	
Homocysteine			<0.0001
• Mean ± SD	31.60 ± 11.72	16.02 ± 11.32	
• Region			
• Urban	30.10 ± 11.43 (n=56)	15.35 ± 10.84 (n=54)	<0.0001
• Rural	33.52 ± 11.95 (n=44)	16.79 ± 11.93 (n=46)	
PASI			
• Range (>12)	40.22 ± 9.29		
• Mean ± SD			

Table 2: Correlation between homocysteine levels and different parameters in patients (n = 100)

	p-value
Age	
• 18–28 years	<0.0001
• 40–50 years	<0.0001
Gender	<0.0001
Occupation	<0.05
Region	<0.0001
PASI	<0.05

This was in concordance with studies by B. Vanizor et al.[5] and Mamoun El Sayed Shalaby.[6] The mean age of cases and controls in study by B. Vanizor et al.[5] was 34.2 and 36.7, respectively. In the study done by Mamoun El Sayed Shalaby[6] the mean age in cases and controls was 36.30 and 35.05, respectively. Results of the present study were in contrast to the study done by Malerba et al.[4] and Tobin et al.,[2] who reported a slightly higher mean age group. The mean age of cases and controls in study by Malerba et al.[4] was 47.4 and 45.8, respectively. In case of Tobin et al.[4] mean age was 41.8 and 41.7, respectively.

Out of 100 cases 63% were males and 37 % were females. Controls were taken as per similar gender distribution. A high male predominance (male: female ratio of 1.7: 1) was observed in our study, which was similar to the study by Mamoun El Sayed Shalaby[6] (67.5% males and 32.5% females), Brazzelli et al.[7] (2010) (71.4% males and 28.5% females) and Malerba et al.[4] (55% males and 45% females). However, the results were contrary to the studies done by Tobin et al., 2010[4] and Ghasem Rahmatpour Rokni et al., 2017[8] in which female predominance was 55% and 73.3%, respectively.

In our study, twenty-five (25%) cases were involved in skilled or semi-skilled occupations like teaching, driving, tailoring, manager and 16% were unskilled workers like farmer, laborers, shopkeepers etc. Twenty-four (24%) cases were either housewives or unemployed.

Out of 100 cases, 56% of cases were from the urban area, whereas 44% were from the rural area. In controls 54% were from the urban area and 46% were from the rural area.

In our study, 42% of cases had duration of psoriasis for more than 4 years and 22% had a duration of less than 1 year. The mean duration of disease was found to be 7.05 ± 7.74 years.

Only eight percent of patients with psoriasis had a positive family history and the remaining 92 patients had no family history of psoriasis.

Nail involvement was observed in 34% of cases. The most common finding was pitting followed by subungual hyperkeratosis.

In our study, 16% of the cases had joint involvement. Majority of the patients in our study (26%) had age of onset between 11 to 20 years. Two peaks were observed between 11 to 20 years and 41 to 50 years.

Out of 100 cases, 68 cases had body surface area of 3% to 10%, and 26 patients had body surface area more than 10% in our study.

In our study, most cases, i.e., 76% had PASI less than 6. Only nine patients with psoriasis had PASI, more than 12. However, in the study done by Malebra et al.[4] out of 40 cases, 62.5% patients had PASI less than 12.

In our study,48 patients had homocysteine levels more than 30 µmol/L. Ninety one cases had homocysteine levels more than 15 µmol/L. However, Malebra et al.[4] found 62.5% patients out of 40 had homocysteine levels more than 15 µmol/L.

The mean serum homocysteine level in our study in cases was 31.60 ± 11.72 and in controls was 16.02 ± 11.32. The result showed that the homocysteine levels were more in cases than in controls. The difference between cases and controls was found out to be statistically significant (p<0.0001). Similar results were seen in Brazzelli et al.[7] study where the mean homocysteine levels in cases and in controls were 19.6 umol/L ± 15.1 and 13.7 umol/L ± 5.56 respectively and there was statistically significant difference between cases and controls (p = 0.0004).This was also following the results of Refsum et al.[3] and Jung Eun Kim et al.[9] where the mean homocysteine levels of the cases was higher as compared to the controls (p <0.05).

The mean homocysteine levels in different age group were calculated in our study. The cases between 18 to 28 and 40 to 50 years age had mean homocysteine levels of 28.06 ± 12.32 and 35.97 ± 10.54, respectively. In controls between 18-28 and 40–50 years, controls have mean homocysteine levels of 11.47 ± 9.21 and 15.66 ± 10.91, respectively. The difference between cases and controls according to age was found out to be statistically significant (p<0.0001). This was in concordance to the study done by Mamoun El Sayed Shalaby[6] and Brazzelli et al.[7] both reported higher homocysteine levels with increase in the age of psoriasis patients (p<0.001). This was in contrast to the study done by Malebra et al.[4]and Rahmatpour Rokni G et al.[8] where both found no statistically significant correlation with p value >0.05. However, no significant trend was observed in our study that is change in mean homocysteine levels amongst different divided groups according to age.

Males showed a significantly higher mean homocysteine levels than females in our study- Males (33.20 ± 12.96) and females (28.88 ± 8.74). In controls, the mean homocysteine levels in males and females were 15.96 ± 11.52 and 16.11 ± 11.12. The difference between cases and controls was found to be statistically significant with p<0.0001. Similar results were observed in Didem Didar Balc et al.[10] in which males had a mean serum homocysteine levels of 30.11 ± 6.81 and females had 21.78 ± 5.36, p<0.001. In contrast, Mamoun El Sayed Shalaby[6] study found no significant correlation between increase in homocystine levels with gender (p=0.356).

In our study, the mean homocysteine level of cases and controls amongst different divided groups according to occupation was found out to be statistically significant. However, the mean homocysteine levels among cases and controls were found out to be highly significant in skilled/ semi-skilled and unskilled workers. (p<0.0001)

In our study, the mean homocysteine level in cases was 30.10 ± 11.43 in urban areas, whereas the mean homocysteine

level in cases was 33.52 ± 11.95 in rural areas. However, there was no correlation observed between 2 groups. But the difference between cases and controls of urban and cases and controls of the rural population was found out to be statistically significant (p < 0.0001).

In our study, the highest mean serum homocysteine levels were found to be 38.67 ± 12.12 in patients according to disease duration ranging from 1 to 2 years. However, no significant correlation was seen between homocysteine levels and disease duration (p = 0.2149). This was in concordance with Uslu et al.,[11] Tobin et al.,[2] Barzzelli et al.,[7] which also showed no statistically significant correlation between the homocysteine levels and duration of the disease.

The mean homocysteine levels in cases with family history was 28.02 ± 11.12, while mean homocysteine levels in cases without positive family history was 31.91 ± 11.78. However, the result did not show any statistical correlation between homocysteine levels and family history.

In our study, the mean homocysteine levels were observed to be slightly raised in cases with nail involvement however there was no correlation seen between homocysteine levels and nail involvement (p = 0.3856).

The mean homocysteine level in cases that had joint involvement was 33.32 ± 9.15 and in those who did not have any joint involvement was 31.27 ± 12.17. No statistical significance was observed between the two groups (p > 0.05). This was in concordance with the study by Giannoni et al.,[12] where no correlation was found between homocysteinaemia and the presence of arthritis (p = 0.62).

In our study, the maximum mean homocysteine levels of 38.75 ± 10.04 were seen in cases according to age of onset with more than 60 years. No trend was observed among different groups and their mean homocysteine levels.

Serum homocysteine showed slight variation in cases among three groups divided according to Body surface area. However, there was no correlation between rising homocysteine levels and increased body surface area. In our study, the results observed were statistically non-significant. (p = 0.2516)

In our study, as the PASI score increased (>12), the mean serum homocysteine levels also increased (40.22 ± 9.29). This was following the results shown in the study by Mamoun El Sayed Shalaby et al.[6] with p < 0.0001, but this was in contrast with the results of the study by Uslu et al.,[11] Tobin et al.,[4] Brazzelli et al.[7] and Mousmi Das et al.[13] which showed that there was no statistically significant correlation between homocysteine levels and severity by PASI score.

CONCLUSION

Psoriasis vulgaris is a common, chronic inflammatory disorder presenting in Dermatology OPD. It has chronic relapsing and remitting course in patients with various therapeutic choices. The chronic nature of the disease and upcoming cases with cardiovascular diseases in patients with psoriasis and homocysteine is now an independent risk factor for cardiovascular diseases. Our findings highlight the need for a more comprehensive investigation into the relationship between psoriasis and homocysteine and to investigate the role of homocysteine as a cardiac marker in patients with psoriasis vulgaris.

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