Psoriatic Nephropathy and its Correlation with hs-CRP: A Case Control Study

Abstract

**Background:** Psoriasis is a multisystem disorder associated with various systemic diseases such as cardiovascular diseases, diabetes mellitus and metabolic syndrome. Renal involvement in patients with psoriasis is sparsely studied and its association is still unclear. **Aim:** The aim of this article was to study causal attributable renal involvement in patients with psoriasis and factors affecting the same. **Methods:** Fifty patients with documented psoriasis were recruited after excluding any secondary causes of renal disease. They were subjected to routine investigations along with hs-CRP and specific investigations for kidney function including urine albumin creatinine ratio (ACR) and estimated glomerular filtration rate (eGFR). The eGFR and ACR of the patients were compared with 50 age- and sex-matched controls. Association with any disease-related factors such as severity and duration were assessed. Renal biopsy was planned in patient with ACR >500 mg/g creatinine. **Results:** The mean eGFR (IQR) (ml/min/1.73 m²) of the case group was found to be 80.00 (71.00–95.75) and in the control group was 88.00 (75.25–99.00). This difference was not significant (P = 0.206). However, in the age group of > 30 years, the eGFR of disease group (78.50 ± 17.94) was significantly lower than that in the control group (88.96 ± 17.01, P = 0.023). The mean urine ACR (mg/g) in the disease group was found to be 13.359 ± 26.01 while that in the control group was found to be 5.66 (3.40–8.08), and the difference was not found to be clinically significant. Four patients with psoriasis had microalbuminuria as opposed to none of the controls. **Conclusion:** Subclinical albuminuria was found in 8 per cent of patients with psoriasis. Glomerular dysfunction with statistically significant reduction in eGFR was seen in psoriasis in age group of more than 30 years and those who had a long-standing disease. The renal involvement had positive correlation with hs-CRP indicating the role of inflammatory milieu. Further large-scale cohort studies would help assess this aspect in further details. **Limitation of the Study:** Sample size was small. Large-scale studies would be required to further substantiate these observations.

**Keywords:** Kidney dysfunction, microalbuminura, psoriasis, psoriatic nephropathy, renal involvement

Introduction

Psoriasis is a chronic inflammatory disease primarily affecting skin, nails and joints. The prevalence of psoriasis varies in different geographical areas of the world.[1] It ranges from 0.8% to 2.8% in India. There is increasing evidence to suggest that psoriasis is causally associated with systemic diseases such as cardiovascular diseases (myocardial infarction, stroke), diabetes mellitus and metabolic syndrome.[2,3] Renal involvement in patients with psoriasis is increasingly being reported in the recent years. This has led to postulation of a cause attributable in psoriasis named psoriatic nephropathy.[4,5]

Although, the exact pathogenesis behind nephropathy in psoriasis is still unclear but auto-immunity is the most popular proposed mechanism with raised circulating levels of IgA antibodies.[6,7] A variety of histopathological and immunological abnormalities in renal biopsies in patients with psoriasis have been described in the literature. IgA nephropathy appears to be a distinct pattern in most of the psoriatic patients with renal involvement.[3]

Methods

Study population

The study was conducted in the outpatient department of dermatology at a tertiary...
care centre in Delhi, India. A total of 50 patients with psoriasis (Group A) were recruited along with 50 age- and sex-matched controls (Group B). Patients with pre-existing renal disease or history of using nephrotoxic drugs like cyclosporine were excluded from the study. Patients with pre-existing secondary causes of kidney disease such as diabetes mellitus, hypertension, metabolic syndrome, connective tissue diseases and vasculitides were also excluded from the study.

**Study design**

After obtaining written consent from the patients, a detailed history was taken for all the subjects regarding the disease duration, symptoms and impact on quality of life. Body mass index, blood pressure and blood sugar of all the cases were recorded to look for any evidence of pre-existing metabolic syndrome. Examination was done to assess morphology, type and severity of psoriasis by means of PASI score and body surface area (BSA). Patients with guttate psoriasis were also screened for anti-streptolysin O titres and throat swab to rule out any possibility of post-streptococcal glomerulonephritis.

Routine investigations including complete blood count, renal function tests, liver function tests, fasting and post-prandial sugar, lipid profile and hs-CRP were done. Estimated glomerular filtration rate (eGFR) was calculated by using serum creatinine levels by modification of diet in renal disease (MDRD) and chronic kidney disease epidemiology collaboration (CKD-EPI) equation.[8-10] Urine albumin was measured by urine nephelometry, and urine creatinine was estimated by alkaline picrate method by using commercial kits. Urine albumin creatinine ratio (ACR) was then calculated by taking ratio of urine albumin and urine creatinine. Renal biopsy was reserved for patients with microalbuminuria of more than 500 mg/g creatinine.

**Statistical evaluation**

Statistical analysis was done by SPSS program version 20.0. Mann Whitney U test was applied to compare the distribution of urine albumin, urine ACR, eGFR, PASI score, BSA, duration of disease and hs-CRP between the two groups. P value <0.05 was considered as significant and P value <0.001 was considered as highly significant.

### Results

#### Demographic data

The baseline characteristics of the subjects and the controls are represented in Table 1. Out of 50 cases with psoriasis, there were 38 males and 12 females (M:F = 3.16:1). The mean age of the cases was 31.94 ± 11.62 years while the mean age of the control group was 35.78 ± 12.33 years.

#### Clinical variants and severity

Chronic plaque psoriasis was the most common clinical variant affecting 31 patients (62 per cent), followed by guttate psoriasis seen in 14 (28 per cent) and psoriatic erythroderma in 4 (8 per cent). The least common variant encountered was pustular psoriasis affecting only one patient (2 per cent) as shown in Figure 1a-d.

PASI Score: PASI score in the disease group ranged from 1.2 to 64 with a mean of 14.25 ± 10.28. Maximum number (52%) of patients had a PASI score ranging from 11 to 20 followed by 36% patients with a score between 0 and 10.

Body Surface Area: The mean BSA was 22.4 ± 24.65 ranging from 1 to 92%. Majority (28) of patients had a BSA >10 per cent followed by 21 patients with a score between 2 and 10%.

**Estimated glomerular filtration rate**

The mean eGFR (IQR) (ml/min/1.73 m²) of the disease group was found to be 80.00 (71.00–95.75) and in the control group was 88.00 (75.25–99.00). This difference was not significant (P = 0.206). The distribution of eGFR was further studied in the cases and controls after dividing each of them into age groups of less than and more than 30 years. The average duration of disease in the age group less than 30 years was 2.06 years while in group more than 30 years was 6.25 years. It was found that the difference among the case and control population of the age groups of <30 years was still insignificant. However, in the age group of >30 years (with a longer average duration of psoriasis), the eGFR of case group (78.50 ± 17.94) was significantly lower than that in the control group (88.96 ± 17.01, P = 0.023) as shown in Figure 2a and b.

### Table 1: Comparison between age and sex distribution of the cases and the controls

| Age group (in years) | Cases | Controls | Significance |
|----------------------|-------|----------|--------------|
|                      | Male  | Female   | Total        | Male  | Female | Total |  |
| < 30                 | 21 (55.3%) | 5 (41.7%) | 26 (52%)     | 19 (52.7%) | 3 (21.4%) | 22 (44%) | 0.648 |
| 31-40                | 10 (26.3%) | 3 (25%)  | 13 (26%)     | 8 (22.3%) | 4 (28.6%) | 12 (24%)  |
| 41-50                | 6 (15.8%) | 1 (8.3%)  | 7 (14%)      | 6 (16.7%) | 4 (28.6%) | 10 (20%)  |
| 51-60                | 1 (2.6%) | 3 (25%)  | 4 (8%)       | 3 (8.3%) | 3 (21.4%) | 6 (12%)   |
| Total                | 38 (76%) | 12 (24%) | 50 (100%)    | 36 (72%) | 14 (28%)  | 50 (100%) |
| Mean age (years)     | 30.5±10.92 | 36.50±13.07 | 31.94±11.62 | 33.50±11.53 | 41.64±12.78 | 35.78±12.33 |
**Urine albumin creatinine ratio**

The mean urine ACR (mg/g) in the disease group was found to be 13.359 ± 26.01, while that in the control group was found to be 5.66 (3.40–8.08). Though this indicated a trend towards ACR being higher in disease group, the difference was not statistically significant [Figure 3].

It was found that four patients with psoriasis had microalbuminuria while none of the controls had microalbuminuria. Clinical characteristics of these patients are represented in Table 2. Out of these four patients, three were males and one was female. All of these cases had severe psoriasis with PASI score >10 and were less than 40 years old.

**hs-CRP**

The mean hs-CRP (mg/l) in disease group was 3.627 ± 0.919 while that in the control group was 0.575 ± 0.2194 (P = 0.00). Out of the disease group (n = 50), 42 had higher levels of hsCRP compared to 0 in the control group and the difference was found to be clinically significant (P = 0.000) [Table 3]. Further, it was observed that the four patients who presented with microalbuminuria had abnormally high levels of hs-CRP. The mean hs-CRP (mg/l) in these four patients with microalbuminuria (5.84 ± 1.37) was found to be significantly higher than that in rest of the patients (3.62 ± 4.26) (P = 0.047) [Figure 4a and b].

**Discussion**

Psoriasis affects multiple systems of the body in addition to skin, nails and joints. The systemic involvement in psoriasis is usually under-investigated by dermatologists. Systemic involvement has a bearing to the morbidity and the choice of treatment in psoriasis. The systemic associations such as metabolic syndrome, accelerated

![Figure 1: Clinical presentation of the subjects including chronic plaque psoriasis (a), guttate psoriasis (b), erythroderma (c), pustular psoriasis (d)](image)

### Table 2: Profile of patients with microalbuminuria

| Patients with Microalbuminuria | Urine ACR (mg/g) | Sex | Age (years) | Duration (years) | PASI | eGFR (ml/min/1.73 m²) | Hs-CRP (mg/dl) | Blood Urea (mg/dl) | Serum Creatinine (mg/dl) |
|-------------------------------|-----------------|-----|-------------|------------------|------|-----------------------|----------------|---------------------|------------------------|
| 1.                            | 176.54          | M   | 35          | 3 years          | 15.2 | 76                    | 5.36           | 25                  | 1.1                    |
| 2.                            | 40.63           | M   | 45          | 5 years          | 11.4 | 100                   | 6.4            | 17.6                | 0.8                    |
| 3.                            | 58.54           | F   | 32          | 15 days          | 29.4 | 70                    | 7.4            | 16                  | 1.2                    |
| 4.                            | 38.72           | M   | 18          | 5 years          | 30.9 | 79                    | 4.2            | 29                  | 1.2                    |

### Table 3: Mean renal function in patients with psoriasis

| Mean                                         | Cases (n=50) | Controls (n=50) |
|----------------------------------------------|--------------|-----------------|
| S. Urea (mg/dl)                              | Male (n=38)  | Female (n=12)   | Male (n=36)  | Female (n=14)  |
|                                              | 22.98±6.23   | 23.58±7.63      | 23.132±6.518 | 31.57±7.00     | 30.64±6.40    |
| S. Creatinine (mg/dl)                        | 0.98±0.22    | 0.94±0.12       | 0.972±0.201  | 0.86±0.14      | 0.81±0.13     | 0.85±0.141     |
| eGFR (ml/min/1.73 m²)                        | 87.32±16.00  | 73.42±20.00     | 83.98±17.86  | 92.11±13.64    | 75.21±12.47   | 87.38±15.26   |
| Urine Albumin (mg/l)                         | 18.19±47.98  | 7.96±3.78       | 15.73±41.97  | 5.67±2.47      | 4.44±2.04     | 4.78±2.215    |
| Urine Creatinine (mg/dl)                     | 1.502±0.877  | 1.51±0.76       | 1.5±0.84     | 0.833±0.200    | 0.839±0.209   | 0.83±0.20     |
| Urine ACR (mg/g)                             | 13.48±28.70  | 12.98±15.59     | 13.35±26.0   | 4.44±2.04      | 6.98±2.89     | 6.004±2.89    |
atherosclerosis, non-alcoholic steatohepatitis and insulin resistance have all been well studied in psoriasis. However, renal involvement in psoriasis has only recently been recognised.\textsuperscript{[3,11‑15]}

For the detection and evaluation of chronic kidney disease, the Kidney Disease Outcomes Quality Initiative (KDOQI) from the National Kidney Foundation (NKF) has developed guidelines that recommends screening with a serum creatinine measurement for use in glomerular filtration rate estimation and analysis of a random urine sample for albuminuria.\textsuperscript{[8,9]} The former can be estimated by MDRD Study equation and the CKD-EPI equation while the latter is to be estimated by urine ACR, which is a more reliable marker than just a urinary albumin concentration.\textsuperscript{[10]}

In our study, a significant decrease in eGFR was seen in psoriasis as compared to control in the age group of >30 years suffering from long-standing disease. The mean urine albumin and urine ACR of patients with psoriasis, though within normal range, was found to be significantly higher than the control group. This indicates a subclinical renal involvement in psoriasis, which if not dealt with may progress to achieve statistical significance over a period of time. The authors feel that such patients are therefore, advised to undergo routine eGFR and ACR monitoring on at least annual basis.

Further in the case group, 8% patients with psoriasis had microalbuminuria in contrast to none in the healthy control group. These patients suffered from severe psoriasis with PASI score >10 and significantly high levels of hs-CRP as compared to the other patients (with normal urine ACR). However, the degree of albuminuria in these patients was not high enough to qualify for renal histopathology as per recommendation taken in our study. We could not find any Indian study to compare our results. To the best of the knowledge of authors, this is the pilot study from Indian population.

Higher values of albuminuria and greater number of patients showing subclinical glomerular dysfunction in the disease group as compared to the control group suggest that the patients with psoriasis have a subclinical nephropathy and are at a greater risk of developing renal dysfunction than non-psoriatic individuals in the future. A regular follow up and monitoring to assess progression of nephropathy may therefore be worthwhile.

The mean hs-CRP was significantly higher in psoriatic patients than the control group with majority (84%)
of the patients showing abnormally higher levels of hs-CRP as compared to none in the control group. This is in concordance with other studies conducted by Agravatt et al.[16] and Vadakayil et al. in which the levels of hs-CRP were found to be raised in patients with psoriasis.[17]

In the present study, the levels of urine albumin and urine ACR were significantly higher in the patients who had high values of hs-CRP. Moreover, all the four patients with microalbuminuria had abnormally high levels of hs-CRP than that of the rest of patients with psoriasis with normal urine ACR. This observation suggests the role of inflammation in the renal dysfunction in psoriasis which is also responsible for the raised levels of hs-CRP (one of the most sensitive markers of inflammation).

Hence, the risk of renal dysfunction is greater in cases where the severity of inflammation is higher causing higher values of hs-CRP. Other authors have also proposed the role of proinflammatory milieu in the pathogenesis of chronic kidney disease. Kumar et al. compared the levels of hs-CRP in 45 cases of chronic kidney disease patients with 35 age- and sex-matched controls and found that the levels of hs-CRP were higher in the patients with CKD, suggesting the role of an underlying chronic inflammatory process in the development of CKD.[18]

Conclusion
Renal involvement in psoriasis is largely in the form of subclinical nephropathy, which manifests in the form of microalbuminuria (more so in patients with higher hs-CRP and sever psoriasis) as well as glomerular dysfunction as measured by urine ACR and EGFR, respectively. These patients need a prolonged monitoring and follow up for early detection of deterioration in renal function when the disease is at its reversible stage.

Limitation of the study
Sample size was small. Large-scale studies would be required to further substantiate these observations.

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Conflicts of interest
There are no conflicts of interest.

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