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Original Article

A study on the clinicopathological correlation of psoriasis with extent of expression of Osteopontin in OPD patients

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Abstract
Objective: *To evaluate the clinico-pathological Correlation of Osteopontin in patients of Psoriasis.*
Methods: *A cross-sectional clinical correlation study was done on 53 clinically diagnosed cases of psoriasis. All clinically diagnosed cases of Psoriasis were included after taking proper consent in a signed proforma. Patients were clinically evaluated and a proper history was taken including patient's age, sex, site, duration, family history, community, Itching, nail involvement, H/O associated endocrine disorder, H/O associated skin disorders. The Psoriasis Area and Severity Index (PASI) score was evaluated on the basis of area coverage and plaque appearance.A detailed study of histopathological features and IHC osteopontin expression was analyzed.*
Results: *About one fourth of patients were 20-30 &>40 years of age (26.4%). More than half of patients were males (69.8%). Lower limb was the most common affected site (75.5%). The duration of disease was 12-24 months in 50.9% patients. Psoriasis vulgaris was the most common clinical diagnosis (26.4%). Induration was among majority of patients (94.3%). PASI score ≥10 was among more than half of patients (60.4%). Parakeratosis and Dermal inflammation were the most common histopathological changes (96.2%). Moderate positivity of Osteopontinin the epidermis which was present among more than half of patients (60.4%) followed by weak (30.2%) and strong positivity (9.4%).In Dermis osteopontin positivity was moderate in (50.9%),followed by weak(39.6%) and strong positivity(9.4%)respectively.*
Conclusion: *Because of varied clinical, histopathological and IHC feature of psoriasis. A definitive diagnosis in doubtful cases can be made by a combination of all the above parameters.*
Keywords: *Psoriasis, Osteopontin, Histopathological changes.*

Introduction

The term psoriasis derived from Greek word "psora" which means "itch". It is a chronic skin disease, touching about 2% of worldwide population. It is non-epidemic infection and horrible skin disorder, which can include a whole system of a person. It is mostly inherited and mainly categorized by sharply marginated crusty,

erythematous plaques that expand in a relatively equal distribution. The majority areas are the scalp, fingers and toes, palms, soles, umbilicus, gluteus, underneath the breasts and genitals, elbows, knees, shins and sacrum (Christophers, 2001; Shrivastav et al, 2009).

Plaque Psoriasis is widely spread, affecting 80–90% of those with psoriasis. Plaques are definite, red, elevated lesions crowned with silvery-white scales and are habitually seen over the extensor surfaces of the limbs, particularly the elbows and knees, over the scalp and at the hairline. Plaques can be huge or little and may itchy, while itching is not an important aspect of plaque psoriasis. Nail concern can occur, manifesting as pitting and departure from the nail bed (onycholysis).

Studies show that between 10% and 30% of people with psoriasis also develop psoriatic arthritis. It is to estimates the prevalence of psoriasis have varied across studies. The prevalence of psoriasis in adults ranged from 0.91 to 8.5 percent, and same in the case of children are in between 0 to 2.1 percent. The study stated that 25% of people with psoriasis could be classified as having sensible to severe psoriasis. Around the world, the one- third of people's affecting psoriasis report a family history of the disease (Parisi et al, 2013; Nickoloff, 1999).

Osteopontin (OPN) is a phosphorylated acidic arg-gly-asp containing glycoprotein implicated biologically in bone remodeling; immune system regulation. OPN is adding to the chronic inflammatory status through anti- apoptotic effects on effectors T cells. It was found that Langerhans cell (LC), myeloid dendritic cells (mDCs) that express intracellular OPN upon their activation polarize naive T cells toward a Th 17 phenotype. Secreted OPN (sOPN) directly stimulates interleukin (IL)-17 productions by T cells (Buback et al, 2009). In PS, OPN has a proangiogenic effect on microvascular endothelial cell. It acts through promoting vessel formation subsequently supporting the influx of inflammatory cells through a mechanism mediated by IL-1 and matrix metalloproteinase-9, induced by OPN and tumor necrosis factor-a, which acts as an angiogenesis promoting factor (Nissinen and Kähäri, 2014).

The present study was designed to evaluate the clinico-pathological Correlation of Osteopontin in patients of Psoriasis.

Material and Methods

A cross-sectional clinical correlation study was done on 53 clinically diagnosed cases of psoriasis who were presented in the Department of Skin & V.D, Hind Institute of Medical Sciences, Safedabad, Barabanki (UP). Skin biopsies were undertaken to study histopathological and immunohistochemical pattern of the lesions and were sent to the Department of Pathology, Hind Institute of Medical Sciences, Safedabad, Barabanki (UP). The study was conducted after obtaining approval from the Institutional Ethical Committee of Hind Institute of Medical Sciences, Barabanki.

All clinically diagnosed cases of Psoriasis were included after taking proper consent in a signed proforma. Patients under treatment, on Anti-cancer drugs and with other systemic manifestation (eg.DM, HTN) were excluded from the study.

Methods

Patients were clinically evaluated and a proper history was taken including patient's age, sex, site, duration, family history, community, Itching, nail involvement, H/O associated endocrine disorder, H/O associated skin disorders. The Psoriasis Area and Severity Index (PASI) score was evaluated on the basis of area coverage and plaque appearance. A well informed written consent both in English and Hindi was taken from the patient. All the data collected were entered in a pre-designed proforma. Mandatory punch biopsy of the skin preferably from the erythematous plaque covered with silvery scales lesions were taken. The tissue was sent to Department of Pathology for tissue processing, sections cutting and embedding for Histochemical and Immunohistochemical study.

Immunohistochemistry study was done on the cut sections using Osteopontin.

All the skin biopsies were fixed in 10% buffered neutral formalin and then entire specimens were submitted for processing. The skin punch biopsies were presented in toto and was carefully section to include the epidermis. Sections of 4-5microns thickness were cut and stained with Haematoxylin & Eosin. For light microscopy, one slide from each cell block was routinely stained with H&E to arrive at a diagnosis. Special immunohistochemical stains were used whenever required.

Method of H & E staining

1) Sections are deparaffinised and hydrated through graded alcohol to water.
2) Stained with alum Hemotoxylin for 1-10 minutes.
3) Washed in running tap water for 5 minutes.
4) Differentiated in 1% acid alcohol for 5 seconds.
5) Washed well in tap water.
6) Blued by dipping in an alkaline solution (ammonia water) followed by a tap water wash.
7) Counterstained with 1% Eosin Y – 15 seconds.
8) Dehydrated in increasing grades of alcohol and cleared in xylene and mounted in DPX.

Immunohistochemical evaluation

Sections were examined under microscope & distinct nuclear staining was taken as positive**.** The staining characteristics were further categorized into strong, moderate and weak positivity.

Statistical Analysis

The results are presented in frequencies, percentages and mean±SD. All the analysis was carried out on SPSS 16.0 version (Chicago, Inc., USA).

Results

About one fourth of patients were 20-30 &>40 years of age (26.4%) followed by <20 (24.5%) and 31-40 (22.6%) years. The mean age of patients was 31.21±15.07 years. More than half of patients were males (69.8%). About half of patients belonged to rural area (50.9%) (Table-1).

Lower limb was the most common affected site (75.5%). Upper limb was the second most common affected site (67.9%). Head was the least common affected site (20.8%) (Fig.1).

The duration of disease was 12-24 months in 50.9% patients followed by <12 (26.4%) and >24 (22.6%) months. The mean duration of disease was 22.49±19.50 months (Table-2).

Psoriasis vulgaris was the most common clinical diagnosis (26.4%). Chronic plaque psoriasis, Palmar psoriasis and Plantar psoriasis were the second most common clinical diagnosis each constituting 13.2%. Guttate psoriasis was least common clinical diagnosis constituting 3.8% (Table-3).

In duration was among majority of patients (94.3%) followed by scaling (81.1%) and erythema (69.8%) (Fig.2).

PASI score ≥10 was among more than half of patients (60.4%). The mean PASI score was 6.88±8.13 (Fig.3).

Itching was the most common symptom (66%). Auspitz sign was the most common sign(62.3%). Associated cutaneous disorder was the least common (1.9%) (Table-4).

Parakeratosis and Dermal inflammation were the most common histopathological changes (96.2%). Acanthosis and Hypogranulosis were the second most common histopathological changes (94.3%). Suprapapillary thinning was the least common histopathological changes (47.2%) (Table-5).

Moderate positivity of Osteopontin in the epidermis was present among more than half of patients (60.4%) followed by weak (30.2%) and strong positivity(9.4%). Moderate positivity of Osteopontin in the dermis was present among about half of patients (50.9%) followed by weak (39.6%) and strong positivity (9.4%) (Table-6).

Table-1: Distribution of patients according to demographic profile

Demographic profile	No. (n=53)	%
Age in years		
<20	13	24.5
20-30	14	26.4
31-40	12	22.6
>40	14	26.4
Mean±SD	31.21±15.07	
Gender		
Male	37	69.8
Female	16	30.2
Place of residence		
Rural	27	50.9
Urban	26	49.1

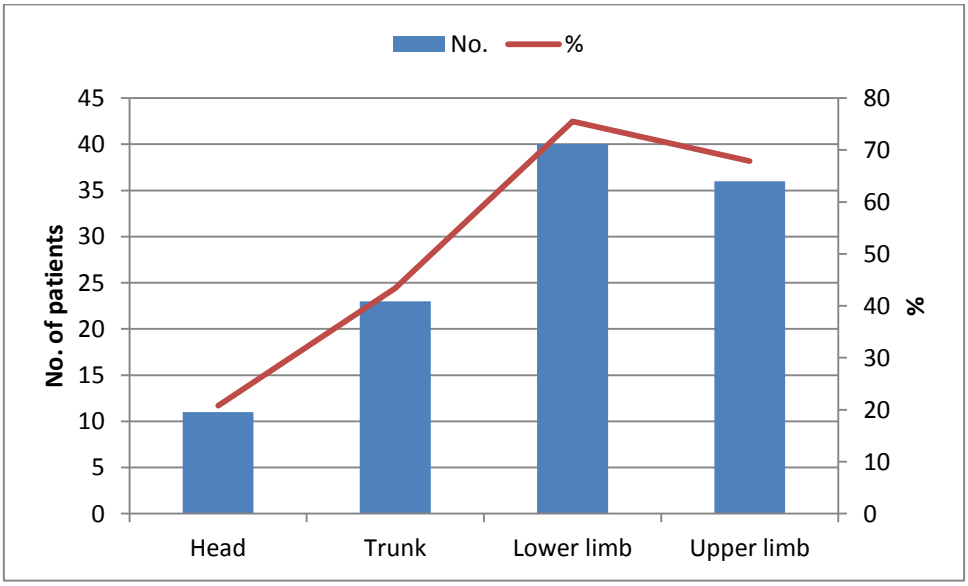

Fig. 1: Distribution of patients according to site of involvement

Table-2: Distribution of patients according to duration of disease

Duration of disease in months	No. (n=53)	%
<12	14	26.4
12-24	27	50.9
>24	12	22.6
Mean±SD	22.49±19.50	

Table-3: Distribution of patients according to clinical diagnosis

Clinical diagnosis	No. (n=53)	%
Chronic plaque psoriasis	7	13.2
Flexure psoriasis	4	7.5
Guttate psoriasis	2	3.8
Palmar psoriasis	7	13.2
Palmoplantar psoriasis	6	11.3
Plantar psoriasis	7	13.2
Plaque psoriasis	4	7.5
Psoriasis	2	3.8
Psoriasis vulgaris	14	26.4

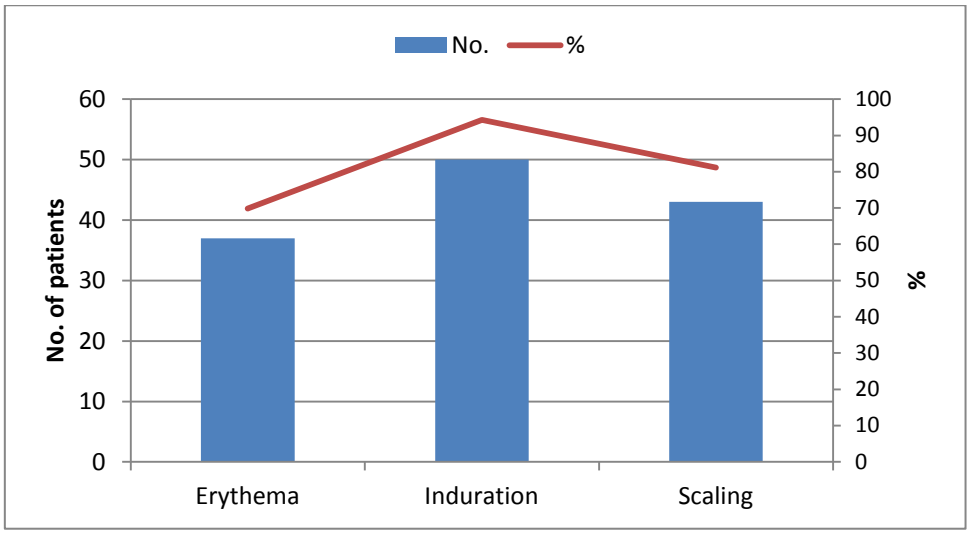

Fig. 2: Distribution of patients according to the Plaque characteristic

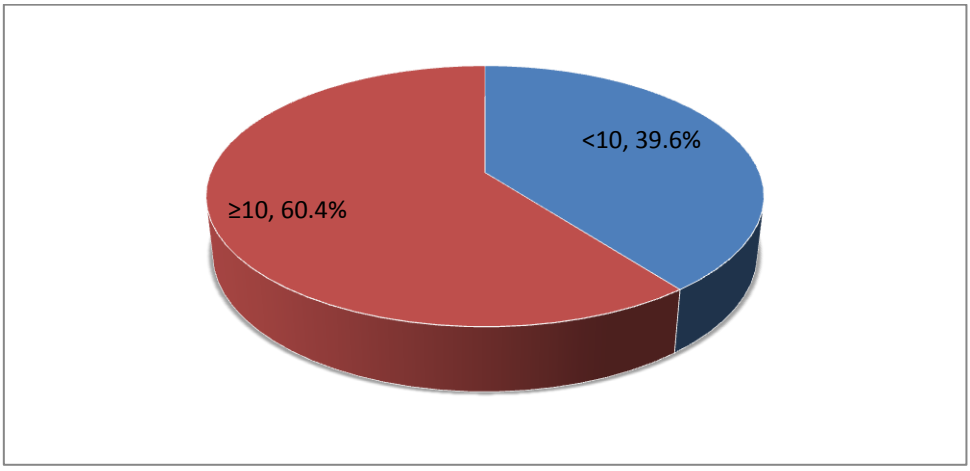

Fig. 3: Distribution of patients according to PASI score

Table-4: Distribution of patients according to Clinical features

Signs and symptoms#	No. (n=53)	%
Itching	35	66.0
Nail affection	16	30.2
Auspitz sign	33	62.3
Joint involvement	0	0.0
Associated cutaneous disorder	1	1.9
Associated endocrine disorders	0	0.0

#Multiple response

Table-5: Distribution of patients according to histopathological changes

Histopathological changes #	No. (n=53)	%
Hyperkeratosis	46	86.8
Acanthosis	50	94.3
Parakeratosis	51	96.2
Suprapapillary thinning	25	47.2
Munro microabscess	31	58.5
Elongated rete ridges	48	90.6
Hypogranulosis	50	94.3
Spongiosis	46	86.8
Dermal inflammation	51	96.2
Vessel changes	42	79.2

#Multiple response

Table-6: Distribution of no. patients according to Osteopontin Expression

Osteopontin Expression	No. (n=53)	%
Epidermis		
Strong positive	5	9.4
Moderate positive	32	60.4
Weak positive	16	30.2
Dermis		
Strong positive	5	9.4
Moderate positive	27	50.9
Weak positive	21	39.6

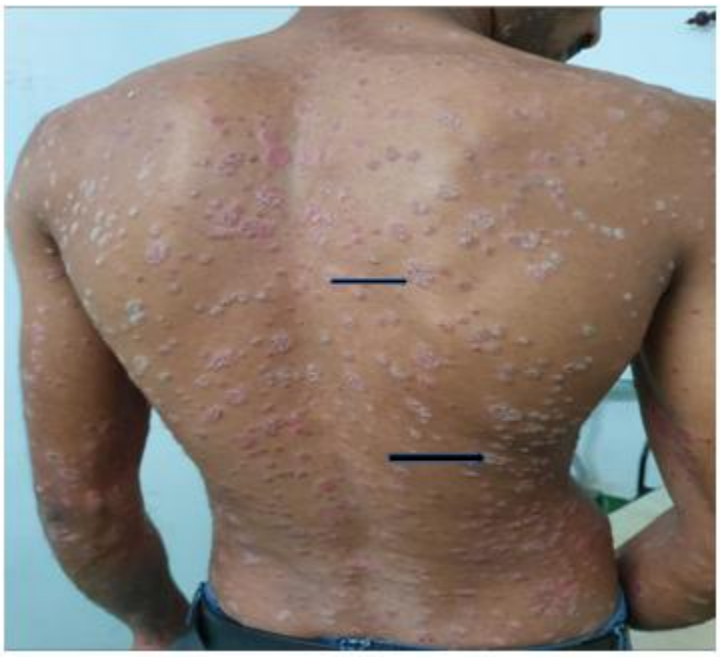

Figure 1- showing psoriasis vulgaris: A typical plaque which is well defined, discoid, erythematous, indurated lesions surmounted with loose silvery scales.

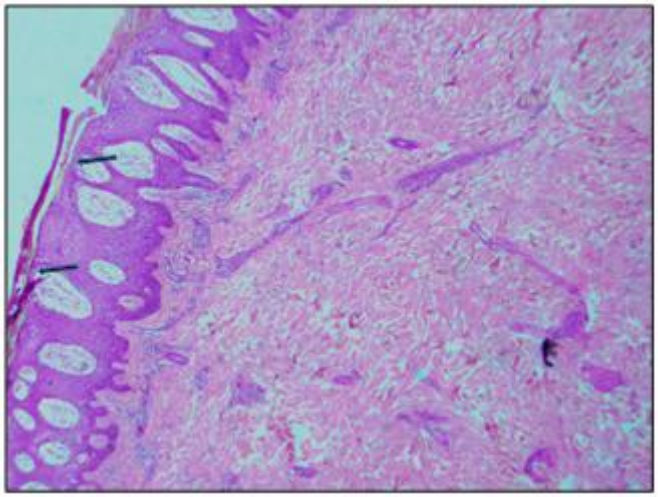

Figure 5: Scanner view 40x magnification, showing hyperkeratosis, acanthosis, suprapapillary thinning (arrow). The dermal papilla shows oedema and prominent small vascular spaces.

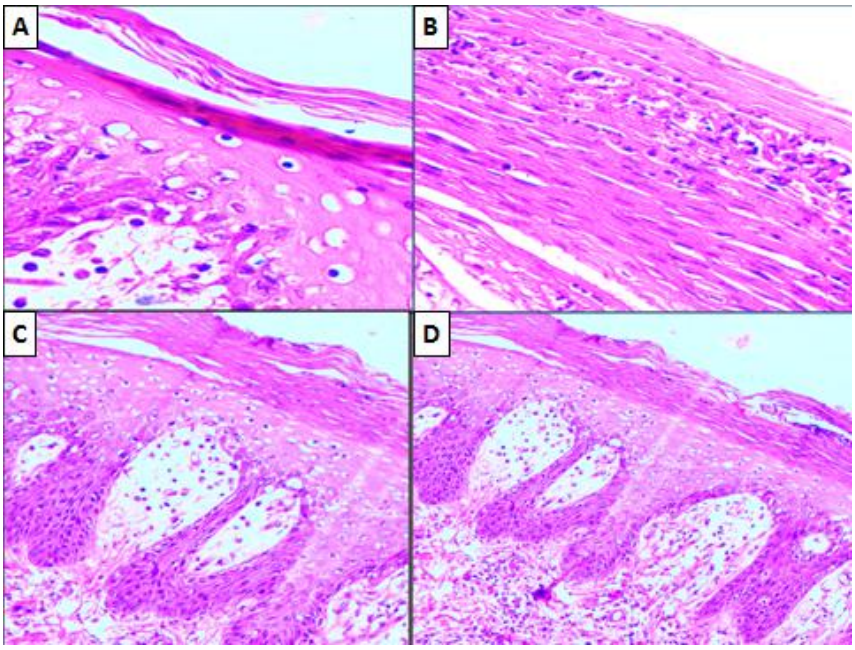

Figure 6- H&E stain. High power view (400x) magnification showing
(a) Parakeratosis (b) Munro-microabscess
(c) Hypogranulosis (d) Spongiosis with elongation of rete ridges

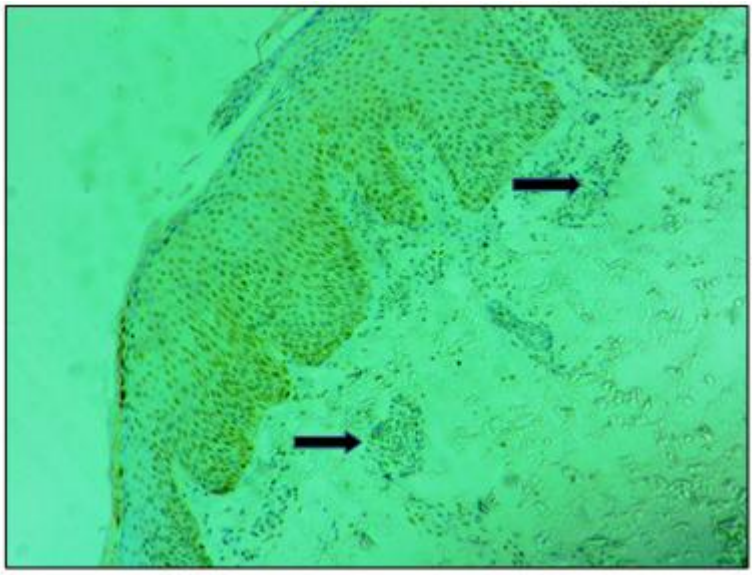

Figure7-In low power view 100x magnification showing moderate positivity in epidermis and dermal inflammatory cells (arrow). [Immunohistochemistry. Osteopontin streptavidin biotin method using haematoxylin as counter stain.

Discussion

Genetic and environmental factors greatly influence the clinical development of psoriasis. This results in wide differences in the prevalence of the disease among different ethnic groups and in different parts of the world. Further, patients with minimal clinical manifestations often do not seek medical attention. Most studies on prevalence are based on information from clinical examinations, interviews, census studies, and mailed questionnaires. Estimates of occurrence of psoriasis in different parts of the world vary from 0.3 to upto more than 2% (Farber and Nall, 1998; Nevitt and Hutchinson, 1996). A few studies that have been performed in India to determine the incidence of psoriasis have been on patients

attending the clinics and hospitals, the incidence of psoriasis among dermatology outpatients was found to be 2.8% (Bedi, 1995; Kaur et al, 1986).

The present study was conducted in the Department of Pathology, HIMS, Barabanki with the objective to study the clinicopathological correlation of psoriasis with extent of expression of Osteopontin in OPD patients. A total of 53 patients were included in the study.

In the present study, about one fourth of patients were 20-30 &>40 years of age (26.4%) followed by <20 (24.5%) and 31-40 (22.6%) years and the mean age of patients was 31.21±15.07 years. Affandi et al (2018) found that the mean age of onset of psoriasis for the study population was 35.14 ± 16.16 years. Song et al (2017) found that the mean age was 47.0 years with a distribution mostly in the 50s (24.9%).. In the study by Chintagunta et al (2018), the mean age of the patients was 30 years among patients with pustular psoriasis.

More than half of patients were males (69.8%) and the male: female ratio is 2.3:1 in the present study. In the study by Affandi et al (2018), male to female ratio was 1.3 : 1. Song et al (2017) found that male to female was 1.47:1 in their study. In the study by Raghuveer et al (2015)male to female ratio was 3:1. Chintagunta et al (2018) found that nine were females and five were males among patients with pustular psoriasis.

The present study observed that according to site of involvement, lower limb was the most common affected site (75.5%). Upper limb was the second most common affected site (67.9%). Head was the least common affected site (20.8%). Raghuveer et al (2015) observed that extremities (lower and upper) (86.5%) were the most common site of involvement followed by trunk (85%) and scalp (75%). Song et al (2017) reported that psoriasis lesions were most frequently found in the lower leg (72.6%, n=913), followed by the back (60.9%, n=766), upper leg (60.8%, n=764), elbow (58.0%, n=729), knee (57.1%, n=718), lower arm (56.8%, n=714), abdomen (55.7%, n=700), upper arm (53.5%, n=672), and scalp (53.1%, n=668). Mikrani and Shrestha (2014) found that extensor surface of the body was most commonly involved.

In the present study, the duration of disease was 12-24 months in 50.9% patients followed by <12months (26.4%) and >24months (22.6%). The mean duration of disease was 22.49±19.50 months. The mean duration of disease was much lower in the present study than the study by Song et al (2017) in which the mean disease duration was 109.2 months. This difference might be due to difference in socio-demographic profile of patients and duration of the study period between the studies.

The present study found that psoriasis vulgaris was the most common clinical diagnosis (26.4%). Chronic plaque psoriasis, Palmar psoriasis and Plantar psoriasis were the second most common clinical diagnosis each constituting 13.2%. Guttate psoriasis was least common constituting about 3.8%. The findings of this study is in agreement with the study by Mikrani and Shrestha (2014) observed that psoriasis vulgaris (PV) was the most common variety of the disease. Raghuveer et al (2015) showed that chronic plaque type was seen in 83% of cases followed by guttate type in 8% of cases.Affandi et al (2018) in which the most common clinical diagnosis was chronic plaque psoriasis (85.1%), followed by guttate psoriasis (2.9%), erythrodermic psoriasis (1.7%), and pustular psoriasis (1.0%). Song et al (2017) observed that plaque and guttate types of psoriasis accounted for 85.8% and 8.4%, respectively. Vijayan et al (2010)reported that chronic plaque was the commonest clinical type (44%) followed by palmar plantar (19%) and scalp psoriasis (12%).

The present study found induration was among majority of patients (94.3%) followed by scaling (81.1%) and erythema (69.8%).Nail involvement was observed in 30.2% of patients. Affandi et al (2018) found that 57.1% of patients had nail involvement. Song et al (2017) found nail involvement in 12.3% of patients. According to Raghuveer et al (2015)nail involvement was present in 75% of cases.

The present study showed that PASI score ≥10 was among more than half of patients (60.4%). The mean PASI score was 6.88±8.13. In the study by Song et al (2017), patients with PASI score≥10 accounted for 24.9%.

In this study, Parakeratosis and Dermal inflammation were the most common histopathological changes (96.2%). Acanthosis and Hypogranulosis were the second most common histopathological changes (94.3%). Spongiosis and Munro-microabscess found to be 86.8% and 58.5% respectively. Suprapapillary thinning was the least common histopathological changes (47.2%). Raghuveer et al (2015) demonstrated that considering only Munromicro-abcesses and Spongiform pustules of Kogoj to be truly diagnostic, only 25% showed definitive evidence of psoriasis. Though most of the biopsy specimen showed histopathological features suggestive of psoriasis, only a few specimens showed diagnostic features, i.e., Munro-microabcesses and spongiform pustules of Kogoj. Various studies on histopathology of psoriasis like Lal et al (1965) also noted parakeratosis, acanthosis, suprapapillary thinning, Munro-microabscess and hypogranulosis in most of the cases.

The histopathological findings in the present study showed features consistent with psoriasis, but there was disparity between findings of other studies (Lal et al, 1965; Cox and Watson, 1972).This can be explained on the basis of varying degrees of activity of the disease. It is clear that there is a wide spectrum of histological change recognizable in psoriatic plaques, even when they have not been subjected to specific treatment and also when the clinical appearance does not deviate from the usual.

In the present study, the extent of expression of osteopontin in the epidermis and the dermis was categorized as strong positive, moderate positive and weak positive. Moderate positivity of osteopontin in the epidermis was among more than half of patients (60.4%) followed by weak (30.2%) and strong positivity (9.4%). Moderate positivity of osteopontin in the dermis was among about half of patients (50.9%) followed by weak (39.6%) and strong positivity (9.4%). In the study done by Abdel Malwa et al (2016) found that the osteopontin was significantly expressed in all the layers of epidermis in all the cases, while in the dermis moderately expressed in 7 patients and strongly expressed in 11 cases out of total 18 cases. Amin and Azim (2012)[97] had found that in psoriatic lesional skin, OPN was expressed in the inflammatory cells and microvasculature endothelial cells of the dermis in all cases. These findings can be explained by that the chemotactic soluble OPN attracts other immune cells to the inflammatory sites such as dendritic cell, neutrophils, natural killer (NK) cells, NK-T cells, and macrophages, which are all known to migrate toward OPN. Abdou et al (2012) reported that there was a correlation of the intensity of OPN expression with the density of the dermal inflammatory infiltrate.

Conclusion

Because of varied clinical, histopathological and IHC feature of psoriasis. A definitive diagnosis in doubtful cases can be made by a combination of all the above parameters.

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