

## OCULAR MANIFESTATIONS IN PSORIASIS

**JigeeshaPreethi. M<sup>1</sup>, Chandrsekaran. B<sup>2\*</sup>**

<sup>1,2</sup>Department of Orthopaedics, SreeBalaji Medical College & Hospital, Chromepet, Chennai, India  
\* balakrishnan.m@bharathuniv.ac.in

### ABSTRACT

Psoriasis is a chronic dermatological disease with multiple extra cutaneous association and eye is one among them. Psoriasis, as a part of its disease process can affect any part of eye ranging from simple eyelid involvement to vision threatening involvement of macula. Not only the disease process but the drugs used for treatment of psoriasis can also cause ocular morbidity which has to be screened.

Blepharoconjunctivitis is the most common manifestation seen among all the other ocular manifestation. Uveitis is the least commonest but a potential sight threatening manifestation seen in both symptomatic and asymptomatics. Detecting this potential complication early and treating promptly can prevent irreversible vision loss.

### Keywords

Psoriasis, Uveitis, retinoscopy, ocular manifestations

### INTRODUCTION

Psoriasis is a fairly common dermatological condition, characterized by reddish/crimson patches that are covered with silvery scales. This condition can occur in any part of the body. It is a noncontagious, autoimmune disease, wherein remissions and exacerbations are the main characteristic of this disease.

It is generally associated with extracutaneous/non- dermatological manifestations like joint and ocular involvement along with an increased risk of coronary artery disease.

Joint involvement can be in the form of peripheral arthritis, spondylitis and enthesitis. This can in turn range from monoarticular involvement to severe destructive forms of arthritis. The occurrence generally follows dermatological lesions, but no correlation is found between the severity of skin lesions and the occurrence of joint disease.

Ocular inflammation occurrence in psoriasis is known for quite some time now, but is not very investigated. It has a very subtle presentation and is often diagnosed after irreversible damage has occurred to the eye. This delay in presentation is maybe due to lack of awareness among patients, lesser signs and symptoms and a delay in referrals.

The various manifestations in Psoriasis maybe due to the disease itself or as a result of the treatment that is being given for the disease. The various findings range from Blepharitis, Conjunctivitis, Dry Eye, Episcleritis, Marginal Keratitis and sight threatening Uveitis.

Psoriasis is also associated with a significant social stigmatization, absenteeism from work, emotional stress and physical pain. Thus, a thorough ocular evaluation and treatment is essential for a wholesome treatment of such patients. <sup>(1)</sup>

### AIM AND OBJECTIVES

#### AIM

Psoriasis is an auto immune disorder with multiple extra cutaneous manifestations. The aim of the present study is to analyze the various ocular manifestations in psoriatic patients.

## **OBJECTIVES**

1. To assess the frequency of ocular manifestations in patients with psoriasis.
2. To study the various clinical presentations of psoriasis in the eye.

## **MATERIALS AND METHODS**

### **Materials and methods**

A prospective study of sample size 100 Patients who are diagnosed to have psoriasis (by dermatologist) attending the dermatology and ophthalmology out patient departments during November 2017 – November 2019 at SreeBalaji medical college.

### **Inclusion Criteria:**

- Patients more than 18 years of age with diagnosis of psoriasis, referred from dermatology OPD
- Patients proven to have psoriasis with ocular manifestation of any severity, duration, sex of the patient and time of presentation of symptoms.
- All types of Psoriasis

### **Exclusion Criteria:**

- Patients with skin diseases other than Psoriasis
- Patients using contact lenses

### **MATERIAL:**

Patients of psoriasis fitting the inclusion criteria are taken as the study subjects. The purpose and details of the study protocol will be explained to each subject and written informed consent will be obtained. Details regarding type and severity of psoriasis, time since diagnosis of psoriasis, specific ocular complaints and their duration, treatment received for psoriasis will be noted from study subjects. Psoriasis extent and severity will be graded by PASI score. Ocular symptoms will be noted using questionnaire. All subjects will be subjected to a complete ocular examination including:

- Head posture, Facial symmetry
- Eyes alignment
- Extra ocular movements
- Visual Acuity using Snellens's chart, retinoscopy and subjective refraction
- Slit lamp examination of anterior segment
- Tearfilmfunctionofallsubjectsevaluatedbythe Schirmer's-1, Schirmer's 2 and TBUT
- Applanation tonometry for measuring IOP
- Posterior segment examination by 90D and, Indirect ophthalmoscopy if needed

### **OBSERVATION**

100 patients of Psoriasis who were referred from department of Dermatology, SreeBalajiMedical College were enrolled in this study after obtaining consent and subjected to complete ocular examination.

## DEMOGRAPHIC DATA

### Age Incidence:

Following graph shows the age distribution of the patient's under this study:

**Table 1 : Age incidence**

Age	Number of Patients	%
≤ 20 years	4	4.00
21-40 years	38	38.00
41-60 years	28	28.00
61-80 years	30	30.00
Total	100	100.00

### Graph 1 : Age incidence

The age of the patients included in the study range from 16 to 79 years. The mean age group of this study is 47.5 years. Maximum number of patients was seen in range of 21 – 40 years group.

### Sex Ratio:

Out of 100 patients included in this study, 59 were males, 41 were females. Psoriasis doesn't show any sex predilection worldwide, but shows slightly high male predilection in India.

### Treatment taken by patients:

In the present study of 100 patients, 28 people were newly diagnosed and were not on any treatment as such unlike the other 72 patients who were on Methotrexate, Methotrexate and Etanercept, etanercept.

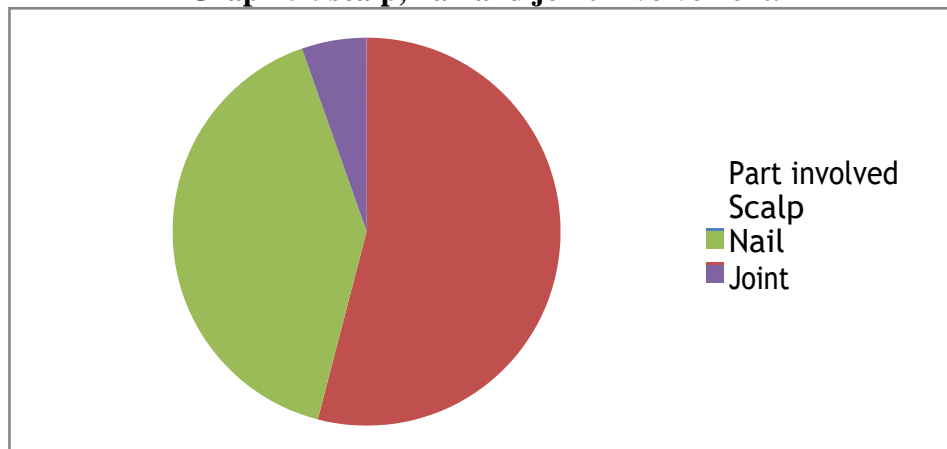
### Scalp, Nail and Joint involvement:

Psoriasis presenting in different types can affect any part of body. In present study scalp involvement of 40% followed by nail 30% involvement was the most common form seen and joint involvement being the least 4%. Psoriasis also occurs in combination involving two different parts, scalp and nail involvement 17% was seen more.

**Table 5 : Scalp, nail and joint involvement**

Part involved	Number of patients	%
Scalp	40	40%
Nail	30	30%
Joint	4	4%
Scalp + nail	17	17%
Scalp + joint	5	5%
Nail + joint	4	4%
Scalp + nail+ joint	0	0%

**Graph 5 : scalp, nail and joint involvement.**



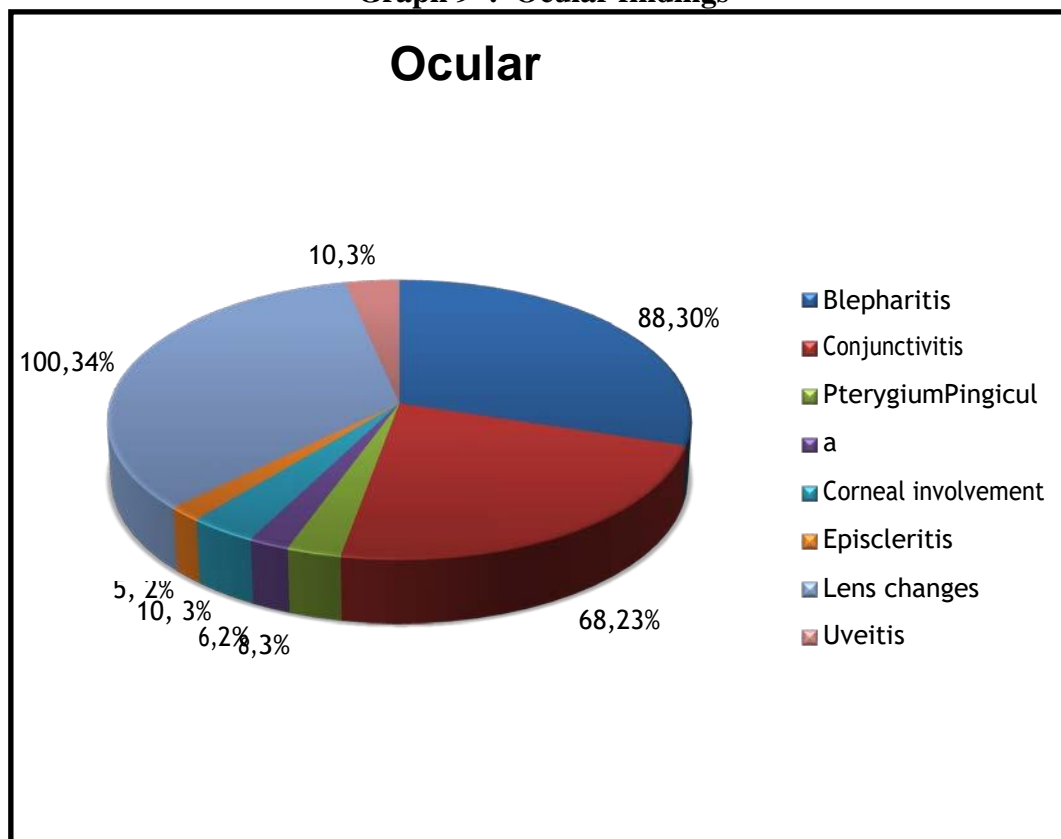
**Duration of disease among patients:**

Following graph shows the duration of disease from diagnosis to present time of this study as follows-

Most of the patients studied were under 5 years of duration of disease and accounts for 54%. The mean average years of duration of Psoriasis disease was 5.95 years.

**OCULAR FINDINGS:**

**Graph 9 : Ocular findings**



In the present study group of 100 patients consisting of 200 eyes, Blepharitis was 42.51 %, Conjunctivitis was 32.85 %, Episcleritis – 2.42%, Pterygium – 3.86 %, Pingiecula – 6%, Uveitis – 4.83 %, Corneal involvement – 4.83% was seen.

Out of 100 patients study group, 42.51% patients had blepharitis which shows positive association with more of scalp and nail involving psoriasis but less commonly in other types of psoriasis.

Conjunctival involvement in the form of Conjunctivitis 32.85%, Pterygium 3.86 %, Pingiecula 2.90%, was seen.

Corneal involvement was seen in 5 patients in which 4 of them had faint nebular type of opacity. No cases of corneal vascularization or active keratitis was seen.

Episcleritis of 2.42% was seen in the study population.

Uveitis was seen in 4.83% population in which 2 patients were referred from orthopaedics department with complaints of pain, photophobia and redness with acute joint involvement. One patient gave history of recurrent similar complaints in past and had bilateral non - granulomatous anterior and intermediate uveitis in both eyes with circumciliary congestion, fine KP's on cornea with 3+ flare and 2+ cells and mild macular odema as posterior segment finding, macular edema confirmed by FFA. The other patient has only anterior uveitis with 2+ cells and flare with minimal KP's. Both the patients responded well to steroids. The other 2 patients had 1+ flare and few fine KP's suggestive of previous attack.



Lid involving Blepharitis



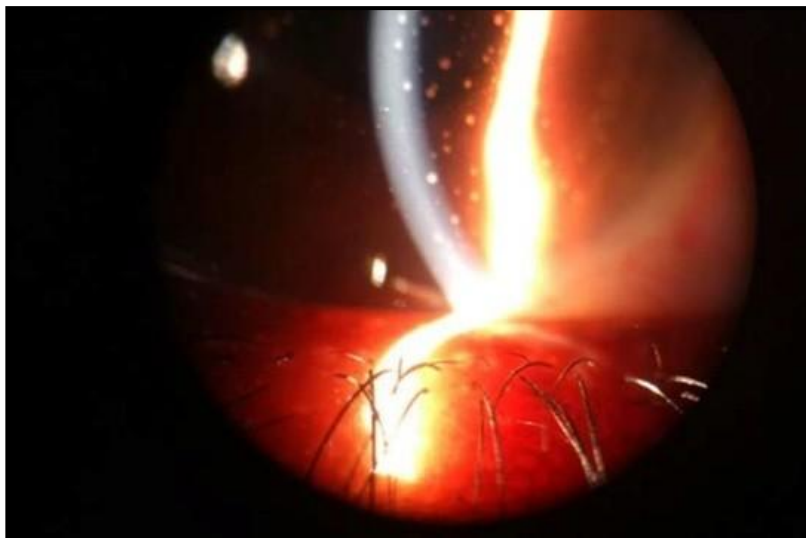
Blepharitis



Conjunctivitis



Episcleritis



Anterior Uveitis – Fine KP's



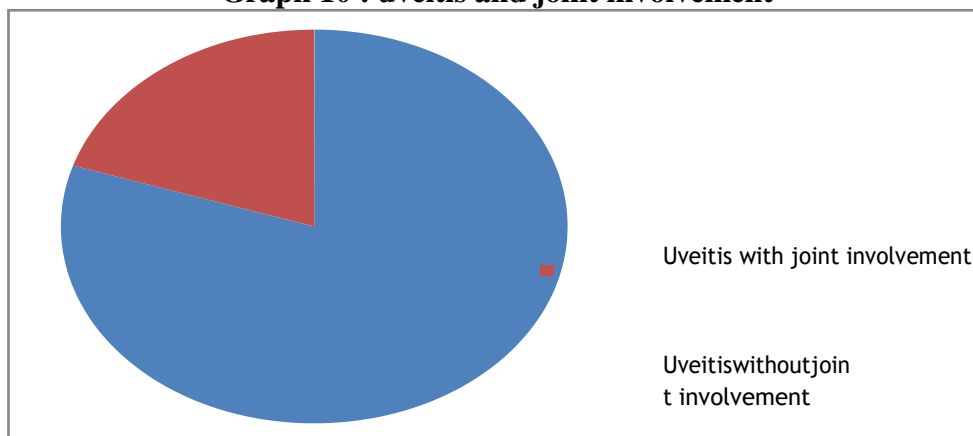
Macular edema

#### UVEITIS AND JOINT INVOLVEMENT:

**Table 10 : uveitis and joint involvement**

Uveitis and joint involvement	No of patients
Uveitis with joint involvement	4
Only uveitis	1

**Graph 10 : uveitis and joint involvement**



Among 5 patients with uveitis, 4 had joint involvement and 1 had active uveitis. Out of which 3 were females and 2 were males. 1 male patient with uveitis and no joint involvement was further evaluated and found to be RA factor negative which shows positive predilection of psoriasis association.

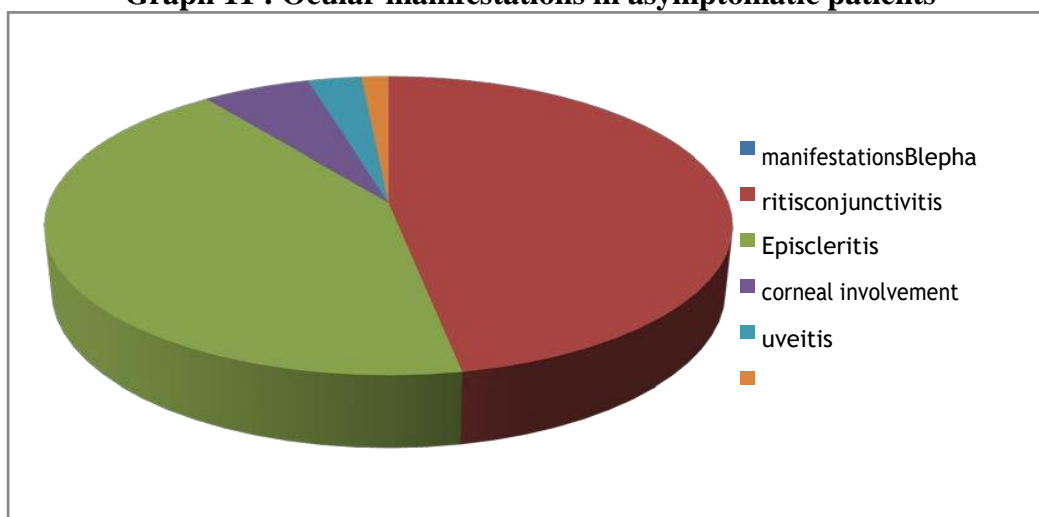
**OCULAR MANIFESTATIONS IN ASYMPTOMATIC PATIENTS:**

Various ocular manifestation seen in the asymptomatic patients were as follows:

**Table 11 : ocular manifestations**

manifestation	Number of patients	%
<b>Blepharitis</b>	32	47.05.%
<b>Conjunctivitis</b>	29	42.64.%
<b>Episcleritis</b>	4	5.88%
<b>Corneal involvement</b>	2	2.94%
<b>Uveitis</b>	1	1.47%

**Graph 11 : Ocular manifestations in asymptomatic patients**





68 patients were asymptomatic among the 100 patients screened. Of which Blepharitis 47.05% was seen more commonly and uveitis with no joint involvement was seen in 1 patient. Other manifestations like conjunctivitis 42.64%, episcleritis 5.88% and corneal involvement in the form of old opacities 2.94% was seen. The importance of screened all the diagnosed patients inspite of absence of any symptoms helps in finding vision threatening conditions like uveitis early.

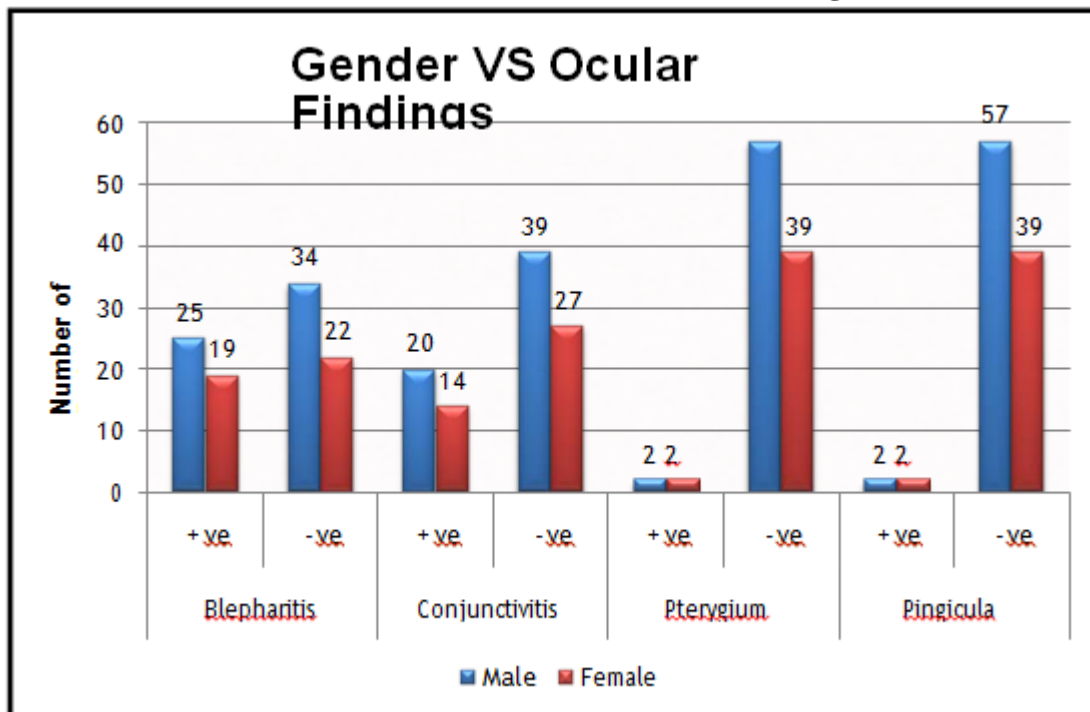
**AGE VERSUS OCULAR FINDINGS:**

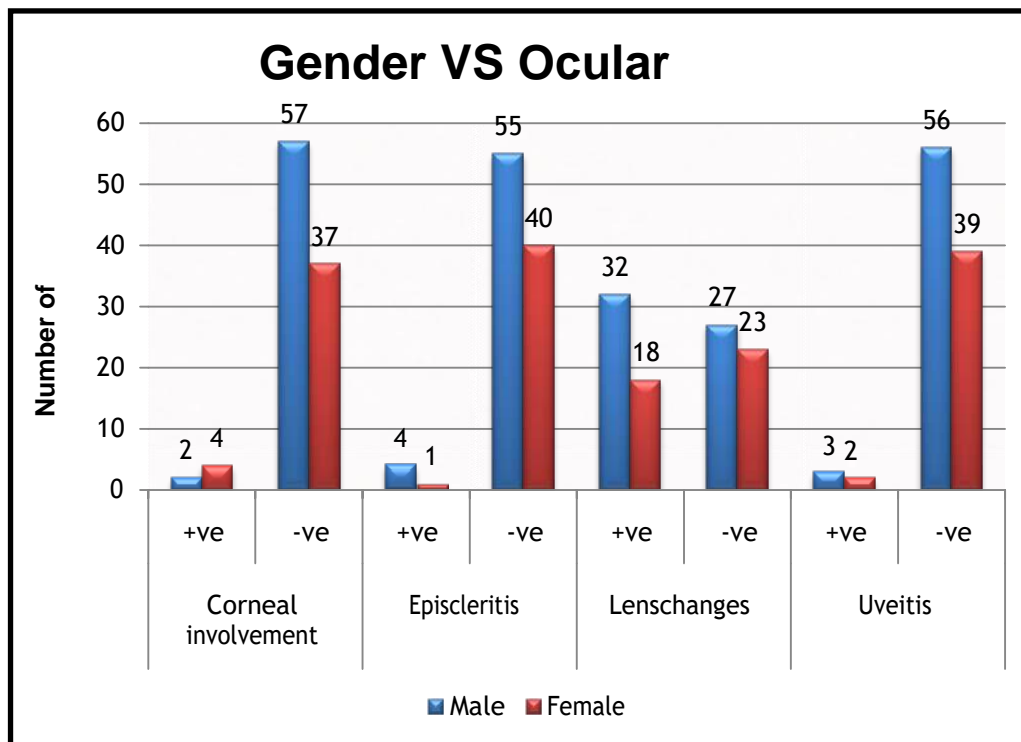
There was no clear association of ocular findings in relation of the age of the 100 screened patients of our study except lens changes which were consistent with age related changes in the eye. There was no incidence of complicated cataract. Ocular changes in Psoriasis is immune mediated than the duration if the disease hence no association was seen.

**GENDER VERSUS OCULAR FINDINGS:**

Of the 100 patients screened in the present study, overall male incidence is more hence overall findings were seen more in male patients, but clear association was not seen between gender and ocular findings.

**Table 13-A : Gender versus ocular findings**





**Table 13-B : Gender versus ocular findings**

**Table 13-A : Gender versus ocular findings**

Gender VS Ocular Findings	Blepharitis		Conjunctivitis		Pterygium		Pingicula	
	+ ve	- ve	+ ve	- ve	+ ve	- ve	+ ve	- ve
<b>Male</b>	25	34	20	39	2	57	2	57
<b>Female</b>	19	22	14	27	2	39	2	39
<b>Total</b>	44	56	34	66	4	96	4	96
<b>P valueChi Squared Test</b>	0.694		0.979		0.709		0.709	

**Table 13-B : Gender versus ocular findings**

Gender VS Ocular Findings	Cornealinvolvement		Episcleritis		Lenschanges		Uveitis	
	+ ve	- ve	+ ve	- ve	+ ve	- ve	+ ve	- ve
<b>Male</b>	2	57	4	55	32	27	3	56
<b>Female</b>	4	37	1	40	18	23	2	39
<b>Total</b>	6	94	5	95	50	50	5	95
<b>P valueChi Squared Test</b>	0.187		0.327		0.309		0.963	

The distribution of patients among two groups is unequal, there was no significant association between duration of the disease and ocular manifestations in this study as the disease is an immune mediated process and many factors are involved in causing disease manifestations per se.

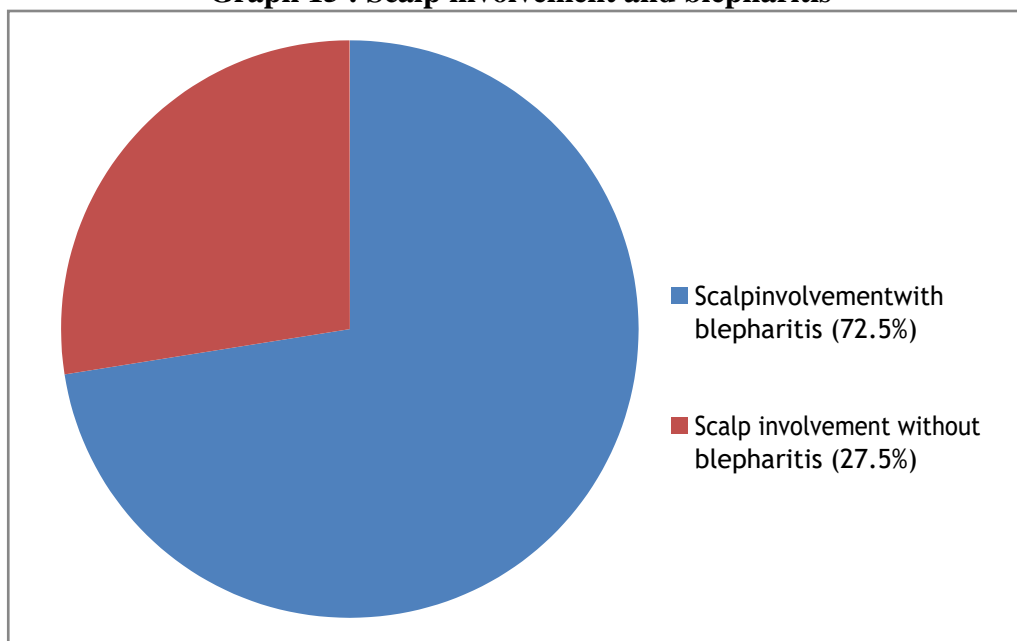
## SCALP INVOLVEMENT AND BLEPHARITIS

The scalp and blepharitis involvement of the present study is as follows,

**Table 15 : scalp involvement and blepharitis**

Scalp involvement	No of patients	Blepharitis	%
Yes	40	29	72.5%
No	60	11	27.5%

**Graph 15 : Scalp involvement and blepharitis**



In the current study, 72.5% of blepharitis was seen most commonly with scalp involving psoriasis than 27.5% of non scalp involving showing positive association.

## DISCUSSION

Ocular manifestations in Psoriasis have been studied by few researchers from different parts of the world. In the present study of 100 patients diagnosed with psoriasis belonged to 16 – 79 years of age (graph 1) with more of patients from age group of 21 – 40 years (table 1). Mean age of the population was 47.5 years (table 1). As male patients access more to health care system than females in our country, similar male preponderance was seen in our study (table 2). Age wise distribution was almost equal in among both genders.

Different types of Psoriasis were seen in the screened group, of which Psoriasis vulgaris 59.00% is commonest and guttate psoriasis 5.00% is the least common (table 3, graph 3).

Patients were given treatment with methotrexate(48 patients), etarnacept(8 patients) and combination of both(16 patients) depending upon disease severity and systemic status. There were 28 newly diagnosed patients and werenot on any treatment at the time of study (table 4, graph 4).

Scalp involvement was seen most (40.00%) and joint involvement was seen least 4.00% (table 5, graph 5). Duration of the disease ranges from few months to many years. Most of the patients screened 54.00% belonged to less than 5 years and least number of patients 2.00% was seen in highest duration of the disease around 16 – 20 years (table 6, graph 6). The average duration of disease was 5.82 years. There was no significant association seen between duration of the disease and ocular manifestations in our study (table14, graph 14). Similar results were published by Okamoto and umebayasi et, al<sup>(1)</sup> in their study regarding severity of disease and age of onset.

68.00 % of patients were asymptomatic irrespective of duration of disease and age of the patients (table 7, graph 7). Ocular manifestations were observed in both symptomatic and asymptomatic patients. Ocular manifestations like blepharitis, conjunctivitis, corneal involvement, episcleritis, uveitis were noted in both the groups (table9, 11 ). Vision threatening complications were of major concern during screening of patients mainly in asymptomatic patients.

### **Blepharitis:**

Burning sensation and redness were most common finding (table 8, 9) seen in all the patients and Blepharitis being most common ocular finding in both groups. Similar reports were found in literature regarding incidence of blepharitis by Limba FB et al. Ibrahim Erbagci et al<sup>(2)</sup> conducted similar study in Turkish population and found to be 64.5%.

<b>Study</b>	<b>Blepharitis %</b>
<b>Limba FB et al<sup>(3)</sup></b>	12.5%
<b>Our study</b>	28%

### **Conjunctival Involvement:**

Conjunctival involvement was seen in the forms of conjunctivitis, pterygium and pinguecula. These ocular findings were seen in both groups. Occurrence of conjunctivitis is more associated with psoriasis than pterygium and pinguecula. The later manifestations were more attributed by dry eye and inflammatory status in eye rather than psoriasis itself.

Similar studies documented conjunctival findings as present study in the literature as follows.

<b>Ocular finding</b>	<b>Limba FB et al<sup>(3)</sup></b>	<b>J R Lambert et al<sup>(4)</sup></b>	<b>Our study</b>
<b>Pterygium</b>	NA	NA	4%
<b>Pingicula</b>	NA	NA	4%
<b>Conjunctivitis</b>	12.5%	19.6%	23%

### Corneal manifestations:

In our study 3 patients with old nebular corneal opacities were seen but no active corneal involvement was seen as reported in the literature by Peter Eustace and Dermot pierse<sup>(5)</sup> in the form of peripheral ulcer with vascularisation and stromal abscess without epithelial involvement by Moadel K<sup>(6)</sup>.

Study	Corneal involvement
Peter Eustace et al <sup>(5)</sup>	2 cases of Peripheralulcerative keratitis
Moadel K et al <sup>(6)</sup>	Stromal abscess
Our study	Old nebular opacities, noactive keratitis

### Uveitis:

Uveitis was seen in 5 patients in our study. Insidious onset, bilateral, chronic mostly anterior uveitis is the most common presentation of Psoriatic uveitis. 1 male patient had non granulomatous anterior and intermediate uveitis with decreased vision. This patient had positive joint association in the form of arthritis in classical form. Decreased vision was due to macular odema which was similar to other studies. Out of 5 patients 4 had strong joint association and HLAB27 positivity. 1 patient with psoriasis duration of 5 years with no joint involvement<sup>(12)</sup> had few episodes of anterior uveitis and was RA factor positive.

Posterior segment involvement in the form of macular odema, sheathing, membrane formation was very less seen than anterior segment involvement in psoriatic uveitis.

The charecteristics of uveitis and joint involvemeny was reported by Eduardo paiva et al<sup>(7)</sup> in the Ann of Rheumatic diseases, they reported 100% of patients with uveitis and axial arthritis to be male which is seen in our study. They reported bilateral involvement of 37.5% and posterior involvement of 44% which is 22 % and 30% respectively in our study.

Study	Uveitis %
J R lambert <sup>(4)</sup>	7.1%
Limba F B at al <sup>(3)</sup>	5.0%
Chandra N S et al <sup>(8)</sup>	2.0%
Ruben Queiro et al <sup>(9)</sup>	18.0%
Our study	4.83%

Parameter	Eduardo Spaiva et al <sup>(7)</sup>	Our study
Patients with axial involvement andmales	100%	100%
Bilateral involvement	37.5%	22.1%
Posterior involvement	44%	30.00%

### Dry Eye:

Dry eye is one of the common findings in patients with psoriasis. Reduced Schirmer's and TBUT levels in our study shows reduced basal level tear production withnormal reflex tear secretion. Similar study reports was published by Her Y et al<sup>(10)</sup> in which reduced TBUT levels and conjunctival cytology with reduced goblet cells were seen. Patients on methotrexate showed more dry eye features than other patients. Keratoconjunctivitissicca was commonest finding reported in a study on Brazilian patients<sup>(11)</sup>.

Study	Dry eye
J R Lambert et al <sup>(4)</sup>	2.7%
Lamba F B et al <sup>(3)</sup>	15 – 22%
Chandran N S et al <sup>(8)</sup>	Increased prevalence
Ibrahim Erbagci et al <sup>(2)</sup>	Increased reduction of TBUT
Her Y et al <sup>(10)</sup>	Reduced conjunctival gobletcells and TBUT
Our study	Reduced tear production andTBUT

## RESULTS

100 patients were studied in the present study with age distribution ranging from 16 – 79 years with average being 47.5 years with male slight male preponderance of 59%.

Psoriasis vulgaris was most commonest seen 59% and guttate psoriasis being least common. Scalp, nail and joint involvement were seen of which scalp involvement of 40% and joint involvement of 4% seen. Majority of the study group 68% was asymptomatic. Irritation, redness, burning sensation, reduced vision, pain and watering were the common complaints seen and burning sensation and redness of eyes 21% was most common complaint. Blepharoconjunctivitis was the most common ocular finding in both symptomatic and asymptomatic group. Strong association of scalp involving psoriasis and blepharitis 72.5% was seen in the present study. 4.83 % of corneal involvement and 2.42% of episcleritis, 4.83% of uveitis was seen.

4 out of 5 patients, 80% with uveitis had joint involvement with positive HLA B-27 association. 2 of them had chronic uveitis. 1 patient had recurrent non granulomatous anterior and intermediate uveitis with reduced vision due to macular odema which showed good response to steroids. 1, 20% patient had anterior uveitis with no joint association was seen. Hence all uveitis patients should be subjected to HLA typing and thorough examination even without joint involvement to rule out complications and vision threatening complications.

Increased incidence of dry eye was seen in the present study, confirmed by reduced Schirmer's test and TBUT time values indicating reduced basal tear secretion with good reflex tear production may be due to meibomian gland dysfunction. Dry eye was seen in association with reduced basal secretion. Increased incidence is due to severity and type of psoriasis rather than duration or gender associated.

Blepharoconjunctivitis being commonest finding in Asymptomatic group of patients. vision threatening conditions like uveitis was also seen in asymptomatic population, which has to be timely diagnosed for proper treatment and less complication, and this indicates the importance of routine ophthalmic evaluation in Psoriasis patients.

## CONCLUSION

The patients are usually asymptomatics and often have mild symptoms and subtle ocular findings which might be missed easily. Uveitis may present with defective vision alone with no signs of anterior uveitis. Hence a high degree of suspicion is required for early and prompt treatment.

The ocular manifestation is usually associated with joint involvement but can be seen without joint involvement also. So all the patients diagnosed to have Psoriasis has to be screened irrespective of disease duration and symptoms.

Association of blepharitis and scalp involving psoriasis was high and all the patients with scalp psoriasis have to be evaluated for blepharitis and lid hygiene must be taught along with proper treatment and to be under follow up.

Incidence of dry eye was seen more in patients with psoriasis and on methotrexate treatment. Hence all the patients must be evaluated thoroughly and adequate treatment to be given based on the severity of dry eye. Care must be taken to identify keratoconjunctivitis sicca early and reduce the morbidity of irreversible ocular surface changes.

Both anterior and posterior segment vision threatening conditions can be easily identified and managed by proper examination and treatment. Posterior segment involvement leads to more morbidity and was seen even in asymptomatic patients irrespective of type and duration of psoriasis. Thus screening all patients as a routine helps in avoiding ocular morbidity and blindness. Association of posterior segment involvement with exacerbations and chronicity of disease could not be established because of the short duration of the study which is a short coming of this study.

The exact mechanism of psoriasis affecting skin, joints and eyes is not known clearly but attributed to T cell mediated responses. Combined treatment approach should be practiced as psoriasis is a multisystem involving disease. Thorough and routine screening along with early and prompt treatment for ocular manifestations irrespective of symptoms should be employed as a routine and complete patient care.

**Funding:** No funding sources

**Ethical approval:** The study was approved by the Institutional Ethics Committee

## CONFLICT OF INTEREST

The authors declare no conflict of interest

## ACKNOWLEDGMENTS

The encouragement and support from Bharath University, Chennai is gratefully acknowledged. For provided the laboratory facilities to carry out the research work.

## REFERENCES

- [1] *Factors associated with increased aqueous flare in psoriasis.* fumikiokamoto, yoshihiroumebayasi, fujiohtsuk a, sachikohommura. s.l. :Japanese journal of ophthalmo l, 2001, Vol. 45.
- [2] *Ocular anterior segment pathologies and tear film changes in patients with psoriasis vulgaris.* Ibrahim Erbagci, Zulal Erbagci, Kivanc Gungor and Necdet Bekir. Gaziantep :Acta Med Okayama, 2003, Vol. 57. 299- 303.
- [3] *Prevalence of eye disease in Brazilian pts with psoriatic art hritis.* Lima FB, Abalem MF, Ruiz DG, Gomes Bde A, Azevedo MN, Moraes HV Jr, Yeskel AS, Kara-Juni or N.
- [4] Saupaulo : clinics of Dermato.l, 2012.
- [5] *Eye inflammation in psoriatic arthritis.* J R Lambert, V Wright. s.l. :ann Rheum Dis , 1976, Vol. 35. 354-356.

- [6] *Ocular psoriasis*. PIERSE, PETER EUSTACE AND DERM OT. s.l. : Brit J Ophthal, 1970, Vol. 54. 810.
- [7] *Psoriatic corneal abscess*. Moadel K, Perry HD,Donnenfeld ED, Zagebaum B and Ingraham HJ.s.l. : Am J Ophthalmol, 1995. 119:800-801.
- [8] *Charecteristics of uveitis in patients with psoriatic art hritis*. Eduardo S Paiva,DamienC Macaluso, Albert ED wards, James T Rosenbaum. 67-70, s.l. :ann Rheum Dis , 2 000, Vol. 59.
- [9] *Psoriasis and the eye: prevalence ofeye disease in Si ngapore Asian patients with psoriasis*. Chandran NS, Greaves M, Goa F, Lim L and Chang BC. s.l. : J Dermatology, 2007.
- [10] *Clinical features and predictive factors in psoriaticarthriti s related uveitis*. Rubén Queiro. spain :s.n.
- [11] *Dry eye and tear film functions in patients with psoriasis*. H er Y, Lim JW, Han SH. 57(4), japan : Jpn J Ophthalmol, 20 13 321-6.
- [12] *Prevalence of eye disease in Brazilian pts with psiriatic art hritis*. Ruiz DG, Gomes Bde A, Azevedo MN, Moraes HV Jr, Yeskel AS, Kara-Junior N. saupaulo : clinicsof Dermato. 1, 2012.
- [13] Kryczek I, Bruce AT, Gudjonsson JE, et al. Induction of IL- 17+ T cell trafficking and development by IFN-gamma: mechanism and pathological relevance in psoriasis. J Immunol. 2008;181(7):4733-41.
- [14] Bettelli E, Korn T, Kuchroo VK. Th17: the third member of the effector T cell trilogy. CurrOpinImmunol, 2007;19(6):652-7.
- [15] Ouyang W, Kolls JK, Zheng Y. The biological functions of T helper 17 cell effector cytokines in inflammation. Immunity. 2008;28(4):454-67.
- [16] Kagami S, Rizzo HL, Lee JJ, Koguchi K, Blauvelt A. Circulating Th17, Th22, and Th1 cells are increased in psoriasis. J Invest Dermatol. 130(5):1373-83.
- [17] Partsch G, Steiner G, Leeb BF, Dunky A, Broll H, Smolen JS. Highly increased levels of tumor necrosis factor-alpha and other proinflammatory cytokines in psoriatic arthritis synovial fluid. J Rheumatol. 1997;24(3):518-23.
- [18] Ettehadi P, Greaves MW, Wallach D, Aderka D, Camp RD. Elevated tumour necrosis factor-alpha (TNF-alpha) biological activity in psoriatic skin lesions. ClinExpImmunol. 1994;96(1):146-51.
- [19] GriffithsCE,StroberBE,vandeKerkhofP,etal.
- [20] Comparison of ustekinumab and etanercept for moderate-to- severe psoriasis. N Engl J Med. 362(2):118-28.
- [21] Gottlieb AB, Antoni CE. Treating psoriatic arthritis: how effective are TNF antagonists? Arthritis Res Ther.2004;6(suppl 2):S31-5.
- [22] Victor FC, Gottlieb AB, Menter A. Changing paradigms in dermatology: tumor necrosis factor alpha (TNF-alpha) blockade in psoriasis and psoriatic arthritis. ClinDermatol.
- [23] Caspi RR, Roberge FG, McAllister CG, et al. T cell lines mediating experimental autoimmune uveoretinitis (EAU) in the rat. J Immunol. 1986;136(3):928-33.



- [24] Brito BE, O'Rourke LM, Pan Y, Anglin J, Planck SR, Rosenbaum JT. IL-1 and TNF receptor-deficient mice show decreased inflammation in an immune complex model of uveitis. *Invest Ophthalmol Vis Sci.* 1999;40(11):2583-9.
- [25] Foxman EF, Zhang M, Hurst SD, et al. Inflammatory mediators in uveitis: differential induction of cytokines and chemokines in Th1- versus Th2-mediated ocular inflammation. *J Immunol.* 2002;168(5):2483-92.
- [26] Kulkarni PS, Srinivasin BD. Cachectin: a novel polypeptide induces uveitis in the rabbit eye. *Exp Eye Res.* 1988;46(4):631-3.
- [27] Rosenbaum JT, Howes EL Jr, Rubin RM, Samples JR. et al. Ocular inflammatory effects of intravitreally-injected tumor necrosis factor. *Am J Pathol.* 1988;133(1):47-53.
- [28] Fleisher LN, Ferrell JB, McGahan MC. Ocular inflammatory effects of intravitreally injected tumor necrosis factor-alpha and endotoxin. *Inflammation.* 1990;14(3):325-35.
- [29] Robertson M, Liversidge J, Forrester JV, Dick AD. Neutralizing tumor necrosis factor-alpha activity suppresses activation of infiltrating macrophages in experimental autoimmune uveoretinitis. *Invest Ophthalmol Vis Sci.* 2003;44(7):3034-41.
- [30] Greiner K, Murphy CC, Willermain F, et al. Anti-TNF alpha therapy modulates the phenotype of peripheral blood CD4+ T cells in patients with posterior segment intraocular inflammation. *Invest Ophthalmol Vis Sci.* 2004;45(1):170-6.
- [31] McPherson SW, Roberts JP, Gregerson DS. Systemic expression of rat soluble retinal antigen induces resistance to experimental autoimmune uveoretinitis. *J Immunol.* 1999;163(8):4269-76.
- [32] Singh VK, Rai G, Agarwal SS. Role of cytokines in experimental and clinical uveitis. *Indian J Ophthalmol.* 2001;49(2):81-90.
- [33] Caspi RR. A look at autoimmunity and inflammation in the eye. *J Clin Invest.* 2010;120(9):3073-83.