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Chronic Ocular Manifestation of Steven Johnson Syndrome along Southern Kerala, India

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Abstract
SJS causes mucosal erosions with wide spread erythematous. Cutaneous macular or target lesions than merge together with subsequent epidermal detachment General drug ethology of SJS and its ocular complications and their management was investigated in present study 52 SJS confirmed cases were studied prospectively at RIO TVPM and the data obtained were statistically analysed. The severity and chronicity of the eye complications depends to a large extent upon the degree of ocular damage during the acute syndrome. Even patient with milder skin involvement may still have severe ophthalmic involvements during the acute phase CHRONIC eye findings noticed are scarring, symblepharon, cicatrization of, conjunctivae, entropion, trichiasis distichiasis and tear film instability. Break down of ocular surface leads to corneal scarring and neovascularisation also. Ectropion noticed may be due to severe mucosal injury leads to scarring of lids. Development of ocular cicatrical pemphigoid : a chronic scarring and neovascularisation also. Ectropion noticed may be due to severe mucosal injury and leads to scarring of lids. Development of the ocular cicatrical pemphigoid a chronic scarring inflammation of the ocular mucosa can leads to blindness. The time interval between the onset of SJS and cicatrical pemphigoid ranges from few months to years. The entropion may be due to contraction of the palpebral conjunctivae. Madarosis due to loss of eye lashes. A more severe chronic problem such as tarsal conjuctival keratinisation may results in chronic keratopathy.
Symblepharm results from adhesion between tarsal and bulbar conjunctivae Late phase corneal complication may develop due to corneal exposure leading to superficial and punctuate epithelial keratitis, recurrent epithelial defect in growth of abnormal new blood vessels with vascularisation, corneal scarring, deep keratinisation corneal thinning and opacity in the visual axis leads to blindness and may corneal perforation results due to uncontrolled infection and leads to endophthalmitis and pan ophthalmitis that finally need evisceration or enucleation. Dry eye being also a late phase complication may develop in a high percentage of patients with SJS. Tear film deficiency may due to conjunctival xerosis or corneal xerosis. Early interference and active treatment regime can reduce the events and further extent of corneal involvement in this study.

Introduction

SJS is a life threatening illness with high incidence of ocular involvement SJS was 1st diagnosed by 2 paediatricians as Dr. S. Albert Slavens and Frank Johnson. Most patients who develop SJS consult a physicians or dermatologist in the acute phase. They consult the ophthalmologist only after the resolution of the skin lesions and are later referred to the tertiary eye care centre. This explains delay in most patients seen at the institute.

Various studies tells about a drug etiology IN 60% of cases. But in SJS role of infectious agents like HSV, Mycoplasma, pneumonial may plays to certain extent (Fitz pal rick et al 1993) other causes have been linked to AIDS, Cox Sackie Virus infection, influenza mumps and hepatitis studies shown that slight male preponderances in SJS (Tasman et al 1996, champion et al 1998)

An idiosyncratic delayed hyper sensitivity reaction has been implicated in the patho physiology of SJS.

SJS causes severe ocular morbidly according to patz (1950) a high percentage of patients with SJS and TES have ocular morbidity so uncontrolled infection if persists due to lack of proper treatment leads to conjunctival, scleral and corneal perforation and even endophthalmilis. Keratinisation of the lid margin and palpebral conjunctival further contributes to discomfort and corneal damage via blink related micro trauma to the corneal epithelium (D Pascuate MA, E spana EM, Livdt et al 2005).

The severity and chronicity of the eye complications depends to a large extent upon the degree of ocular damage during the acute syndrome (Howard 1963, Arstikaitis 1973). Among the chronic eye findings the scarring and cicatrisation of the conjunctivae may result from initial inflammatory process. This may leads to entropion; trichiasis and instability of tear film (Dohl man CH, Dough MAN D 1972) Wright P Collin JR (1983). Arstikaitis MJ (1973). Break down of ocular surface leads to corneal scarring and neovascularisation Blepharilis is mentioned in 12% of (TINHC and Adam's 1985 series) Ectropion may be due to severe mucosal injury (chan LS et al (1991) entropion due to contraction of the palpebral conjunctivae.

Trichiasis: a posterior misdirection of eye lashes. It has been reported by (Dipasculae MA, E spana EM, Liv DT et al (2005)

Distichiasis: An aberrant lashes may arise from the openings of the damaged meibomian glands Anderson et al 1981 reported case of SJS with Acquired distichiasis - Madarosis noticed A study by (RAMON RUIZ Maldonado 1985) noticed this in 2% of cases Mebomian gland dystuntion Lid margin Inflammation can cause wide spread destruction of meibomian gland orifices and the gland themselves (YIPIW N, Thong by, Limj et al (2005)

Symblepharon : It results from adhesion between tarsal and bulbar conjunctivae. It follows as a sequalae of late complications due to conjunctivae Healing by scarring and may leads to symblepharon or an kyloblepharon (Lee Muta Phong et al 1993) found symble pharon in 20 of 78 patients with SJS.

Soren Jenson (1967) had case of Phensuximide induced SJS who developed symble pharon in both eyes in the late phase. Dry Eye: due to deficiency of tear film mucin layer of deficiency and Aqueous layer of deficiency is noted. The most common tear film deficiency associated with SJS and TEN is mucous deficiency (Wilkins et al 1992) due to destruction of conjunctival goblet cells (Nelson et al 1984, ormerod et al 1988).This causes abnormalities IN tear break up time (TBUT) A study by arstikartis M7 (1973) revealed cicatrisation of the conjunctival goblet cells may leads to a severe dry eye state.

Cicatrisation of the lacrimal ducts IN association with destruction of the conjunctival goblet cells may leads to a severe dry eye state (Arstikartis MJ 1973) Ralph RA (1973) Dryeye secondary to goblet cell destruction is the most common long term ocular complication in patients with various ocular surface diseases Lehman S S, Clin Redial (1999), Nelson JD, wright JC (1984), oh JIM oh

MG kiritoshi A, kinoshi S (1987). Another study by chang Y, Huang any F, Tsings et al (2007) stated that the intense Pseudo membranous and membranous leads to destruction of goblet cells and accessary lacrimal glands as well as the secretory duds of the main lacrimal gland.

Kerato conjunctivitis Sicca or aqueous layer deficiency is usually results from scarring of lacrimal ducts orifice: schirmer test is used to diagnose kcs Ponlaja et al (1966) Roujeau et al (1985), wilkins et al (1992), Tasman et al (1996). Schirmer test is used to diagnose kcs pohloja et al (1966). Roujeau et al (1985), Wilkins et al (1992), Tasman et al (1996)

Corneal Involvement

Destruction of the corneal lumbal stem cells is perhaps the most direconsequences of the A fore mentioned pathologies and can leads to vascularisation and thickening of the corneal epithelium (de Rojas MV, Dart JK, SAWVP (2007)

The conjunctivization of the cornea accompanied by the abnormal tear film produces severe visual loss. There were reported cases of keratization of the lid margins and Palpebral conjunctival further contributes to discomfort and corneal damage via blink related micro trauma to the corneal epithelium (YIP LW, Thong BY, LIMJ et al (2005) late phase corneal complications develop due to corneal exposure leading to punctate epithelial keratitis recurrent epithelial defects in growth of abnormal blood vessels opacification in the visual axis and blindness (wright P, colliN JR 1953)

Uncontrolled infection may leads to perforation; endophthalmitis and panophthalmitis that finally need evisceration as enucleation (power WJ 1995, Tabbora K, shamma H (1975) study by (Dr Rojas MV, Dact JK, Saw VP, 2007) stated as destruction of the corneal Limbal stem cells is perhaps the most dire consequences of the afore mentioned pathologies and can lead to vascularization and thickening of the corneal epithelium.

Tear film deficiency is often troublesome and leads to late phase complication (Barun J 1985) which in turn leads to conjunctival and corneal xerosis with ocular surface problems Late phase corneal complications develop due to corneal exposure lending to punctuate epithelial keratitis (wright P Collin JR (1983) recurrent epithelial defects in growth of abnormal new blood vessels, opacification in the visual axis and blindness.

Chronic keratopathy occur due to the abrading action of the keratinized tarsal conjunctiva, abrading action of the misdirected eye lashes, tear film deficiency and lagophthalmos (Albert and Jacobie et al 2000). The chronic ocular disease may often the most devastating result of survivors of the acute reactions. The outcome depends upon the severity of the initial events made more that it does in the initial treatment.

To minimize visual impairment the prevention of complication is the key to success and careful attention to ophthalmologic examination during the early period of the skin reaction and recognizing the complication and secondary infection can improve the outcome.

Aim of Study

To describe various chronic ocular manifestation of SJS.

Materials and Methods

A descriptive study follow up of 52 cases were included. All cases were initially examined at M.C.H TVPM. Referring from physician, dermatologists were included in this study patients were examined and called for detailed evaluation at RIO TVPM. Duration of the study period from 2009-2011 August. All patients were subjected to detailed examination followed with torch light, slit lamp examination. Initial Vn acuity and corrected Vision acuity was noted. Ry is offered and effect of Ry is studied during the follow UP period. Patient can be called up for follow up periods visit for 2 weeks, 4weeks, 2months, 6months, 12months and 18 months. Data collected will be

analysed information about the chronicity of the disease.

Data were Analysed using computer software statistics package for social science (spss) version '10' Data are expressed in its frequency and percentage as well as mean and standard deviation. To elucidate the association and comparison between different parameters chi square (X2) test was used as non-parametric test for all statistical evaluation a two tailed probability of value <0-05 was considered significant.

Results

Table 1 Showing Sex distribution

Gender	frequency	per cent
Male	19	36.5
Female	33	63.5
Total	52	100.00
Sex ratio	0.57	

Fig: 1 Gender distribution

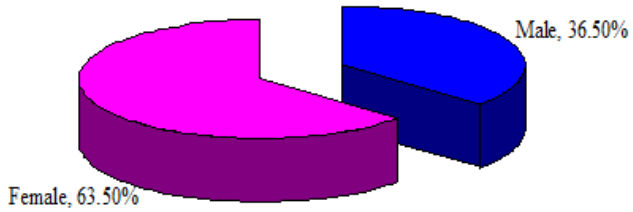


Table -2 Table showing the causative drugs

Drug Intake	Frequency	Percent
No Drug Intake	2	3.8
Ciproflaxacin	12	23.1
Paracetamol	9	17.3
Brufen	3	5.8
Sulphamethaxazone	8	15.4
Allopurinol	3	5.8
Carbamazepine	4	7.7
Phenytoin	6	11.5
Others	5	9.6
Total	52	100

Fig: 2 causative drug administered

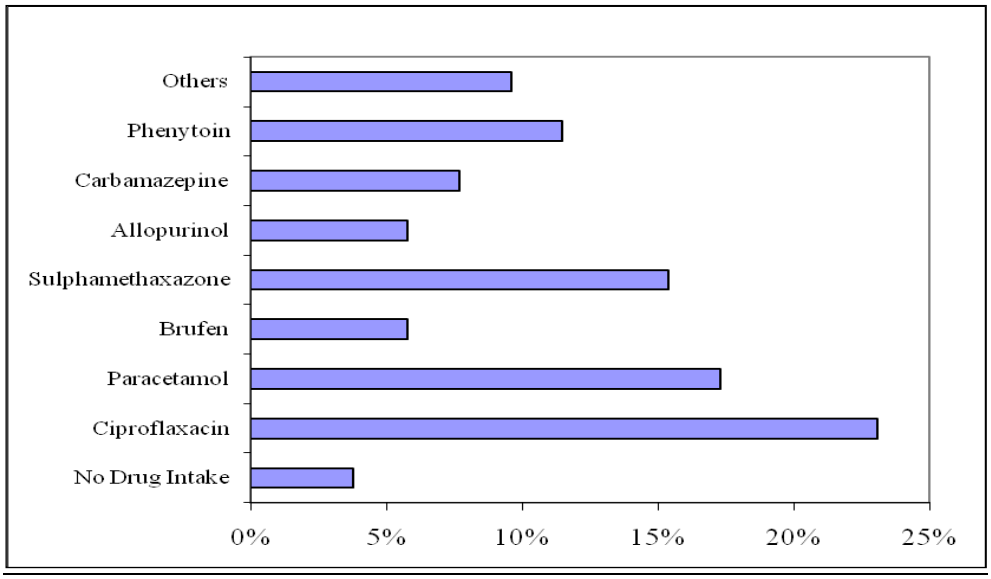


Table 3 Table showing frequency of age distribution

Age	Frequency	Percent
< 20 yrs	7	13.5
20 - 29	8	15.4
30 - 39	14	26.9
40 - 49	8	15.4
50 - 59	6	11.5
>= 60 yrs	9	17.3
Total	52	100
Mean Age	39.56 (SD ± 16.77)	

Figure - 3

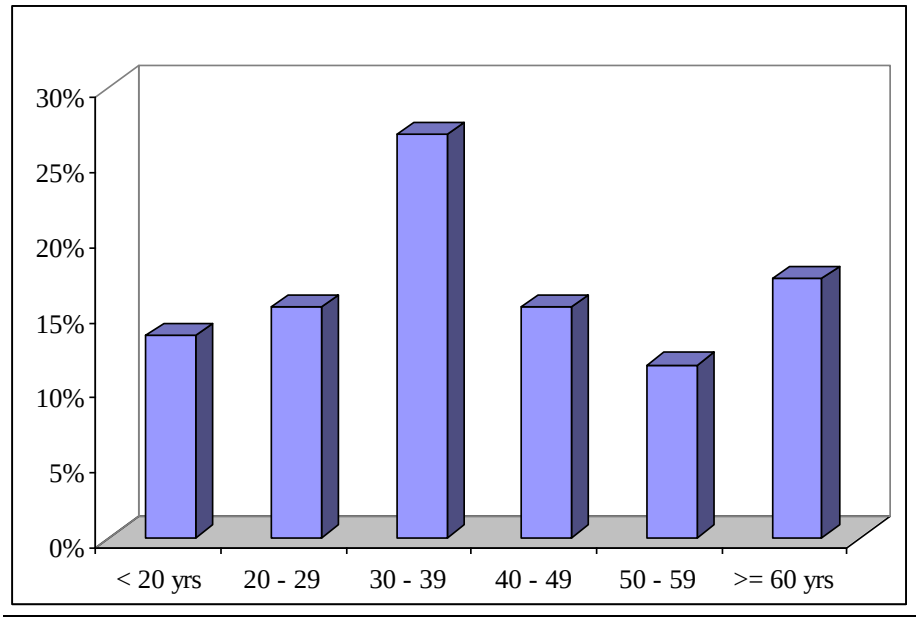


Table 4 showing Chronic ocular involvement other than corneal complications

Chronic ocular Involvement Other than corneal complications	Frequency	Percent
Trichiasis	4	7.7
Blephaulis	2	3.8
HI	2	3.8
Lid oedema	4	7.7
MC	2	3.8
Absent	24	46.2
No follow up	14	26.9
Total	52	100

Figure - 4

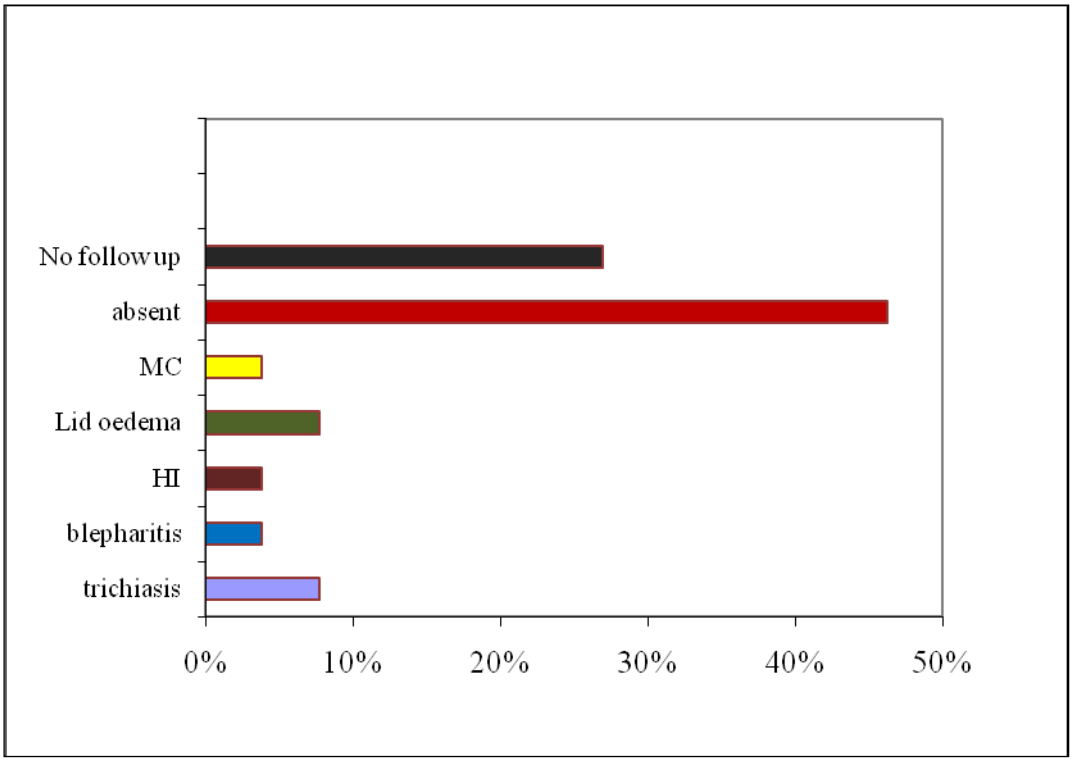


Table 5 Showing simblepharon at the time of follow up visit

Symblepheron	Right Eye		Left Eye	
	Frequency	Percent	Frequency	Percent
UL +	1	1.9	1	1.9
LL +	3	5.8	2	3.8
Absent	34	65.4	35	67.3
No Follow Up	14	26.9	14	26.9
Total	52	100	52	100

Figure - 5

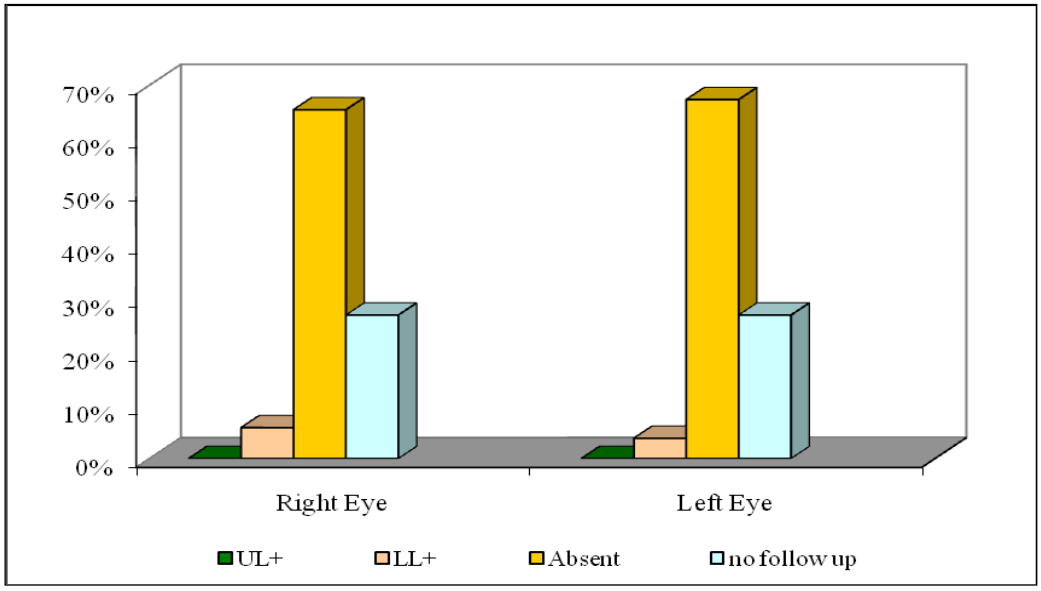


Table 6 Corneal involvement in chronic stage

Chronic Corneal Involvement	Frequency	Percent
PEE	5	9.6
Erosion	3	5.8
SPEE	2	3.8
Corneal Opacity	1	1.9
Absent	27	51.9
No Follow Up	14	26.9
Total	52	100

Figure - 6

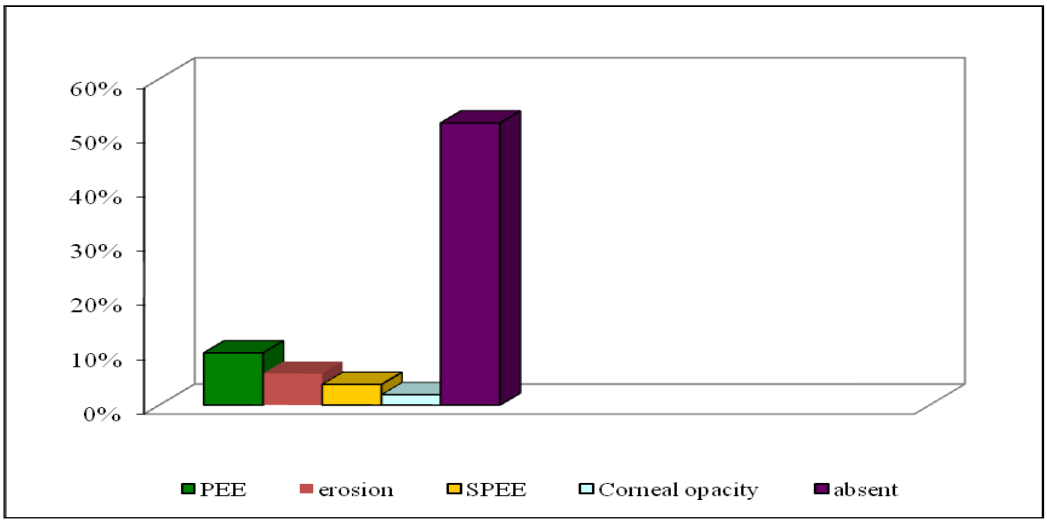


Table: 7 Shirmer score in chronic stage

Chronic Stage Shirmer Score	Frequency	Percent
< 9	9	17.3
10 – 15	13	25.0
> 15	16	30.8
No Follow Up	14	26.9
Total	52	100

Figure - 7

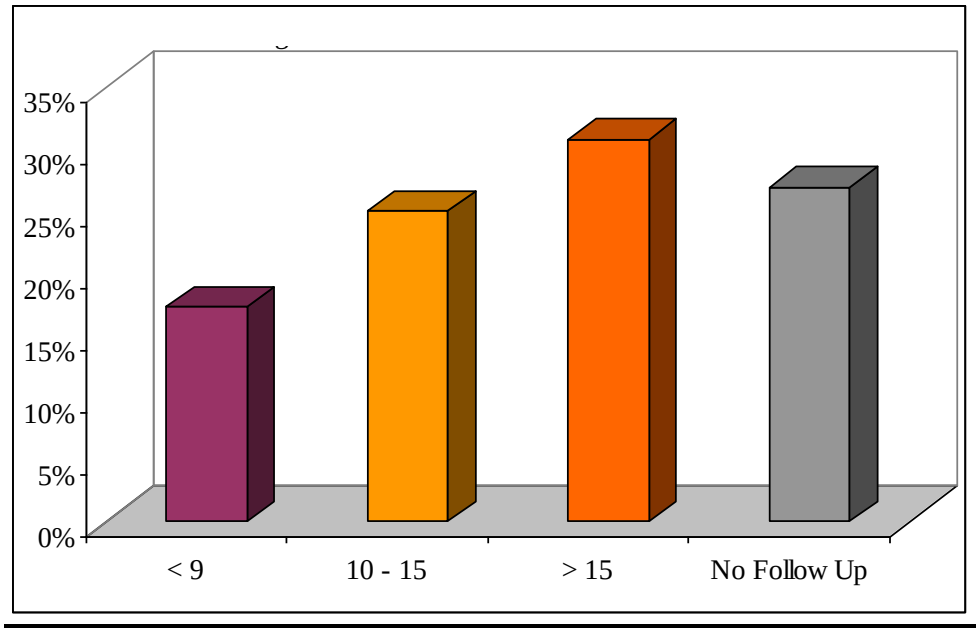
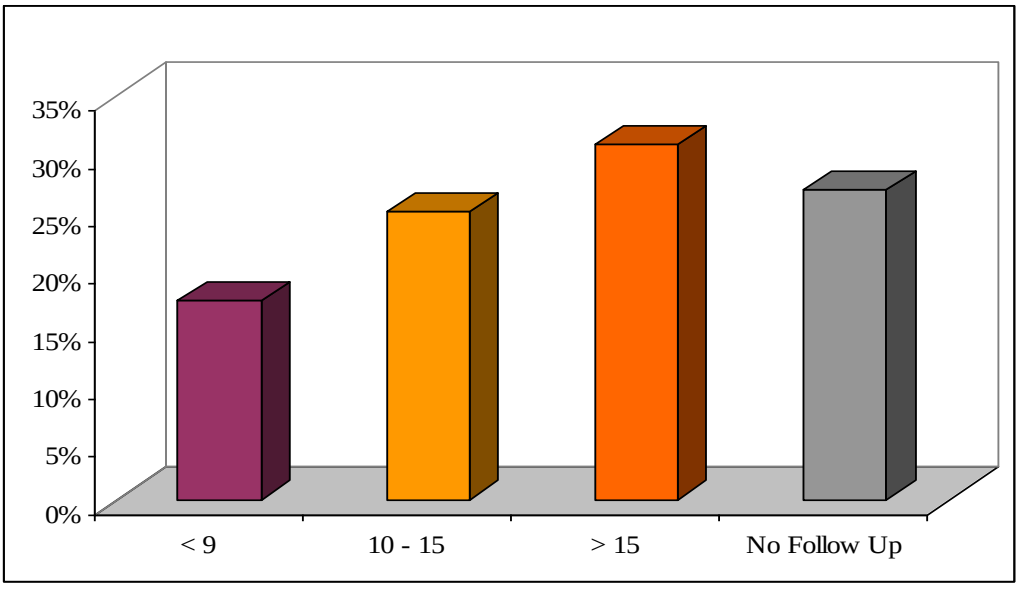


Table: 8 T But score IN Chronic stage

Chronic Stage TBUT	Frequency	Percent
< 9	9	17.3
10 - 15	13	25.0
> 15	16	30.8
No Follow Up	14	26.9
Total	52	100

Figure - 8



Discussion

In this study ophthalmic manifestation in 52 patients of Steven Johnson syndrome along southern Kerala, India at RIO Thiruvananthapuram was investigated showed high ophthalmic involvements beyond the acute period.

Table I Figure I

Sex distribution

Out of 52 patients there were 19 males (36.5%) and 33 females (63.5%) in this study. Female preponderance is more. A study by ward K.E, Arch. Archambault R, MerstelderT.h (2010), Showned female predominance.

Causative drugs

Table II figure II

Ciprofloxacin as 12 (23.1%) followed by paracetamol 9 (17.3%) and sulphamethaxole 8 (15.4%) followed by Antiepileptics (pheny to IN) and (Casbamazepine) as 6 (11.5%) and 4 (7.7%) and non-steroidal Antiinflamatory drugs (Brufen) as 3(5.8%) and other groups of drug as 5 (9.6%).

Study by Hallgren J, TengVall Linder M, Person N, Wahlgren CF also mentioned about SJS associated with ciprofloxacin.

A study by Mockenhaupt M, Messen J, Tennies P, schlingmann (2005) mentioned about in new users of antiepileptic adverse reactions. In this study also antiepileptic contributes a percentage of 19.2%.

A retrospective study at TAIWAN between In this study Allopurinol showed 5-85 (3 people showed).

Age distribution

Table 3 figure 3 commonest age group were 30-39 yrs.

Ophthalmic manifestation

Ophthalmic involvements is higher in this study.

Table 4 figure 4 showed chronic ophthalmic involvements other than corneal involvements.

In this study Trichiasis were shown by 4 patients 7.7%. Trichiasis is a constant and recurrent problem in patients presented with SJS

Epilation, Cyrotheraphy, argon laser treatment, electrolysis or blepharatony can be used to destroy lashes. Rotation of the entire lid margin can also peformed 2 out of 4 patients were treated by epilation followed by Cryo and one were treated surgically by rotation of the entire lid margin technique. Yet one patient was presented with severe abrading of the corneal surface and corneal ulceration later and had undergone penetrating keratoplasty to restore vision. A similar study conducted at Tan Toch Seng Hospital Singapore revealed (1993-2002) patients presented with SJS/TEN out of 44 patients with 6 months follow up showed Trichiasis IN 7(16%)

Blepharitis: 2 patients showed blepharitis and were treated with local application of steroid ointment and followed Lid hygiene.

Lid Oedema: 4 patients showed and it is subsided by regular treatment regime.

Hordeolum internum: 2 patients were shown and was treated by proper lid hygiene and antibiotics ointment were given Tobramycin /dexametha sone eye ointment at night time application reduced the incidence to certain extent.

1988 – 2004 at National cheng KUNG University Hospital revealed allopurinol was the most cause.

Membranous Conjunctivitis: 2 patients showed. The raw surface can leads to adhesion formations between the palpebral and bulbar conjunctivae. Combination regime of moxifloxacine 0.5%, cyclosporine 0.1% and dexametha some 0.10% drops twice daily is advocated for a period and follow up necessary.

Table 5, figure 5 showing symblepharm at follow up visits

Symble pharon showed by 4 patients in both eyes. Upper eye lid involvement IN RE as I (1.9%) and LE also as I (1.9%) lower lid involvement in 3 persons in RE (5.8%) and lower lid involvement IN LE by 2 persons 2 (3.8%).

Table -6, Figure -6 showing corneal involvement in chronic stage

The percentage of punctuate epithelial erosions and superficial punctuate epithelial erosions were shown by 5(9.6%) and 3 (5.8%) respectively. A retrospective study conducted at HenRI Mondor Hospital France between 1994-2002 among

SJS/TEN showed out of 49 patients 14 (29%) showed punctuate epithelial erosion and superficial punctate epithelial erosion as late phase complications.

I patient with punctate epithelial erosions out of 5 showed superficial vascularisation in RE and corneal opacity and has undergone penetrating keratoplasty and preserved ocular integrity IN RE.

Table-7, Figure 7 showing shirmer score in the chronic stage

Patients were presented with moderate to severe dry eye manifestations due to loss of goblet cell contribute greately to the dry eye state.

A study at TAN TOCH seng Hospital (1993-2002) for SJS/TES patients out of 117 patients 46% were showed severe dry eye manifestation and they followed the regime of cyclosporine for a period along with intravenous immune globulins .

In this study moderate to severe dry eye presented with 9 were treated with lubricant eye drop like methyl cellulose, artificial tear drop and cyclosporine eye drop. 2 cases presented with severe dry eye with total loss of stem cell deficiency due to chronic irritation caused by Trichiasis caused ocular surface damage. They are treated with cryo preserved amniotic membrane adhesion using fibrin glue to RE (3.5 cm 2 piece of amniotic membrane is used IN one eye)

Table -8, Figure - 8 figure showing T But score IN chronic stage

9 patients were showed T But score less than 9 seconds and 13 showed between 10-15 seconds as moderate T BUT and 16 showed no abnormally IN T BUT value. The T BUT score and shirmer score shows a gross similarity and management was same as mentioned above.

Conclusion

SJS is a life threatening illness with high incidence of ocular involvement.

Antibiotics and antipyretics, antiepileptic's followed by NSAIDS and analgesic and Antimalarial too were the common cause of drug etiology in this study.

The chronic ocular manifestations in this study are symblepharon, ectropion, trichiasis, corneal erosions, corneal vascularisation.

Dry eye being the late phase complication can develop lates on in a high percentage of patients with SJS. Tear film deficiency may due to conjunctival xerosis or corneal xerosis.

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