CLINICOPATHOLOGICAL STUDY OF LICHENOID REACTIONS: A RETROSPECTIVE ANALYSIS

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ABSTRACT: BACKGROUND: Lichenoid dermatoses refer to various, clinically different inflammatory dermatoses which share in common, various essential lichenoid histologic features. AIMS AND **OBJECTIVE:** In this study we have analysed the different clinicopathological aspects in lichenoid reactions, as prompt diagnosis of these lesions can greatly influence the morbidity associated with the disease. STUDY DESIGN: This was a 14 month retrospective analysis of cases presenting to the department of dermatology from June 2013 till July 2014. MATERIALS AND METHODS: All new patients diagnosed with lichenoid reaction clinically and histopathologically were included in the study. INCLUSION CRITERIA: All newly diagnosed cases of Lichenoid tissue reactions within the time period mentioned above. **EXCLUSION CRITERIA:** Patients whose adequate records were unavailable Statistical Analysis: The SPSS, version 13 software was used to statistically analyse the data. **RESULTS:** A total of 66 cases were diagnosed as lichenoid reactions, 51 were lichen planus and 15 had lichenoid eruptions. Males (53%) were more commonly affected than females (47%), with lower limbs (69.69%) being the most common site of predilection. Oral lesions were seen among eleven patients. Histopathologically, the most consistent findings with lichenoid reaction was the presence of a lymphocytic infiltrate followed by vacuolar degeneration of basal cell layer, hyperkeratosis, hypergranulosis, acanthosis, pigment incontinence and a band like infiltrate over the basal layer. **CONCLUSION:** In our study, Lichenoid reactions were more common among adults from the 2nd to 4th decade and can showed a male preponderance, with the most frequent archetype being lichen planus. Thus this study emphasises on the need of histological analysis in various clinically similar cases of lichenoid dermatoses in order to arrive at a definitive diagnosis.

KEYWORDS: Lichenoid reactions, Lichen tissue reactions, lichen planus.

INTRODUCTION: Lichenoid tissue reactions (LTR) are among the most frequently presenting clinical and histopathological conditions in dermatology. They represent a diverse group of conditions which are comparable to lichen planus (LP) clinically and histopathologically referred to as the lichenoid tissue reaction.¹

Histologically LTR are characterised by a inflammatory cell infiltrate obscuring the dermoepidermal junction (DEJ) in a band like fashion with associated vacuolar degeneration of basal layer.² LTR can also be referred as "interface dermatitis",³ that refers to histological finding of inflammatory infiltrate that abuts dermoepidermal junction.⁴ LTR can be subdivided into cell rich and cell poor categories on the basis of intensity of interface inflammation. Cell rich LTRs include lichen plaus with its variants and cell poor LTRs include conditions like autoimmune connective tissue disorders and erythema multiforme.⁵

This study focuses on the clinical and histopathological spectrum of various LTR as prompt diagnosis of these lesions can greatly influence the morbidity associated with the disease.

OBJECTIVES OF THE STUDY:

- 1. To find out the age & sex distribution of patients with LTR.
- 2. To review common histopathological findings in various LTR.

MATERIAL & METHODS: Retrospective analyses of the cases diagnosed with LTR clinically and histopathologically from June 2013 to July 2014 at Father Muller Medical College Hospital were included in the study. Clinical details were obtained from the case records and the histopathological features were studied again from the paraffin wax embedded tissue specimens. The data obtained was statistically analysed.

RESULTS: A total of 66 cases were studied, which were diagnosed as LTR clinically & histopathologically. Out of 66 cases, 51 cases were of lichen planus and its variants, 15 cases were of lichenoid eruptions.

(Table 1) Out of 66 cases, 35 were male and 31 were females. The oldest patient was of a 80 year male patient, and the youngest was a 11 year female patient. Male patients were more compared to female patients in our study. Most common age group was 4^{th} decade followed by 2^{nd} and 3^{rd} decade. 11 patients were below 18 years of age (16.67%)

Age in years	No. of males	No. of females	Total cases	Percentage (%)
1- 9	0	0	0	0
10 - 19	5	6	11	16.6
20 – 29	5	5	10	15.15
30 – 39	30 - 39 9		16	24.24
40 – 49	3	5	8	12.12
50 – 59	4	2	6	9.09
60 - 69	5	4	9	13.63
70 – 79	3	2	5	7.57
>80	1		1	1.51
Total	35	31	66	100

Table 1: Age and sex distribution of LTR

(Table 2) Most common site of lesions were lower limbs followed by upper limbs, trunk, oral lesions, face & neck, scalp and genital area in decreasing order of frequency.

Site involved	No. of patients	Percentage (%)
Upper limb	40	60.60
Lower limb	46	69.69
Trunk	19	28.78
Oral	11	16.66
Genital	2	3.03
Face & neck	8	12.12
Scalp	2	3.03

Table 2: Distribution of lesions

(Table: 3) Among 51 cases of lichen planus type, classical lichen planus was the commonest presentation with 25 cases and 26 cases were morphological/ histopathological variants of lichen planus.

Sl. No.	Diagnosis	No. of patients	Percentage (%)
	Lichen planus & variants		
1	Classical lichen planus	25	37.87
2	Lichen planus pigmentosus	11	16.66
3	Follicular lichen planus	1	1.51
4	Bullous lichen planus	1	1.51
5	Hypertrophic lichen planus	11	16.66
6	Oral lichen planus	2	3.03
	Lichenoid eruptions		
1	Lichenoid drug eruption	1	1.51
2	Fixed drug eruption	1	1.51
3	Lichen sclerosus et atrophicus	2	3.03
4	Lupus erythematosus (systemic/discoid)	3	4.54
5	Lichen nitidus	2	3.03
6	Lichen striatus	1	1.51
7	Pityriasis lichenoids chronica	4	6.06
8	Lichenoid tattoo reaction	1	1.51
	Total	66	100

Table 3: Histopathological diagnosis of different lichenoid reactions

Table 4, enlists various epidermal histopathological features in LTR. The common epidermal changes were vacoular basal cell degeneration, hyperkeratosis, hypergranulosis, & acanthosis in decreasing order of frequency.

Sl. No	Epidermis	No. of Cases
1	Atrophy	14
2	Hyperkeratosis	47
3	Parakeratosis	11
4	Hypergranulosis	43
5	Acanthosis	40
6	Spongiosis	6
7	Papillomatosis	2
8	Elongated rete ridges (saw tooth)	4
9	Loss of rete ridges	2
10	Civatte bodies	17
11	Vacuolar basal cell degeneration	49
12	Max joseph space	2
13	Basement membrane thickening	2
14	Follicular plugging	5

Table 4: Epidermal histopathological changes

Table 5, showing in dermis most common histopathological feature dermis was melanin incontinence, followed by band like infiltrate over DEJ, infiltrate was predominantly composed of lymphocytes.

Sl. No	Dermis	No. of cases			
1	Band like inflammatory infiltrate over DEJ	32			
2	Melanin incontinence	42			
3	Melanophages	16			
4	4 Predominantly lymphocytic infiltrate				
5	Mixed inflammatory infiltrate	18			
6	Perivascular inflammatory infiltrate	40			
7	Periadnexal inflammatory infiltrate	24			
8	Subepidermal bulla	1			
9	Plasma cells	3			
10	Eosiniphils	3			

Table 5: Dermal histopathological changes

(Table 6) Based on the intensity of inflammation, LTR were subdivided into cell rich & cell poor Lichenoid tissue reaction/ interface dermatitis.

Sl.	Cell- rich	No. of	Sl.	Cell- poor	No. of
No	LTR	cases	No	LTR	cases
1	Lichen planus	25	1	Fixed drug eruption	1
2	Lichen planus pigmentosus	11	2	Lichen sclerosus et atrophicus	2
3	Hypertrophic lichen planus	11	3	Systemic lupus erythematosus	1
4	Bullous lichen planus	1	4	Pityriasis lichenoides chronica	4
5	Drug induced lichen planus	1	5	Follicular lichen planus	1
6	Discoid lupus erythematosus	2			
7	Lichen striatus	1			
8	Lichen nitidus	2			
9	Lichenoid tattoo reaction	1			
10	Oral lichen planus	2			

Table 6: Classification of LTR based on the intensity of inflammatory infiltrate

LP, Lichen planus pigmentosus, hypertrophic lichen planus were the main components of the cell rich LTR and Pityriasis lichenoides chronica, drug induced/ fixed drug eruption, lichen sclerosus et atrophicus were cell poor LTRs mainly, seen in this study.

Besides the classical LTR changes in the HPE following frequent/characteristic changes were noticed in different conditions:

Lichen planus pigmentosus showed thinned out epidermis (8 cases) and pigment incontinence (11 cases), in most of HPE. Characteristic claw clutching the ball appearance was noticed on HPE of lichen nitidus. Discoid lupus erythematosus specimen on examination showed follicular plugging in both samples & thickening of basement membrane with epidermal atrophy was noticed in systemic lupus erythematosus specimen. Pityriasis lichenoides chronica specimens

showed spongiosis in all of its samples. Characteristic follicular plugging was noticed in follicular lichen planus specimen. Hypertrophic lichen planus showed hypertrophy in 12 cases most of specimen with irregular acanthosis (10 cases) as second most common finding. Sub epidermal bulla was noticed in bullous lichen planus specimen. Lichen sclerosus et atrophicus showed follicular plugging in both of the specimen. Parakeratosis was seen in oral lichen planus specimen.

DISCUSSION: LTR can be part of histological presentation of various diseases, lichen planus is the prototype of lichenoid reactions. As seen in this study 51 patients were of lichen planus and its variants. The term "lichenoid" refers to shiny, flat topped, polygonal papules of different sizes and occur in clusters creating a pattern resembling lichen growing on a rock.⁶ In this study 25 cases were of classical lichen planus (37.87%), was the largest single group, followed by lichen planus pigmentosus 11 cases (16.66%), hypertrophic lichen planus 11 cases (16.66%), pityriasis lichonides chronica 4 cases (6.06%), Lupus erythematosus 3 cases (4.54%), 2 cases (3.03%) each of oral lichen planus, lichen nitidus, & lichen sclerosus et atrophicus. One case (1.51%) each of drug induced lichenoid reaction, fixed drug eruption, follicular lichen planus, bullous lichen planus, lichen striatus, & lichenoid tattoo reaction.

Banushree et al,⁷ showed the distribution of cases in their study as follows:

Classical lichen planus 73.3% cases was the most common diagnosis, which was followed by lichen planus pigmentosus 8.3% cases, follicular lichen planus 5% cases, lichen nitidus 3.3% cases, each of lichen planus hypertrophicus, lichen planus atrophicus, lichen planus actinicus, benign lichenoid keratosis, lichenoid eruption, and lichen striatus as 1.7% cases.

Mahesh kumar et al⁸ in their study showed prevalence of different lichenoid tissue reactions with the following distribution: Classical lichen planus was 26. 66% of cases, as most frequent diagnosis. Followed by lupus erythematosus 10% cases, lichen sclerosus et atrophicus 7.77% cases, lichen planus pigmentosus 6.66% cases, each of follicular lichen planus, lichen nitidus, pityriasis lichenoides, and erythema multiforme had 5.55% cases, diagnosis of 4.44% cases were seen with lichen sclerosis and lichen striatus, 3.33% cases were of actinic lichen planus, drug induced lichenoid eruption, and poikiloderma, hypertropic lichen planus, eruptive lichen planus & lichen spinulosus each had 2.22% cases and lichen planus like keratosis as 1.11% cases.

The present study shows a slight predilection for males (53 %), when compared to females (47 %). Multiple studies Fordyce et al 9 White C J et al 10 Banushree et al 7 Mahesh kumar et al 8 all have shown predilection for females. There also have been studies that have shown equal incidence in both the sexes Schmidt H 11 In present study it showed that most of the cases were in the age group of 11- 40 years of age, maximum in the 4 th decade, similar to findings of Sehgal at al 12 (11- 4 0 years) . 11 patients were below 18 years of age, comparable to Parihar A et al 13 Mahesh kumar et al 8 where most of the cases were in 1-30 years of age.

In our study, we found lower limbs (69.69%) were the most common site of presentation of lesions in the LTRs. Similar observation was found in study by Parihar et al, other sites in order of frequency were upper limbs, trunk, oral mucosa, face & neck and genital area. Oral mucosa was involved in 11 patients (16.66%).

Histopathological features of LTR are mainly attributed to its immunopathogenesis caused by T cell mediated autoimmune attack against the epidermal basal layer cells.¹⁴ The damage and disorganisation of the cells in epidermal basal layer is the characteristic epidermal change in the LTR.⁵ The basal layer degeneration is described as hydropic/ liquefactive/ vacuolar degeneration.⁵

Two types of cells are seen in the dermal layer in the lesions of lichen planus, attributed to the basal cell injury, that are melanophages and colloid bodies. Majority of inflammatory infiltrate cells in LTR are T lymphocytes, macrophages, dendritic cells.

For the diagnosis of LTR/ interface dermatitis, minimum of different combinations of leucocyte infiltration in dermis, vacuolar degeneration of the basal layer of epidermis, necrotic keratinocytes and accumulation of melanophages in papillary dermis must be present. This study showed predominant lymphocyte infiltration in dermis in 48 cases (72.72%), & mixed inflammatory infiltrate in 18 cases (27.27%). Vacuolar degeneration of basal layer of epidermis was seen in 49 cases (74.24%). Necrotic keratinocytes (Civatte bodies) were seen in 17 cases (25.75%) and melanophages in papillary dermis were seen in 16 cases (24.24%).

	Features	Present study	Banushree et al, ⁷	Mahesh kumar et al ⁸	Ellis Francis (1965) ¹⁶
1.	Atrophy	21.21%	8.33%	15.55%	47%
2.	Hyperkeratosis	71.21%	80%	93.33%	
3.	Parakeratosis	16.66%	5%	666%	12%
4.	Hypergranulosis	65.15%			
5.	Acanthosis	60.60%	73.33%	83.33%	23%
6.	Spongiosis	9.09%	70%	67.77%	
7.	Papillomatosis	3.03%	16.66%	24.44%	
8.	Elongated rete ridges (saw tooth)	6.06%	33.33%	60%	
9.	Loss of rete ridges	3.03%			
10.	Civatte bodies	25.75%	80%	21.11%	37%
11.	Vacuolar basal cell degeneration	74.24%	83%	96.66%	100%
12.	Max Joseph space	3.03%	13.33%	10%	17%
13.	Basement membrane thickening	3.03%			
14.	Follicular plugging	7.57%	5%	13.33%	6%
15.	Band like inflammatory infiltrate over DEJ	48.48%	96.6%	93.33%	100%
16.	Melanin incontinence	63.63%	93%	93.33%	
17.	Melanophages	24.24%			
18.	Predominantly lymphocytic infiltrate	72.72%	100%	100%	100%
19.	Mixed inflammatory infiltrate	27.27%			
20.	Perivascular inflammatory infiltrate	60.66%			
21.	Periadnexal inflammatory infiltrate	36.36%			
22.	Subepidermal bulla	1.51%			
23.	Plasma cells	4.54%	3.33%	8.88%	3%
24.	Eosiniphils	4.54%	3.33%	4.44%	

Table 7: Comparative findings in this study and previous studies

In cases of lichen planus pigmentosus, most of our specimens showed thinned out epidermis with pigment incontinence, similar changes were noticed in study by Parihar A Et al.¹³ Characteristic "Claw clutching the ball" appearance was noticed in the slides of lichen nitidus which has also been mentioned by various authors.^{17,18,19} Discoid lupus erythematosus showed follicular plugging on examination as the most consistent finding which was also noticed in multiples studies.^{20,21}

Thickening of basement membrane zone was observed in systemic lupus erythematosus specimen which was concurrent to findings of Alahlafi AM et al.²² HPE of follicular lichen planus showed characteristic follicular plugging, similar findings were noticed by Wilk M et al.²³ in fully developed lesions of follicular lichen planus. Subepidermal bulla noticed in the bullous lichen planus was a typical feature as reported by authours^{24,25} in earlier reports and studies. Lichen sclerosus et atrophicus characteristic feature of follicular plugging was seen in both the specimen which has also been noticed by Kowalewski et al.²⁶ Parakeratosis was seen in oral lichen planus specimen. Parakeratosis was most consistent finding in specimen of oral lichen planus which was analogous to findings of Chatterjee K et al. in their study.²⁷

CONCLUSION: Lichenoid reactions were more common among adults from the 2^{nd} to 4^{th} decade and can show a male preponderance, with the most frequent archetype being lichen planus. Thus this study emphasizes on the need of histological analysis in various clinically similar cases of lichenoid dermatoses in order to arrive at a definitive diagnosis which will help in specific treatment.

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Figure 1: 4x view, showing hyperkeratosis, focal hypergranulosis, with irregular acanthosis and band like inflammatory infiltrate at dermo-epidermal junction.

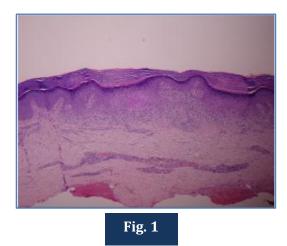


Figure 2: 10x view showing basked weave hyperkeratosis, basal cell degeneration and max josephs space.

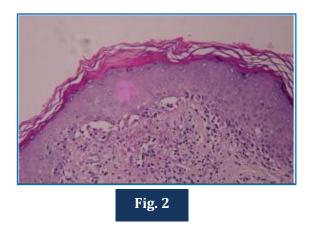


Figure 3: 10x view showing lichen nitidus- claw shaped elongation of epidermal rete ridges encircling well defined inflammatory infiltrate- claw clutching the ball appearance.

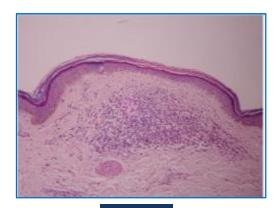


Fig. 3

Figure 4: 40x view showing spongiosis with occasional basal cells degeneration, melanin incontinence and melanophages in the dermis.

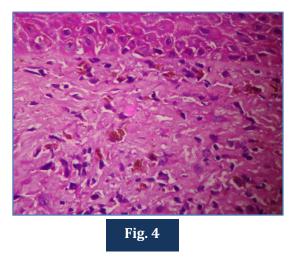


Figure 5: 40x view showing lupus erythematosus -thickened basement membrane.

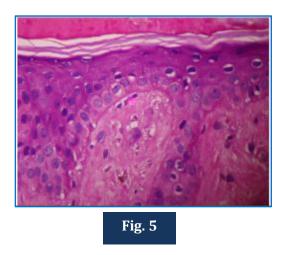


Figure 6: Bullous LP-multiple violaceous papules and plaques with bullae over dorsum of ankle and foot.



Fig. 6

Figure 7: Discoid lupus erythematosus- multiple dusky red to violaceous plaques with erythematous margins over fore head, maxilla, cheeks and post auricular areas.



Figure 8: LICHEN PLANOPILARIS- multile grouped violaceous papules with irregular distribution and areas of cicatricial alopecia over occipital area of head.



Figure 9: LICHEN PLANUS- multiple skin coloured to erythematous, symmetrical, plane topped, polygonal papules over dorsum of hands.



Figure 10: ORAL LICHEN PLANUS- well defined violaceous plaque over buccal mucosa.



Fig. 10

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