"STUDY OF ASSOCIATION BETWEEN LICHEN PLANUS AND HEPATITIS C VIRUS INFECTION"

This dissertation is submitted to

THE TAMILNADU DR.M.G.R.MEDICAL UNIVERSITY

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DERMATOLOGY, VENEREOLOGY AND LEPROSY

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DECLARATION BY THE CANDIDATE

I solemnly declare that the study titled "**Study of association between Lichen planus and Hepatitis C virus infection"** was done by me at **Government Stanley Medical College and Hospital during 2012-2015** under the guidance and supervision of my HOD, **Prof. Dr. V. Anandan.**

The dissertation is submitted to **THE TAMILNADU DR. M.G.R.MEDICAL UNIVERSITY** towards the partial fulfillment of requirement for the award of **M.D. Degree (Branch XX) in DERMATOLOGY, VENEREOLOGY & LEPROSY.**

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ABSTRACT

INTRODUCTION: Lichen planus is an immunologically mediated skin and mucous membrane disease, which can affect oral mucosa, the skin, genitalia, hair follicles, nails, esophagus, urinary tract, nasal mucosa, larynx and even the eyes. Lichen planus has been found in patients with Hepatitis C virus related liver disease, with variable frequency in several studies till date. However an association between HCV infection and lichen planus is uncertain because prevalence of HCV infection in patients with lichen planus varies considerably from one geographic area to another. If there is a true association, lichen planus in certain populations may be used as a sign of HCV infection in asymptomatic patients, leading to early diagnosis and treatment, and a better prognosis of infected patients.

AIM AND OBJECTIVE: To study the association between Lichen planus and Hepatitis C infection in this geographical region.

MATERIALS AND METHODS:
PLACE: GOVT. STANLEY MEDICAL COLLEGE, CHENNAI
TYPE: Prospective, Observational
TIME: July 2013 to June 2014
SAMPLE SIZE: 100 lichen planus patients, 100 controls

RESULTS AND CONCLUSION: The present study shows no association between lichen planus and hepatitis C infection. Based on this result, it can be concluded that anti-HCV antibody testing is not necessarily required in lichen planus patients having no risk factors for HCV infection in this geographic region.

KEY WORDS: Lichen Planus, Hepatitis C virus

INTRODUCTION

Lichen planus is a chronic inflammatory disease of skin and mucosa, which exhibits distinct morphology and histopathology. It can affect skin, genitalia, hair follicles, nails, oral mucosa, nasal mucosa, esophagus, larynx and eyes.[1] Out of enormous number of associations reported, Hepatitis C virus (HCV) infection is one of them.

Lichen planus was first described by Hebra, but later named by Erasmus Wilson in 1869. The word Lichen comes from Greek word '*leichen*', which means tree moss.[1] It refers to a unique group of flower-less vegetation. And the word Planus (Latin- '*planus*') means flat. Lichen planus is a self-limiting condition which commonly affects middle-aged adults. It involves skin, mucous membranes, hair and nails.

In skin, the hallmark of lichen planus is its clinical manifestation as itchy, violaceous, flat-topped, glistening, polygonal papules and plaques, most commonly occurring over flexor aspect of extremities, especially wrist. Nail changes include ridging, thinning and sub-ungual hyperkeratosis. Scalp involvement leads to scarring alopecia.

Variants of lichen planus include hypertrophic, atrophic, actinic, follicular, bullous, annular, linear and lichen planus pigmentosus.[1] Oral lichen planus has low tendency for spontaneous regression as compared to cutaneous type. Clinically, oral lichen planus can be of reticular, bullous, plaque, erosive or atrophic types.

Many factors are reported as far as the etiology of lichen planus is concerned. Hepatitis C virus infection is one of them. The association between lichen planus and Hepatitis C infection was first reported in 1991.[3,12] Since then, many studies have supported this view and have suggested the importance of liver monitoring in patients of muco-cutaneous lichen planus.

As HCV infection is usually indolent[4], patients may present only in late stages of the disease with serious complications like cirrhosis and chronic liver disease. So, if association between lichen planus and HCV infection is found to be true, screening of patients with lichen planus may help in early diagnosis, treatment as well as decreased transmission of HCV infection in asymptomatic individuals.

But on the contrary, if the same is not a true association, screening of lichen planus patients may result in unnecessary use of medical resources, along with financial and mental trauma to those being tested.

The study will help in further supporting this fact and hence moving a step closer to frame the guidelines regarding HCV screening in lichen planus patients.

Diagnosis of lichen planus is mostly clinical, but can be confirmed by histopathology in doubtful cases. Treatment options include corticosteroids, retinoids, immunosuppressive agents and other newer agents.

AIMS AND OBJECTIVES

1. **To study the association between lichen planus and Hepatitis C virus infection in this particular geographical region.**

2. **To study various clinical presentations of lichen planus.**

REVIEW OF LITERATURE

HISTORICAL ASPECTS

The name ‘lichen planus’ was given by Erasmus Wilson in 1869. The term ‘lichen’ was applied because of its clinical presentation of flat-topped lesions similar to dry excrescences of symbiotic vegetation known as lichen.

Hebra described the condition as Leichen Ruber/ Lichen Ruber Planus.[1] Hallopeau (1887) and Darier (1892) considered it as a modification of lichen sclerosus et atrophicus because of morphological similarity.[5]

Kaposi described first variant of the disease in 1892 and used the term Lichen Ruber Pemphigoides for widespread bullous eruption complicating typical lichen planus.[56] Louis Frederick Wickham (1895) described characteristic whitish striae on the top of flat papules.[7,8]

Lichen planopilaris (Pringle, 1895) and Follicular lichen planus (Silver et al) are clear terms that describe clinical syndrome of lichen planus associated with cicatricial alopecia.[9] Darier (1909) described histopathological findings and attributed the appearance of Wickham’s striae to increase in granular cell layer.[1,5]

Graham Little (1915) reported scalp involvement in lichen planus.[41] Schreiner (1930) divided bullous lichen planus into lichen planus vesiculosus and lichen planus pemphigoides. Niles (1941) described actinic lichen planus.[6]

Thyresson and Meberger demonstrated colloid bodies at dermo-epidermal junction and suggested these to be degenerating epithelial cells.[5,8] Glickman (1964) attributed pallor, which produces appearance of Wickham striae, to the absence of papillary capillaries in centre of the lesion. But, Ryan in 1966 attributed violaceous hue, which surrounds the areas of pallor, to the radially arranged capillaries.[5,8]

Pinkus and Mehregan (1969) suggested damage to the basal cell layer as basic histopathological feature.[8] Zaias (1970) described histology of nail lesions in lichen planus.[6]

Lichen planus-Lupus erythematosus overlap was first described in 1970.[55] Aronson and Soltani reported triad of lichen planus, myasthenia gravis and thymoma in 1978.[6] Further, Pelisse et al described Vulvo-vaginal gingival syndrome[10] in 1982.

In 1989, perforating variant of lichen planus (Hanav and Sengel) and another entity called Grinspan syndrome (Triad of lichen planus, hypertension and diabetes mellitus) were described.[11] Cribier et al described male equivalent of vulvo-vaginal-gingival syndrome as Peno-gingival syndrome[10] in 1993.

Hepatitis C virus was discovered as a single stranded RNA virus in 1989 and testing for anti-HCV antibodies started from 1991. Thereafter, association between lichen planus and hepatitis c virus infection came to light.[3]

Hard and Humberg used penicillin for treating lichen planus in 1954. Sehgal et al reported effectiveness of griseofulvin (1971) and levamisole (1978) in recalcitrant lichen planus. Many other drugs and modalities like isotretinoin, dapsone, phenytoin, cyclosporine and PUVA have been tried with variable success in treating lichen planus.[6]

EPIDEMIOLOGY

Incidence: Exact incidence and prevalence of the disease is not known. But it has been estimated to be about 1% of general population worldwide.[6] Studies have shown the incidence to range from 0.38% (in India)[14] to 1.2%. About 15% cases have lesions confined to mouth.[33] Lichen planus has no racial predisposition.

Age/Sex: Females are usually affected in sixth decade. But males have an earlier age predisposition (fourth decade). The disease is less common at extremes of age. There is no sex predilection, except female preponderance in some studies.[6,13]

Seasonal Variation: Increased frequency of cases has been reported in rainy season.[15]

Genetics: Association with HLA-B7, -Aw19, -B18 and -Cw8 has been found in familial cases and HLA-A3, -A5, -A28, -B8, -B16 and -Bw35 have been reported in non-familial cases of lichen planus.[1,20] HLA-DQ1 may be associated with resistance to the disease.[16] Oral lichen planus is associated with HLA-B8 and carbohydrate intolerance in Jews has been linked to HLA-28.[17]

Symptomatic lichenoid reactions: These are associated with exposure to paraphenylene diamines, methacrylic acid esters, gold, nickel, musk ambrette and aminoglycoside antibiotics.[58]

PATHOGENESIS

Lichen planus is immunologically mediated, with cell-mediated immunity playing a major role and humoral immunity playing a secondary role in the pathogenesis. Both CD4+ and CD8+ T-cells have been found in lesional skin, but progression of disease leads to preferential accumulation of CD8+ cells. Another type of lymphocytes in the infiltrate of lichen planus is CD45RO+ (memory) cells, which are not found in normal skin.[1]

Epithelial-lymphocyte interaction in lichen planus involves antigen recognition, cytotoxic lymphocyte activation and keratinocyte apoptosis.[1]

Antigen recognition: CD8+ cytotoxic T-cells within epithelium and those adjacent to basal keratinocytes recognize lichen planus- specific antigens associated with major histocompatibility complex (MHC) class-I on lesional keratinocytes. Exact nature of antigen is unknown but it may be an autoreactive peptide or an exogenous factor like altered protein,

infectious agent (HCV, HSV, HIV or Helicobacter pylori), drug, contact allergen or dental amalgam (mercury and gold).[1]

Role of T-helper (CD4) cells in lichen planus is unclear, but it is proposed that these cells are activated via antigen-presenting cells like Langerhans cells or epidermal keratinocytes, in association with members of MHC class-II, and may propagate CD8+ cells through release of cytokines.[1]

Lymphocyte activation: Activated cytotoxic lymphocytes undergo oligoclonal proliferation and release cytokines and chemokines like interleukins (IL-2, 4, 6, 10 and 1β), interferon (IFN-γ), tumor necrosis factor (TNF-α) and transforming growth factor (TGF-β). Both Th1 and Th2 products (pro-inflammatory and anti-inflammatory) are released simultaneously,[1] and balance between these determines the clinical behavior of the disease. These cytokines upregulate the expression of specific keratin genes like K1, K6, K10, K16 and K17. In contrast, K4 and K13 are reduced.

T-cells secrete RANTES (regulated upon activation, normal T-cell expressed and secreted), which leads to mast cell degranulation and consequent release of TNF-α, and this again upregulates RANTES secretion. This process may contribute to chronicity of the disease.[21]

IFN-γ produced by T-helper cells during antigen recognition stage induces keratinocytes to produce lymphotoxin-α and TNF-α and to up-regulate MHC class-II, thus increasing interactions with T-helper cells. IFN-γ also up-regulates expression of intercellular adhesion molecule (ICAM-1) and vascular cell adhesion molecule (VCAM-1) by basal keratinocytes and langerhans cells.[1] ICAM-1 is a ligand for the β_2-integrin, leukocyte function-associated antigen-1, on the surface of lymphocytes. The ligands for β_1-integrin of lymphocytic surface are laminin-5 and collagen- IV and –VII, which are also increased in lichen planus. These interactions also increase the association of lymphocytes with the basement membrane. Further, integrin-α3 is present on activated, skin-homing T-cells and it leads these effector cells to epidermal-dermal interface and basement membrane (which contains laminin-5, the ligand for this integrin).

Finally, this close interaction between lymphocytes and basement membrane leads to alteration in extracellular matrix (through matrix metallo-proteinase) causing apoptosis, basement membrane disruption, reduplication and sub-epidermal cleft formation.[2]

Keratinocyte apoptosis: Exact mechanism is unclear but possible ones are (1) binding of TNF-α (secreted by T-cells) to TNF-α R1 receptor on keratinocyte surface, (2) binding of T-cell surface CD95L (Fas ligand) on CD95 (Fas) of the keratinocytes, (3) over-expression of bone morphogenic protein (BMP-4) in mucosal lichen planus leading to apoptosis of oral epithelial cells[18], (4) entry of granzyme-B (secreted by T-cells) into keratinocyte through perforin-induced membrane pores initiating caspase activity, and (5) loss of basement membrane-derived cell survival signal (basement membrane disruption), which normally prevents apoptosis.

Association with dental amalgam: Mercury in dental amalgam fillings may be a causative agent in cases of oral lichen planus.[54] Increased risk of lichen planus is due to corrosion of amalgam and the galvanic effect from dissimilar dental material in continuous contact with oral mucosa (called as Bimetallism).

CLINICAL FEATURES

Classical cutaneous lesions in lichen planus are plain-topped, violaceous/purplish, polygonal, pruritic papules and plaques of varying sizes. Highly characteristic Wickham's striae (fine whitish reticulated networks) can be observed with hand-lens after applying oil, xylene or water over the surface of lesions.[7,8,20]

Lesions are distributed in a bilaterally symmetrical fashion over flexural areas of wrists, arms and legs. These are grouped and tend to coalesce. Thighs, trunk, back and neck may also be involved in later stages. Face is usually spared and palmo-plantar involvement is unusual.[1,6]

In active stage of the disease, any injury/scratching/trauma leads to an isomorphic phenomenon named as Koebner's isomorphic phenomenon.[20] Lichen planus usually heals with hyperpigmentation[1,19,20] which is more prominent in darker individuals.

CLASSIFICATION[1,20]

Morphology: Hypertrophic, Atrophic, Erosive/ulcerative, Bullous, Annular, Linear, Follicular, Actinic, Guttate, Perforating, Lichen planus pigmentosus

Site: Mucosa, Nails, Scalp, Inverse, Palmo-plantar

Special Forms: Lichen planus pemphigoides, Keratosis lichenoides chronica, Lichenoid drug eruption, Lichenoid dermatitis, Lichenoid keratosis, Lichen planus- Lupus erythematosus overlap syndrome, Lichenoid reaction of GVHD & Malignant transformation.

ANNULAR LICHEN PLANUS: Occuring in about 10% cases, this form presents as arcuate grouping of papules, which develop rings or peripheral extension of clustered papules with central clearing. Annular lichen planus is usually seen over penis and scrotum and is more common in blacks.[1,19]

LINEAR LICHEN PLANUS: Spontaneous isolated lesions of lichen planus (not as part of Koebner's phenomenon), measuring several inches, occur in linear distribution. Sometimes these may involve whole length of a limb. This form is usually seen in childhood. Differential diagnoses include nevus unius lateris, lichen striatus and linear psoriasis.

A zosteriform pattern has been described and lichen planus can even occur at site of healed herpes zoster.[22] Multiple linear lesions along the lines of Blaschko may also occur (due to post-zygotic somatic mutations).[23,44]

HYPERTROPHIC LICHEN PLANUS (Lichen planus verrucosus): Considered as the most pruritic variant of lichen planus, lesions usually occur over shins and interphalangeal joints, and are thickened, hyperkeratotic and elevated, with occasional verrucous plaques. These heal with atrophic scar. Common association is with chronic venous insufficiency.[20] Keratoacanthoma[40] and squamous carcinoma have been reported to arise from long-standing lesions.[24,25]

ATROPHIC LICHEN PLANUS: This rare form is usually seen over lower extremities and trunk and is characterized by few well-demarcated papules or plaques with central superficial atrophy.[20] Atrophy may be a result of faded annular type or resolved hypertrophic type of lichen planus. Morphology may resemble lichen sclerosus et atrophicus or guttate morphea.

BULLOUS LICHEN PLANUS: Vesicles and bullae may develop within the pre-existing lesions of any type of lichen planus during acute flare-up. These develop commonly over lower extremities and are associated with mild constitutional symptoms.

Familial type of bullous lichen planus[26] is a rare autosomal dominant disorder. Onset is bimodal, with peaks at 1-3 years and 13-17 years of age. Lesions are most common over shins. Earlier onset and widespread distribution differentiates it from the non-familial type.

LICHEN PLANUS PIGMENTOSUS: It is seen among darker races and Latin Americans, and is not associated with typical papules of lichen planus.[20] Asymptomatic, hyperpigmented dark-brown macules are seen in sun-exposed areas and flexural folds.[27] Mucosa, palms and soles are never involved. Erythema dyschromicum perstans (Ashy dermatosis of Ramirez) bears significant similarity to lichen planus pigmentosus. Case has been reported in association with Acrokeratosis of Bazex.[46]

EROSIVE/ULCERATIVE LICHEN PLANUS: This rare variant is clinically seen as painful bullae and ulcerations of feet.[48] Permanent loss of toe nails, webbing of toes and cicatricial alopecia of scalp are usually present. Squamous cell carcinoma has been reported. Other rare associations of erosive lichen planus are Castleman's lymph node hyperplasia and malignant lymphoma.

LICHEN PLANO-PILARIS (Follicular lichen planus/ lichen planus acuminatus or peripilaris): It may occur alone or may co-exist with other variants. Keratotic, spiny, hyperpigmented, follicular papules are seen over trunk and extremities. Involvement of scalp can lead to cicatricial alopecia. Inflammatory infiltrate targets stem cell containing region (infundibulo-isthmic) of follicles.[28]

Associations reported are dermatitis herpetiformis[52] and etanercept therapy.[43] Graham-Little-Piccardi-Lassueur syndrome[41] (or Graham-Little-Feldman) is the triad of follicular lichen planus of skin (lichen planus spinulosus) and/or scalp, multifocal cicatricial alopecia of scalp and non-scarring alopecia of axillary and pubic areas. Some variants of lichen plano-pilaris have also been described, like pseudopeladic form of Brocq[53], tumidus form with oval plaques of mastoid area, post-menopausal frontal fibrosing alopecia[42] and lichen plano-poritis.[29]

LICHEN PLANUS PEMPHIGOIDES: It is a controversial entity in which there is co-existence of bullous pemphigoid and lichen planus. Proposed mechanism is that basal cell keratinocyte damage by lymphocytes unmasks hidden antigenic determinants, which leads to autoantibody formation through epitope spreading. These antibodies react with BP-180 kDa and BP-200 kDa antigens.[30] Clinically, tense blisters occur over lesional as well as normal uninvolved skin, usually over extremities. It may be associated with paraneoplastic pemphigus[57] and PUVA therapy.[31]

ACTINIC LICHEN PLANUS: Also called as lichen planus actinicus, lichen planus subtropicus, summer time actinic lichenoid eruption, lichen planus atrophicus annularis and lichenoid melanodermatitis, this form is seen during the spring and summer season, usually affecting children and young adults in tropical countries.[32,45] Sunlight is considered as a predisposing factor. In contrast to the classical lichen planus, this variant is characterized by minimal itching and scaling. Lesions occur over exposed areas of face, hands, arms and nape of neck and are annular with violaceous colour, surrounded by a thready, rolled, hypopigmented edge showing well-defined borders.

GUTTATE (ERUPTIVE) LICHEN PLANUS: Widely scattered discrete lesions resembling guttate psoriasis are seen.

EXFOLIATIVE, EXANTHEMATOUS FORMS: These may be seen as a part of manifestations of lichenoid drug reactions and are very rare.

INVISIBLE LICHEN PLANUS (de Gougerot): Inflammatory phase is minimal and lesions are visible only under Woods lamp.[1]

MUCOSAL LICHEN PLANUS: Various mucosal surfaces in the body like those of mouth, vagina, esophagus, conjunctiva, urethra, anus, nose, tympanic membrane or larynx may be involved. It may be the sole manifestation in 20-30% cases of lichen planus.

Oral mucosa is involved in about 60-70% of patients with lichen planus. Prolonged emotional stress may be a precipitating factor (psychosomatization).[34] Humoral autoimmunity (Anti-desmoglein1 and anti-desmoglein3 antibodies in case of erosive variant of oral lichen planus) seems to be involved in the pathogenesis of oral lichen planus.[37] Buccal, gingival and glossal mucosae are commonly affected. Lesions are bilaterally symmetrical and are usually asymptomatic. Differential diagnoses include leukoplakia, candidiasis, smoker's patches and white-sponge naevi. Gingival stomatitis or desquamative gingivitis may be the sole presentation in some cases.

Various types of oral lichen planus include reticular, bullous, plaque-type, erosive and atrophic.[35] Out of these, the reticular type is commonest, which is seen as atrophic plaques with raised whitish streaks in a lacy pattern over buccal mucosa. Plaque-type of oral lichen planus is seen as multiple raised white plaques, usually over buccal mucosa and tongue. Erosive type is common in elderly patients and is extremely

painful. It is more prone to develop squamous cell carcinoma. Low rate or complete absence of apoptosis in inflammatory infiltrate and epithelial cells in cases of oral lichen planus potentiates the molecular defects in epithelial cells, leading to carcinogenesis.[38] Higher expression of cyclo-oxygenase-2 is also postulated as a cause for carcinoma.[50] Most commonly, tongue is the site for malignancy, followed by buccal mucosa. Concurrent tobacco use and long duration of the disease are the risk factors.[1] Lesions may extend to posterior pharynx, larynx and esophagus.[36] Atrophic type may occur simultaneously with erosive or reticular types, over gingival mucosa.

Genital: Male genital involvement in lichen planus has been described in about 25% of cases with typical lesions. Glans and shaft of penis are commonly involved. Most of the lesions are of annular morphology and are symptomatic with pruritus and burning sensation.

Females are affected in peri- and post-menopausal period. Patches of leukoplakia or erythroplakia are seen, occasionally with generalized desquamative vaginitis. Painful vulval introital erosions with white lacy reticular borders extending into vagina are characteristic. Marked structural changes like loss of labia minora, clitoral burying and vaginal

adhesions may result. Anal mucosal lesions present as hyperkeratosis and fissuring.

Decreased antioxidant defense of basal cells results in oxidative stress and damages the cellular lipids, proteins and DNA. This initiates the immune process leading to lesions of vulval lichen planus.[39]

Vulvovaginal-gingival syndrome is combination of desquamative gingivitis and vulvovaginal erosive lichen planus, leading to burning pain, dyspareunia and vaginal discharge.[10]

Cicatricial conjunctivitis may occur if lichen planus involves conjunctiva.[51] Direct immunofluorescence can differentiate between ophthalmic lichen planus from cicatricial pemphigoid.

PALMO-PLANTAR LICHEN PLANUS: This acral variant is rare. Lesions lack characteristic shape and colour of lesions elsewhere and are firm to touch.[47] Erythematous scaly plaques are seen on the internal plantar arch and yellowish compact keratotic papules are present on lateral margins of fingers and hand surfaces. Pruritus may be absent. Clinically, there may be close resemblance to psoriasis vulgaris, warts, callosities, porokeratosis or secondary syphilis. Rarely, chronic ulcerative variant of lichen planus can occur over soles.

LICHEN PLANUS OF NAILS: Nail is involved in 10-15% of patients. Lichen planus may be limited to nails or it may be a part of widespread disease. Finger nails are more commonly involved.[49] Thinning, longitudinal ridging and onychoschizia are commonest findings. Onycholysis, onychorrhexis, sub-ungual hyperkeratosis, trachyonychia and even anonychia (especially toe nails) may also occur. Pterygium (forward growth of eponychium with adherence to proximal nail plate) is a classic finding, indicating severe nail matrix involvement. Pup-tent sign occurs because of nail bed involvement, leading to elevation of nail plate. In children, idiopathic atrophy of the nails has been associated.

LICHEN PLANUS OF SCALP: In typical cases, keratotic follicular papules coalescing to form plaques are seen over scalp. Perifollicular erythema and acuminate keratotic plugs are characteristic. Women are more commonly affected. End stage leads to extensive scarring alopecia, because of which various terms are used like lichen plano-pilaris and folliculitis decalvans et atrophicus.

INVERSE LICHEN PLANUS: Lesions occur in flexural areas like axillae, groin, infra-mammary and rarely, popliteal and antecubital areas.[1]

LICHENOID DRUG REACTIONS: These develop after ingestion, inhalation or contact with certain drugs, with lesions occurring symmetrically over trunk and extremities. Latency period ranges from weeks to months. Mucosae are usually spared. Resolution occurs in 3-4 months, except in gold-induced eruption, which may take up to 2 years to resolve, after stopping the drug.

Common drugs causing lichenoid eruptions include gold, mercury, quinine, mepacrine, demeclocycline, furosemide, thiazides, NSAIDs, PUVA therapy, isotretinoin, amlodipine, ethambutol, carbamazepine, 5-fluorouracil, streptomycin, isoniazid, pyrazinamide, methyldopa, propranolol, enalapril, captopril, clopidogrel and interferon/ribavirin treatment of hepatitis C. Penicillamine can cause oral lesions.[1,20]

LICHEN PLANUS-LUPUS ERYTHEMATOSUS OVERLAP: Classic lesions of lichen planus are absent. Atrophic hypopigmented patches and plaques having livid red or blue-violet colour, along with telangiectasia, occurring usually over extremities are characteristic. Some cases may progress to systemic lupus erythematosus. The disease runs a chronic course and is resistant to therapy. Histologically features of both lichen planus and lupus erythematosus are present.

KERATOSIS LICHENOIDES CHRONICA (NEKAM'S DISEASE): This rare dermatosis (also known as lichen ruber moniliformis or orokeratosis striata lichenoides) clinically presents as violaceous or erythematous, verrucous papules and nodules arranged in linear or reticular pattern over hands, feet, extremities and buttocks.[1,59] Lesions are covered with hyperkeratotic plug. Oral manifestations include recurrent aphthous ulcers and erythrokeratotic papules.

LICHEN PLANUS AND MALIGNANCY: Risk factors for malignant transformation include long-standing disease, erosive and atrophic variants and tobacco usage. Incidence of squamous cell carcinoma is reported in 0.5-5% of cases with oral lichen planus. Most common site for malignancy is tongue, followed by buccal mucosa, gingiva and lip.[1] Lesions occur as indurated, non-healing ulcers or exophytic lesions with keratotic surface. Nodal metastases and death can occur in more advanced cases.

LICHENOID GRAFT VERSUS HOST DISEASE: Lichenoid eruption occurs over trunk, lower extremities, palms and soles as a part of chronic GVHD. Xerostomia and oral ulcers may also occur.

LICHENOID KERATOSIS: (Solitary lichen planus or Lichen planus-like keratosis)[63] This condition probably represents inflammatory stage of involuting solar lentigines.[64] It presents as a non-pruritic, bright red to brown, scaly, papule or plaque over sun-exposed areas of trunk and extremities, which is almost always solitary, though multiple lesions have also been reported. Histologically, parakeratosis, presence of eosinophils and plasma cells in the infiltrate, are seen in addition to features of lichen planus. Frequent associations are seborrheic keratosis, actinic keratosis and solar lentigines.

ASSOCIATIONS

Cutaneous:[60,65]

Alopecia areata, Vitiligo, Systemic lupus erythematosus, Morphea, Dermatomyositis, Lichen sclerosus et atrophicus, Pemphigus vulgaris and Paraneoplastic pemphigus.

Lichen plano-pilaris is reported in association with dermatitis herpetiformis.

Systemic:[60,61]

Thymoma, Myasthenia gravis, Diabetes mellitus, Hypertension, Ulcerative colitis and Hepatic disorders like primary biliary cirrhosis, chronic active hepatitis.

HISTOPATHOLOGY[1,20]

Typical lesion of lichen planus shows compact hyperkeratosis, wedge-shaped hypergranulosis, irregular acanthosis, basal cell degeneration and dense band-like lympho-histiocytic infiltrate in upper dermis closely approximating the epidermis. Focal hypergranulosis is seen clinically as Wickham's striae. Flattened rete ridges lead to 'saw-tooth' appearance. Dermal melanophages are also present. Max-Joseph space is an artefact, present occasionally as focal dermo-epidermal separation.

Colloid bodies (Civatte bodies/ Cytoid bodies) are seen as homogenous and eosinophilic structures in papillary dermis, about 20μm in diameter. These represent apoptotic basal cells or necrotic keratinocytes.

HYPERTROPHIC LICHEN PLANUS: Hyperkeratosis, acanthosis and papillomatosis are seen. In chronic cases, dermal fibrosis adjacent to inflammatory changes is present.

ATROPHIC LICHEN PLANUS: Epidermis is thinned out, but relative compact hyperkeratosis is still present. Rete ridges are completely effaced with relatively fewer colloid bodies.

LICHEN PLANO-PILARIS: Infiltrate surrounding and sometimes permeating the base of hair follicles is present, along with follicular keratin plugging.

ACTINIC LICHEN PLANUS: Epidermis shows orthokeratosis and hypergranulosis. Prickle cell layer at center of the lesion is atrophic, with loss of rete pegs, but at borders it is acanthotic with saw-tooth appearance. Dense band-like infiltrate is present as in classical lichen planus.

LICHEN PLANUS PIGMENTOSUS: Pigment incontinence extending deep into the reticular dermis.

BULLOUS LICHEN PLANUS: Sub-epidermal bulla, heavy dermal infiltrate, numerous colloid bodies.

ORAL LICHEN PLANUS: Characteristic features are presence of parakeratosis and thinned-out epithelium. There are fewer colloid bodies and dense band-like infiltrate is composed mainly of plasma cells.

ELECTRON MICROSCOPY[1]

1. Basal keratinocytes show degenerative changes.
2. Loss of desmosomes and disruption of tonofilaments in basal layer.
3. Reduplication of basal lamina.
4. Dermal infiltrate invades the epidermis and causes changes in lamina densa such as fragmentation, irregular folding and duplication.
5. Colloid bodies are seen in papillary dermis.
6. Split in lamina lucida in case of lichen planus pemphigoides.
7. Separation between basal lamina and cytomembrane of basal keratinocytes in bullous lichen planus.

IMMUNOFLUORESCENCE[1]

Direct immunofluorescence shows shaggy deposits of fibrinogen at dermo-epidermal junction. Occasionally granular or linear deposits of IgM (and rarely IgG or IgA) in basement membrane zone may be seen. Necrotic keratinocytes may be seen. In lichen plano-pilaris, fibrinogen

deposits around follicles and IgM and IgG or rarely C3 deposits at the level of infundibulum and isthmus are present. Lichen planus pemphigoides shows linear deposits of IgG and C3 along basement membrane zone of perilesional skin. Both direct and indirect immunofluorescence are negative in bullous lichen planus.

COMPLICATIONS

Cicatricial alopecia: (Lichen plano-pilaris)

Erythroderma: (Generalized lichen planus)

Pterygium

Twenty-nail dystrophy

Anonychia

Deformity: (Ulcerative lichen planus of feet)

Malignancy: (0.5-5% cases of oral lichen planus)

DIFFERENTIAL DIAGNOSIS[1,20]

Classic lichen planus: Psoriasis, lichen simplex chronicus

Annular lichen planus: Granuloma annulare, dermatophytosis

Hypertrophic lichen planus: Lichen simplex chronicus, prurigo nodularis, papular lichen amyloidosis, warts, kaposi sarcoma

Linear lichen planus: Nevus unius lateris, lichen striatus

Atrophic lichen planus: Lichen sclerosus et atrophicus, morphea

Follicular lichen planus: Lichen nitidus

Actinic lichen planus: Polymorphous light eruption

Guttate lichen planus: Guttate psoriasis, secondary syphilis

Lichen plano-pilaris of skin: Lichen nitidus, lichen spinulosus

Lichen plano-pilaris of scalp: Cicatricial pemphigoid, alopecia areata, lupus erythematosus, inflammatory folliculitis

Childhood lichen planus: Lichen nitidus, lichen striatus

Nail involvement: Psoriasis, alopecia areata, onychomycosis

Mucosal lichen planus: Leukoplakia, oral pemphigus, candidiasis, secondary syphilis, lupus erythematosus, paraneoplastic pemphigus

Lichenoid Drug Eruption:

	Classic lichen planus	**Lichenoid drug eruption**
Lesion	Small	Large and scaly
Wickham's striae	Present	Absent
Distribution	Flexural	Symmetrical over trunk and extremities; Photodistributed pattern
Mucosal involvement	Common	Rare
Alopecia	Rare	Common
Colloid bodies seen higher in epidermis	Absent	Present
Lymphocytic exocytosis	Absent	Present
Parakeratosis	Not seen	Present
Eosinophils	Not present	Present

TREATMENT

Lichen planus is usually benign and self-limiting. Various treatment modalities include:

Topical: Steroids, tacrolimus, pimecrolimus

Systemic: Steroids, retinoids, dapsone, anti-malarials, immuno-suppressants, photochemotherapy, anti-histamines

CUTANEOUS LICHEN PLANUS:

Topical: Steroids, tacrolimus, photochemotherapy

Systemic: Steroids, etretinate, acitretin, isotretinoin

Second-line: Cyclosporine, dapsone, hydroxychloroquine, azathioprine

ORAL LICHEN PLANUS:

Topical: Steroids, Lidocaine, Tretinoin, Isotretinoin, Tacrolimus

Systemic: Steroids, Etretinate, Acitretin, Isotretinoin, Anti-candidal

Second-line: Cyclosporine, Griseofulvin, Thalidomide, Hydroxy-chloroquine, Azathioprine, Cyclophosphamide, Photodynamic therapy

OTHER VARIANTS:

Lichen planus pemphigoides: Doxycycline, Tetracycline, Nicotinamide

Generalized lichen planus: Interferon-α 2b, Metronidazole

Refractory cases: Cyclophosphamide, Methotrexate

CORTICOSTEROIDS

Corticosteroids are the drug of choice for treating lichen planus. These can be used in topical, systemic or intralesional formulations.

Topical steroids: These are used in patients with mucosal and limited cutaneous involvement. Topical clobetasol propionate (0.05%) under occlusion leads to regression of lesions in most of the cases of limited cutaneous disease. Cortisone vaginal/rectal suppositories are used for mucosal lichen planus. Triamcinolone acetonide lozenges or betamethasone valereate aerosols can be used for oral lesions.

Systemic steroids: Oral steroids are indicated for extensive skin lesions, ulcerations over oral/vaginal mucosa, pterygium formation, bullous lichen planus and lichen planus of scalp.

Most commonly, prednisolone is used in dosage of 5-20 mg/day for 4-6 weeks and then gradually tapered over another 6 weeks. In patients requiring long duration of therapy, oral mini pulse can be given as oral betamethasone 5mg on two consecutive days per week.

Intralesional steroids: Triamcinolone acetonide 5-10 mg/ml may be used in hypertrophic and nail lichen planus.

RETINOIDS

Topical retinoids: Isotretinoin gel (0.1%) and etretinate has been used in cases of oral lichen planus.

Systemic retinoids: Acitretin is given as a dose of 30mg/day for eight weeks in severe cutaneous lichen planus and for two weeks in LP-LE overlap syndrome.

PHOTOCHEMOTHERAPY

PUVA therapy may be used in generalized cutaneous and erosive oral lichen planus. Initial dose is 0.5-2 J/cm^2 and it should not exceed 7 J/cm^2 in a single session, given for 3 times/week.

IMMUNOSUPPRESSANTS

Cyclosporine is used in severe cutaneous, oral and nail lichen planus cases, at dosage of 3-10 mg/kg/day. Azathioprine is useful for generalized cutaneous involvement and lichen planus pemphigoides. Mycophenolate mofetil (1.5g twice a day) is also useful in oral and bullous forms. 0.1% tacrolimus ointment is useful in erosive oral lichen planus, as is 1% pimecrolimus cream.

MISCELLANEOUS

Anti-malarials like hydroxychloroquine (200-400 mg/day) has been used for actinic and erosive lichen planus. Thalidomide can also be used for resistant cases of erosive lichen planus. Dapsone (200 mg/day) is useful in bullous and erosive types. Other drugs include griseofulvin (1g/day), phenytoin (100-200 mg/day) and metronidazole (500 mg twice daily).

Low-molecular weight heparin has anti-proliferative and immunomodulatory actions and is used as injection (3 mg/week) for 6-10 weeks.

Interferon-α 2b can also be used in generalized cutaneous involvement, but it has also been implicated as a causative/aggravating factor of lichen planus.

Extracorporeal photopheresis and photodynamic therapy mediated methylene blue (MB-PDT) are used for oral lichen planus.

Split skin grafting has been used in ulcerative lichen planus of feet.[103]

COURSE AND PROGNOSIS[1]

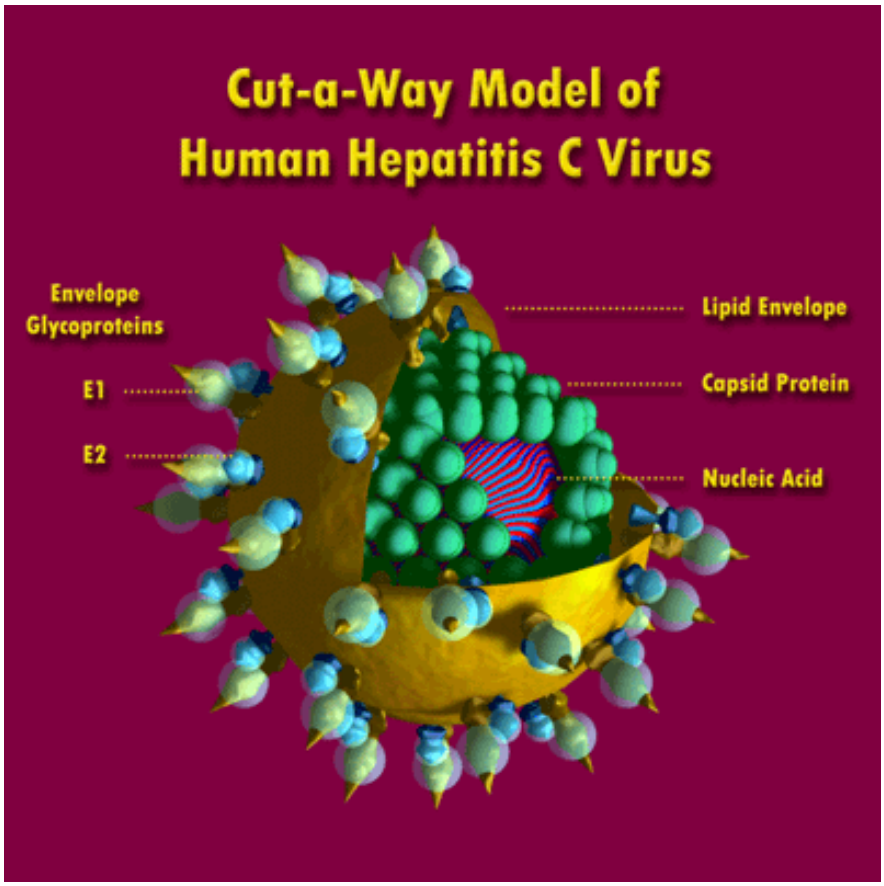
Lichen planus typically persists for 1-2 years, but course is unpredictable. It may follow a chronic relapsing course for many years. Generalized cutaneous lesions heal spontaneously and faster than limited cutaneous involvement. Lichen plano-pilaris is most chronic and progressive variant with permanent hair loss. Hypertrophic lichen planus also follows protracted course. Oral lichen planus has a mean duration of about 5 years. Usually, the duration of disease follows this order (shortest to longest): generalized, cutaneous, cutaneous + mucosal, mucosal, hypertrophic and lichen plano-pilaris.

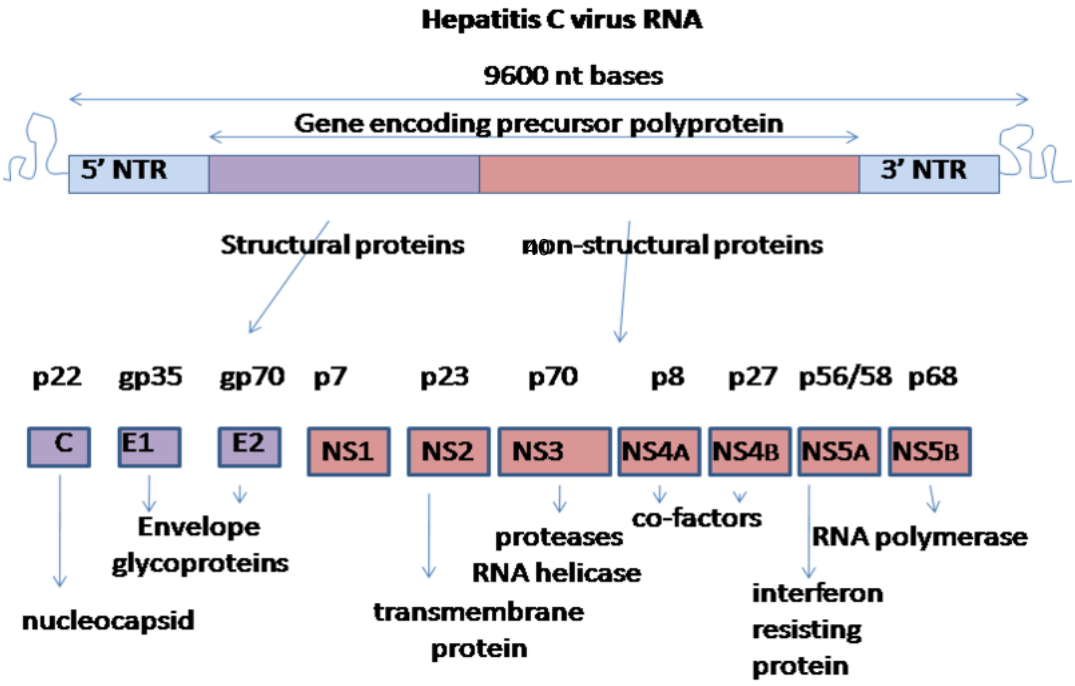
Relapses occur in 15-20% cases and are more commonly reported in generalized disease. Serum neopterin level reflects the extent and progression of the lesions. Serum angiotensin converting enzyme (ACE) activity can be used for assessing the treatment response.[62]

HEPATITIS C VIRUS

Hepatitis C virus (HCV) was discovered in 1989.[72] More than 170 million people are infected with HCV worldwide.[69] Although the incidence of HCV infection is much lower than that of hepatitis B virus (HBV) infection, the rate of chronically infected individuals is much higher.[71] Morbidity associated with HCV infection is not only due to the sequelae of chronic liver disease, but also due to a variety of extrahepatic manifestations.[70] It is not only the principal cause of post-transfusion chronic hepatitis, but is also associated with a number of cutaneous disorders other than lichen planus, like porphyria cutanea tarda, cryoglobulinemia, leukocytoclastic vasculitis and livedo reticularis.

Structure: Hepatitis C virus is a 55-65 nm, ss-RNA virus belonging to genus hepacivirus under the family flaviviridae, that replicates in hepatocytes and peripheral blood mononuclear cells. It consists of positive-sense, single-stranded, extremely variable[70], RNA genome placed inside an icosahedral shell/nucleo-capsid and surrounded outside by a lipid envelope derived from host membrane. Viral envelope glycoproteins (E1 and E2) are embedded into this envelope. Genome of HCV consists of about 9600 nucleotide bases, which translates into very long protein containing about 3000 amino acids.


Cut-a-Way Model of
Human Hepatitis C Virus
Envelope
Glycoproteins
E1
E2
Lipid Envelope
Capsid Protein
Nucleic Acid


Hepatitis C virus RNA
9600 nt bases
Gene encoding precursor polyprotein
5' NTR
3' NTR
Structural proteins
non-structural proteins
p22
gp35
gp70
p7
p23
p70
p8
p27
p56/58
p68
C
E1
E2
NS1
NS2
NS3
NS4A
NS4B
NS5A
NS5B
nucleocapsid
Envelope
glycoproteins
transmembrane
protein
proteases
RNA helicase
co-factors
interferon
resisting
protein
RNA polymerase

Types:(Six genotypes)[70]

Type 1- United States

Type 2- Not common

Type 3- India, Pakistan, Australia

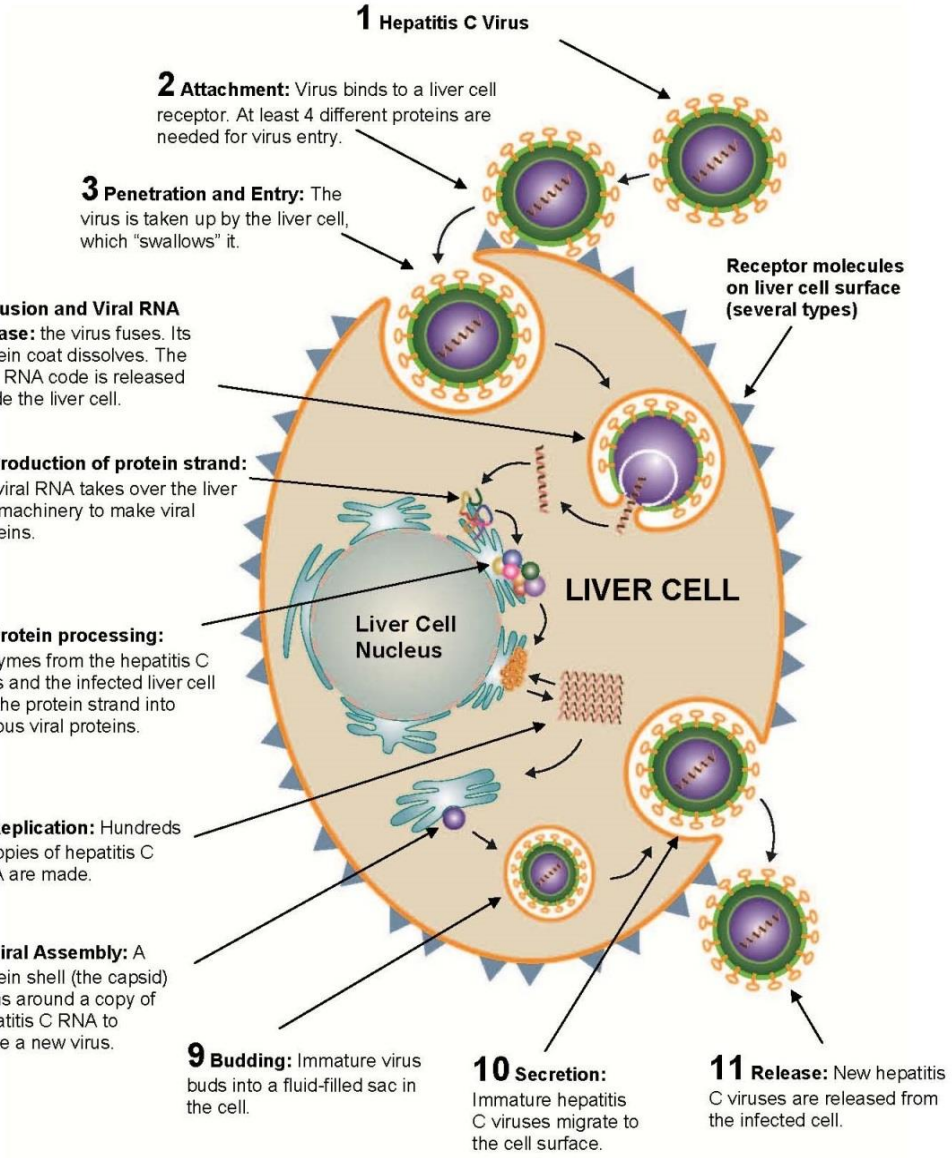
Type 4- Middle East

Type 5- South Africa

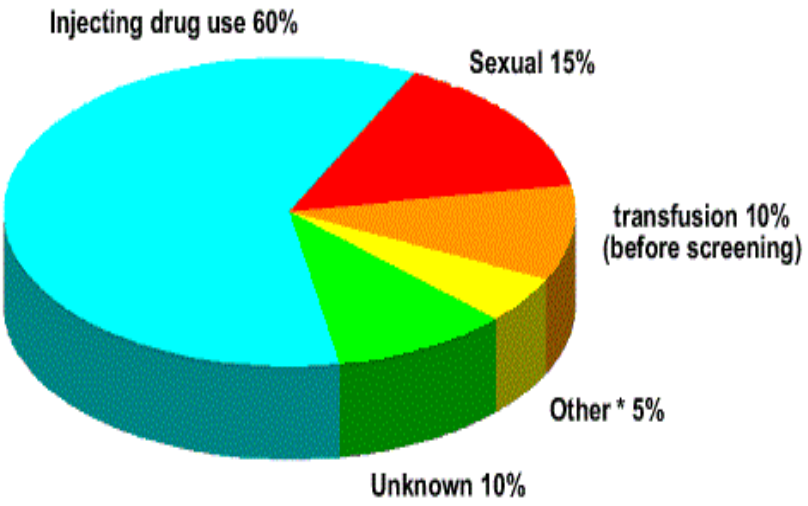
Type 6- Asia

Modes of transmission: HCV is mainly transmitted through blood transfusion (developing world) and intravenous drug usage (developed countries). Other modes include nosocomial, vertical and sexual transmission.[66]

Immunology: Both humoral and cell-mediated immunity play role in pathogenesis. The antibodies developing against viral structural and non-structural proteins are the basis for the assay. Cellular response includes action of CD4 and CD8 cells against HCV antigens. However, inspite of these defense systems of the host, reasons for chronicity of hepatitis C are attenuated antigenicity, restricted expression of MHC proteins in infected hepatocytes and emergence of virus quasispecies.



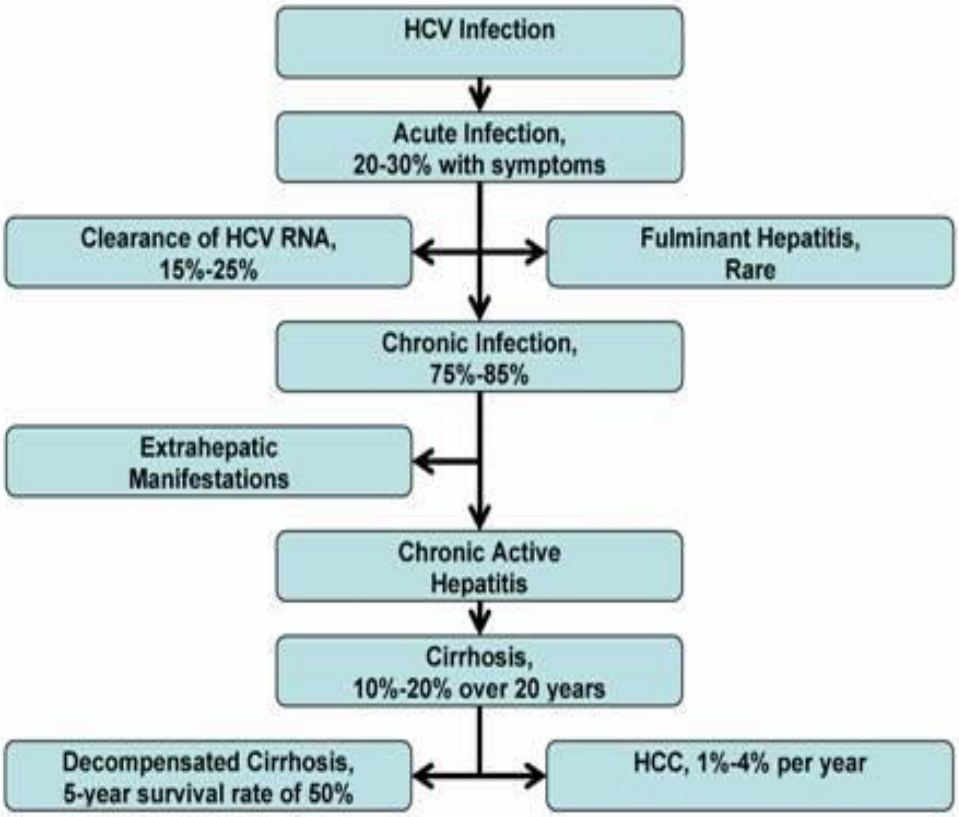
LIFE CYCLE OF HEPATITIS C VIRUS[68]



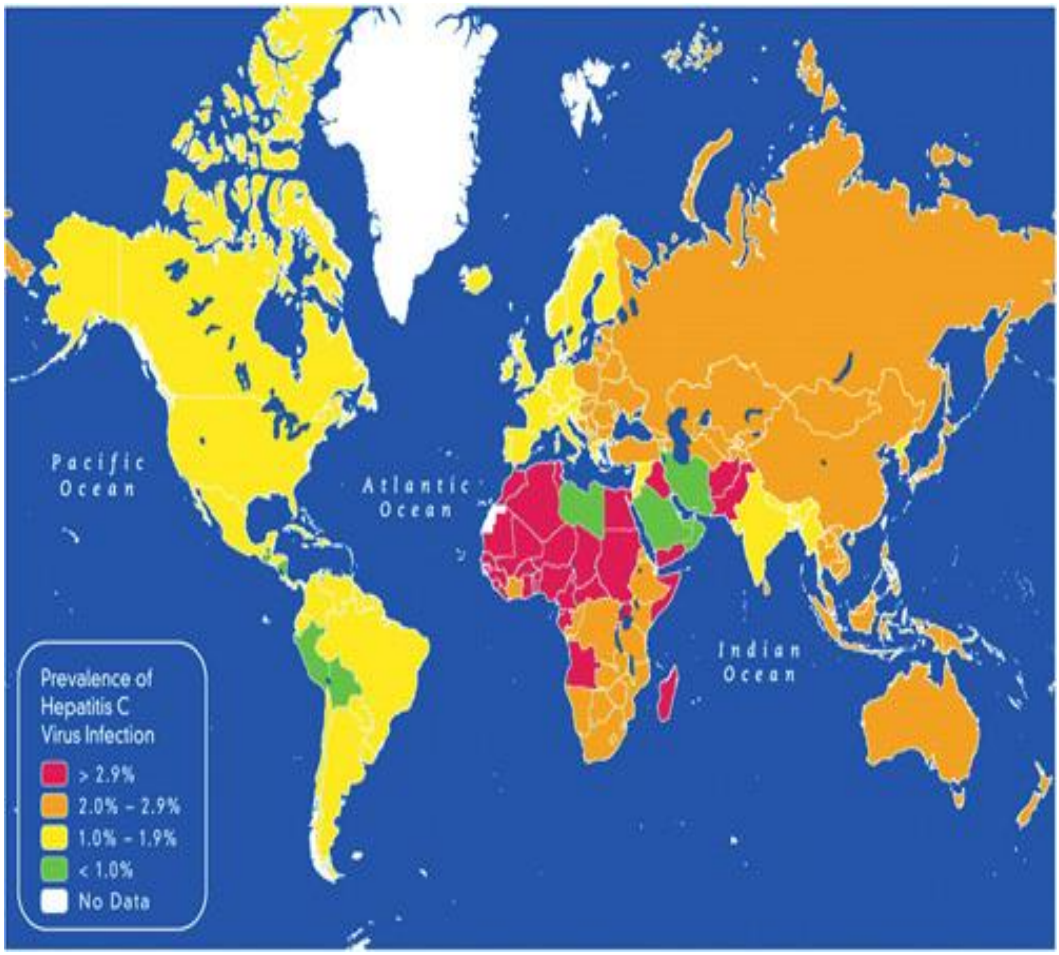
*Nosocomial: Health-care work; Perinatal

Source: Centers for Disease Control and Prevention

SOURCES OF INFECTION FOR HEPATITIS C



NATURAL HISTORY OF HCV INFECTION[4]



GLOBAL BURDEN OF HEPATITIS C INFECTION[67]

Clinical effects:

HEPATITIS

CUTANEOUS: Lichen planus, cryoglobulinemia, porphyria cutanea tarda, leukocytoclastic vasculitis, livedo reticularis and Sjogren's syndrome

Diagnosis: Two types of tests are available. Serological assays detect anti-HCV antibodies (ELISA and RIBA) and Molecular assays detect HCV RNA (Polymerase chain reaction).

Enzyme Linked Immunosorbent Assay (ELISA): Antibodies to several HCV antigens are simultaneously detected. First generation ELISA uses recombinant antigen C100-3 derived from NS4 region of HCV genome. Second generation ELISA incorporates recombinant proteins from nucleo-capsid core (C22-3 and NS3 region). Third generation ELISA incorporates proteins from NS5 region and replaces some recombinant proteins with synthetic peptides.

Radio Immunoblot Assay (RIBA): This is a supplementary test. Reactivity is confirmed by incubation with nitrocellulose strip that contains individual bands of recombinant or synthetic HCV proteins.

Polymerase Chain Reaction (PCR): This technique is very sensitive but complicated, expensive and time-consuming. Qualitative PCR used for confirmation of HCV infection detects fewer viral particles (< 50 mRNA/ml) as compared to Quantitative PCR which detects > 500 mRNA/ml. The latter is used for monitoring disease activity and response to treatment.

Treatment:

- Rest, diet and vitamins offer NO benefit
- Pegylated interferon-alpha
- Pegylated interferon-alpha 2a with ribavirin
- Boceprevir or telaprevir
- Sofosbuvir with interferon and ribavirin
- Urso-deoxycholic acid
- Hepatic iron removal
- Liver transplant is last option
- Alternative therapies- Milk thistle (Silybum marianum), ginseng, colloidal silver

LICHEN PLANUS IN HCV INFECTION

Lichen planus in HCV infection is mainly associated with class II HLA-DR6 allele. Various researchers have suggested that simultaneous appearance of lichen planus and HCV infection can be due to genetic, environmental, geographic or other factors.[74]

Proposed mechanisms for this association are local induction of an immune response specific for HCV epitopes[70], selective presentation of certain HCV-encoded peptides by HLA-DR6 molecules on surface of monocytes to the CD4+ cells, cytopathic replication of HCV in extra-hepatic tissues, keratinocyte antigenic changes leading to cell-mediated response and lastly the auto-immunity.

Correlation of HCV infection with lichen planus has been reported to be statistically significant in various studies from Japan, Spain, Germany, USA, Italy and Europe. On the other hand, many researchers did not report any association. Most likely hypothesis describing this non-homogeneity in results from different geographical areas is the regional-based correlation.

Many of the reports for lichen planus come from registries of hospitals or university affiliated clinics. These cannot represent the real situation in the general population. Difficulties in making a definite diagnosis for lichen planus make the interpretation even more complex.

Estimation of the point prevalence of HCV infection in the general population and how well the control group was selected are other contributing variables which may lead to divergent results. Also, as HCV treatment, especially interferon-α, may provoke oral lesions similar to oral lichen planus, lack of information on the treatment status of enrollees with HCV infection in the studies makes summarizing the results challenging.[73] Genetic factors and prevalence of certain HCV genotypes in certain geographical areas also influence the result.

No correlation was observed between the viral load and HCV genotype and the likelihood of developing lichen planus in HCV-infected patients.[74] Interestingly, co-infection with HIV decreases the possibility of lichen planus in HCV-infected patients, probably through immunodeficiency.[75]

Overall, it can be concluded that HCV-infected patients may have increased risk of developing lichen planus or alternatively, patients with lichen planus may be at a higher risk for developing HCV infection. More prospective well-designed studies are necessary to clarify the issue.

Clinically, lesions are similar to classic lichen planus, but mucosal involvement is more common especially erosive and reticular types. Lesions are symmetrically distributed over gingiva, tongue and lips. Mega et al reported three types of oral lichen planus: 1) Associated with a HCV infection (OLPHCV), 2) Oral lichen-contact sensitivity reaction (OLCSR), and 3) Idiopathic oral lichen planus (IOLP).

MATERIALS AND METHODS

STUDY DESCRIPTION:

PLACE: Dept. of Dermatology, Govt. Stanley Medical College, Chennai

DESIGN: Prospective, Observational

TIME PERIOD: July 2013 to June 2014

SAMPLE SIZE: 100 patients, 100 controls

SOURCE OF PATIENTS: Patients attending Dermatology OPD of Govt. Stanley Medical College& Hospital Chennai, from July 2013 to June 2014, clinically diagnosed as lichen planus (involving skin, mucous membrane or both).

SOURCE OF CONTROLS: Voluntary blood donors being screened in Govt. Stanley Hospital, Chennai.

INCLUSION CRITERIA:

1) Male with Lichen planus (>18years and <60 years of age)
2) Female with Lichen planus (>18 years and <60 years of age)
3) Patients willing to follow-up

EXCLUSION CRITERIA:

1) Patients taking drugs causing lichenoid eruptions like beta-blockers, anti-malarials, diuretics, ACE inhibitors, chlorpropamide, simvastatin.
2) Pregnant/Lactating woman

3) Pre-existing liver disease
4) Past history of blood transfusion
5) Intravenous drug users
6) Blood dyscrasias like haemophilia
7) Patients not willing for screening

The study was conducted in accordance with ethical committee approval (**ANNEXURE 3**). Demographic data and detailed history for each patient (including duration and location of lesions, extent of involvement and any risk factors) were noted in a pre-designed proforma (**ANNEXURE 1**) after taking informed consent (**ANNEXURE 2**). Diagnosis was made by clinical examination.

Following investigations were done in all patients:

Hemogram (Hb, TC, DC, ESR, Platelet count)

Liver function tests (S.Bil., SGOT, SGPT, SAP, STP, S.Alb.)

Renal function tests (S. urea and creatinine)

Random blood sugar

Hepatitis C antibody test (SD Bioline- Immunochromatography)

IMMUNOCHROMATOGRAPHIC HCV TEST

(SD BIOLINE HCV 02FK10I)

ONE STEP, RAPID IMMUNOCHROMATOGRAPHIC TEST FOR THE DETECTION OF ANTIBODY AGAINST HEPATITIS C VIRUS IN HUMAN SERUM, PLASMA OR WHOLE BLOOD

Explanation of the test

HCV diagnostic kit detects the presence of HCV antibodies in human serum by immunoassay. HCV genes are constructed for the expression of recombinant antigens in bacterium systems like E. coli. The major immunoreactive antigens of these proteins are Core, NS3, NS4 and NS5 regions of HCV genome. For diagnosis, these recombinant proteins are used as capture materials and coated on the membrane of the rapid test. Compared to the first generation HCV test using single recombinant antigens, multiple antigens using recombinant proteins have been added in new generation of tests to avoid non-specific cross-activity and to increase the sensitivity of test.

The SD BIOLINE HCV test is an immunochromatographic (rapid) test for the qualitative detection of antibodies specific to HCV, in human serum, plasma and whole blood. This test contains a membrane strip, pre-coated with recombinant HCV capture antigen (core, NS3, NS4 and NS5) on test band region. The protein A-colloid gold conjugate and serum sample moves along the membrane chromatographically to the test region (T) and forms a visible line as the antigen-antibody-protein A gold particle complex forms with high degree of sensitivity and specificity. The SD BIOLINE HCV test window is clearly labelled- 'T' for 'Test line' and 'C' for 'Control line'. Both the Test line and Control line in the result window are not visible before applying any samples. The Control line is used as a control and it should always appear if the test procedure is performed correctly.

Materials provided

1) SD BIOLINE HCV test device individually foil pouched with a desiccant
2) Capillary pipette
3) Assay diluent
4) Package insert

Precautions/ Kit storage

1) The test device should be stored at room temperature.
2) The test device is sensitive to humidity as well as to heat.
3) Perform the test immediately after removing the test device from pouch.
4) Do not use it beyond the expiry date.
5) The shelf-life of the kit is as indicated on outer package.
6) Do not use the test kit if the pouch is damaged or seal is broken.
7) Do not re-use the test device.
8) Do not freeze.
9) Assay Diluents contain sodium azide as a preservative. In case of contact with skin wash immediately, wear gloves and eye protection.

Warnings

1) For in vitro diagnostic use only.
2) Wear protective gloves while handling specimens.
3) Avoid splashing or aerosol formation.
4) Clean up spills thoroughly using an appropriate disinfectant.
5) Decontaminate and dispose of all specimens, reaction kits and potentially contaminated materials in a biohazard container.
6) Do not mix and interchange different specimens.

7) Anticoagulants like heparin, EDTA and sodium citrate do not affect result.
8) Use of hemolytic samples, rheumatoid factors-contained samples and lipidemic, icteric samples can lead to impair the results.
9) Do not use any of the components beyond expiry date.
10) Assay diluents contain sodium azide as a preservative. If these materials are to be disposed off through sink or other common plumbing system, flush with generous amount of water to prevent accumulation of potentially explosive compound.

Specimen collection, storage and precaution

1) Whole blood

1) Collect the whole blood into the collection tube (containing anticoagulants such as heparin, EDTA and sodium citrate) by venipuncture.
2) If blood specimens are not immediately tested, they should be refrigerated at 2-8 degree Celsius.
3) When refrigerated, the specimens should be used within 3 days.
4) For storage period longer than 3 days, freezing is recommended. They should be brought to room temperature prior to use.
5) Using the blood specimens in the long-term keeping more than 3 days can cause non-specific reaction.

2) Plasma or serum

1) [Plasma]- Collect the whole blood into the collection tube (containing anticoagulants such as heparin, EDTA and sodium citrate) by venipuncture and then centrifuge blood to get plasma specimen.
2) [Serum]- Collect the whole blood into the collection tube (Not containing anticoagulants such as heparin, EDTA and sodium citrate) by venipuncture, leave to settle for 30 minutes for blood coagulation and then centrifuge blood to get serum specimen of supernatant.
3) If plasma or serum specimens are not tested immediately, they should be refrigerated at 2-8 degree Celsius. For storage period longer than 2 weeks, freezing is recommended. They should be brought to room temperature prior to use.
4) Plasma or serum specimens containing a precipitate may yield inconsistent test results.

Test procedure

1) Remove the test device from the foil pouch, place it on a flat, dry surface.
2) Using a capillary pipette, add 10µl of serum, plasma or blood specimen (up to the black line) into the sample well(s).

3) Add 4 drops (about 120µl) of assay diluent into sample well(s).
4) Interpret test results in 5-20 minutes.
5) Reading too late can give false results.

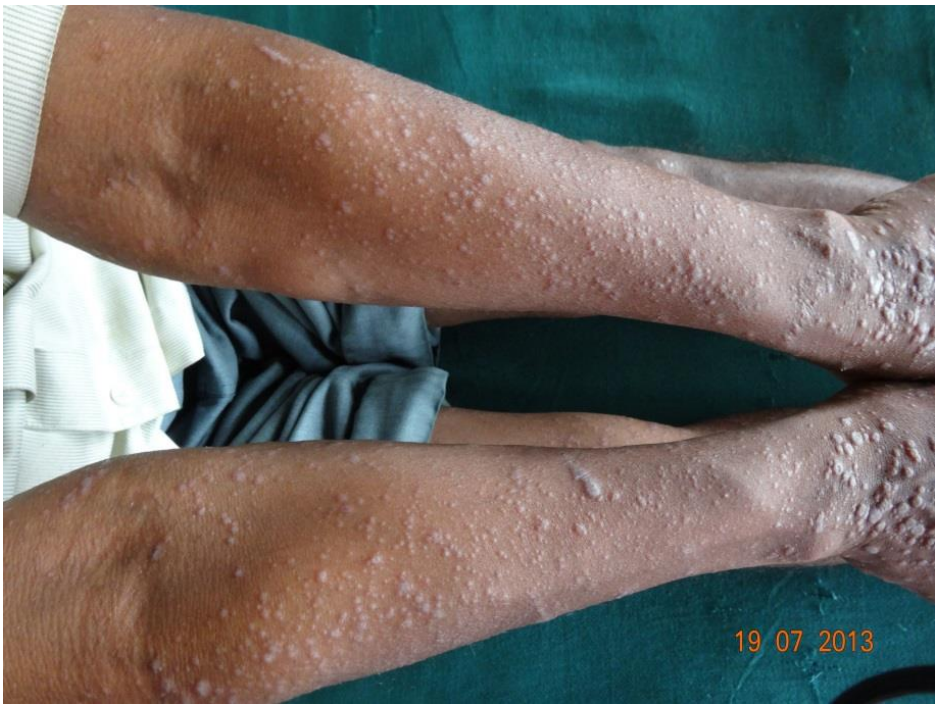
Interpretation of results

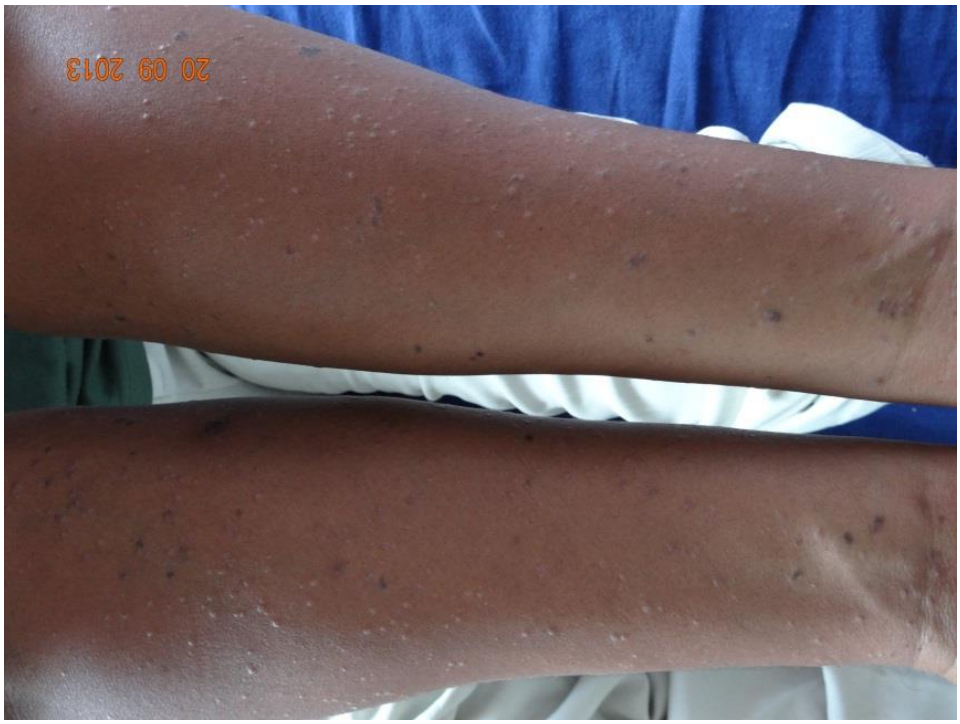
1) A color band will appear in the left section of the result window. This band is control line (C).
2) Color band appearing in the right section of result window is test line (T).
3) **Negative Result:** The presence of only one color band (C) in the result window.
4) **Positive Result:** The presence of two color bands (C and T) in the result window.
5) **Invalid Result:** If the control band (C) is not visible in result window, result is considered invalid and the specimen must be retested using a new test device.

Limitations of the test

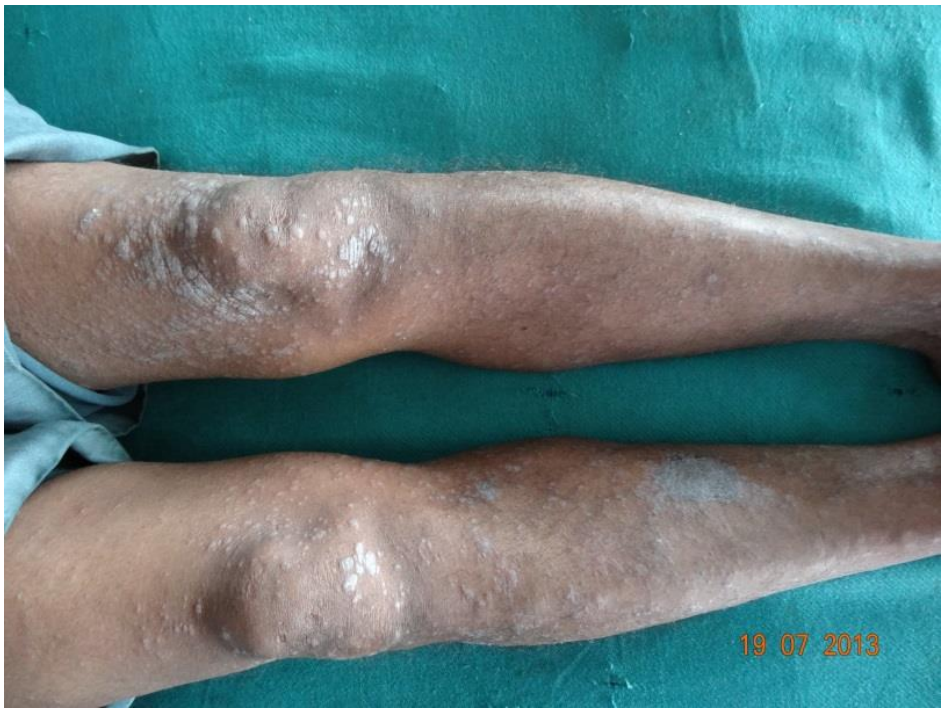
1) Negative result does not preclude the possibility of HCV infection.
2) Specimens repeatedly tested positive should be retested using another testing method.
3) A definitive clinical diagnosis should not be based on the results of a single test, but should only be made by the physician after all clinical and laboratory findings have been evaluated.

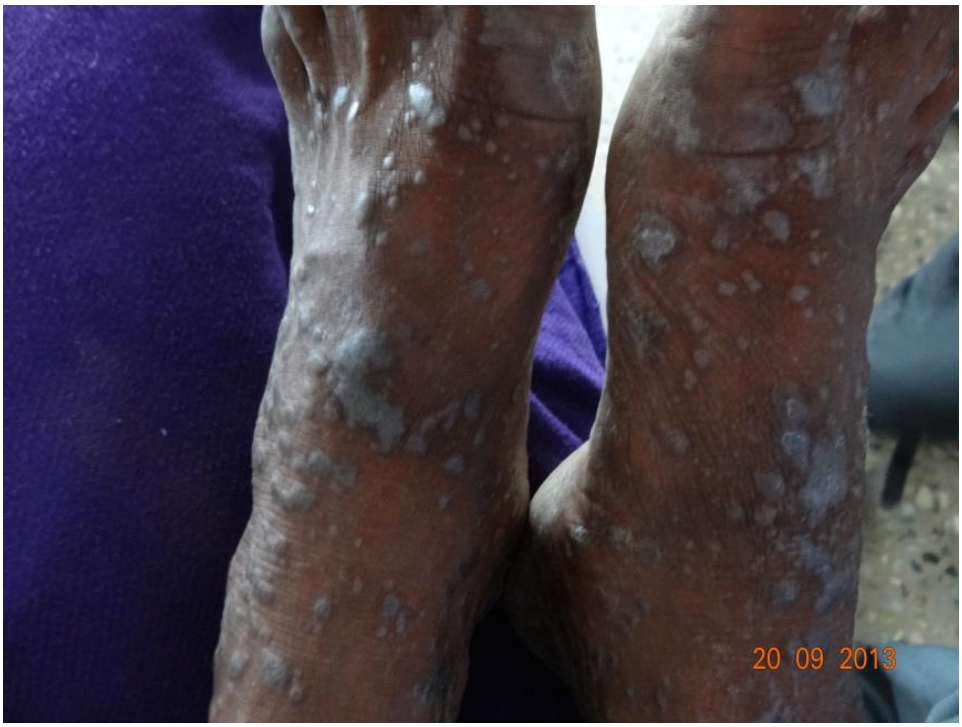
CLINICAL PHOTOS



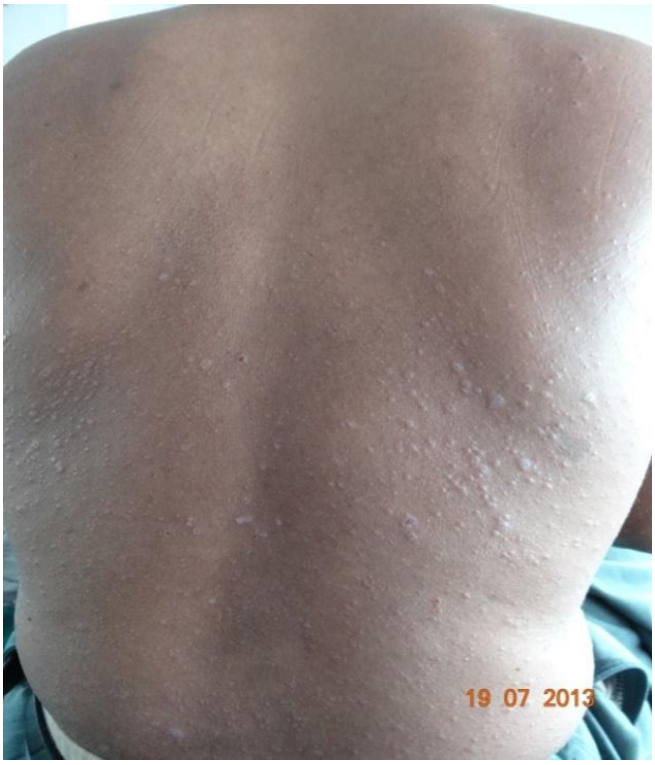


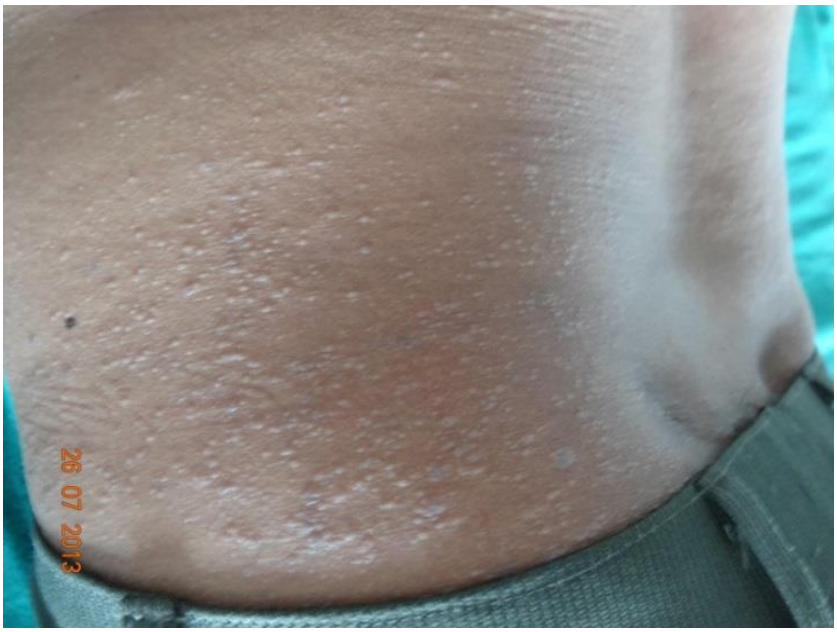
CLASSICAL LICHEN PLANUS



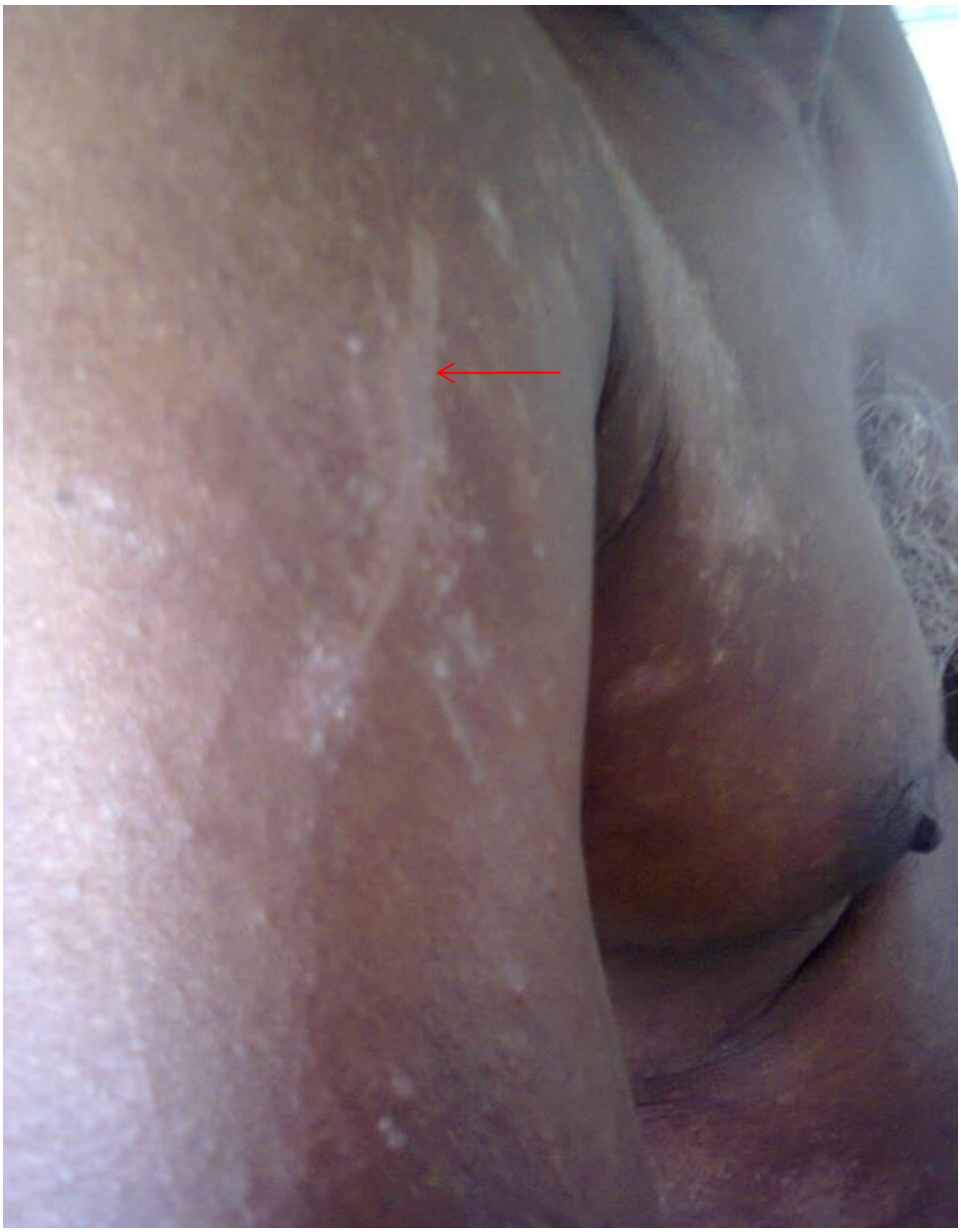


LOWER LIMB INVOLVEMENT

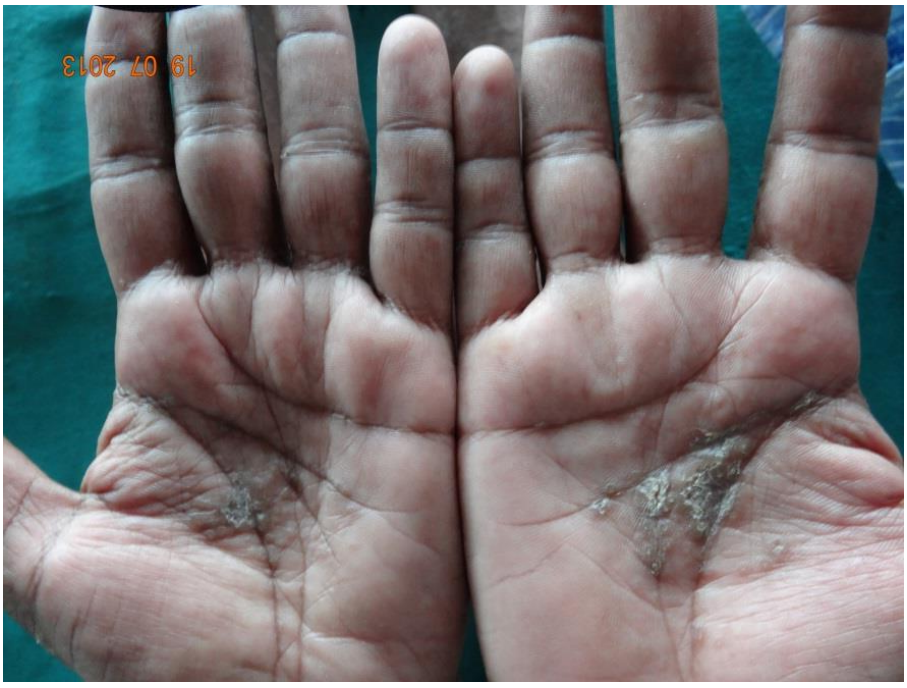


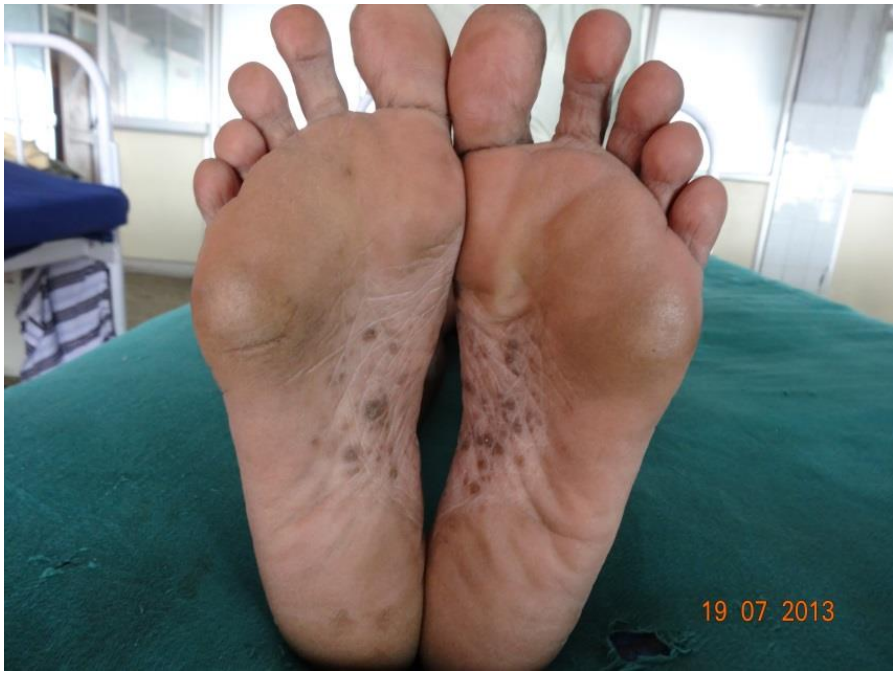


TRUNK INVOLVEMENT

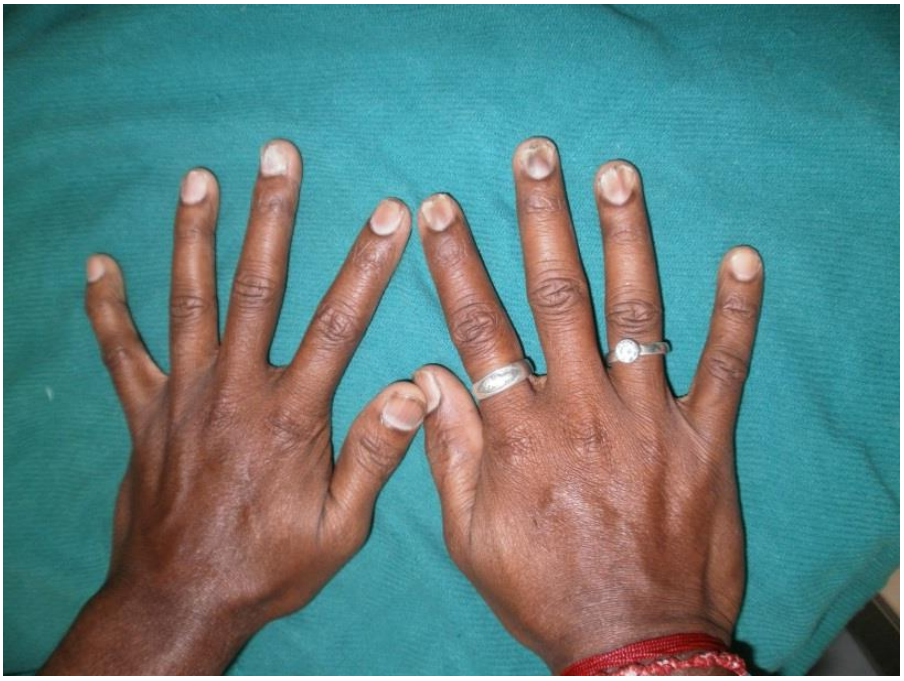


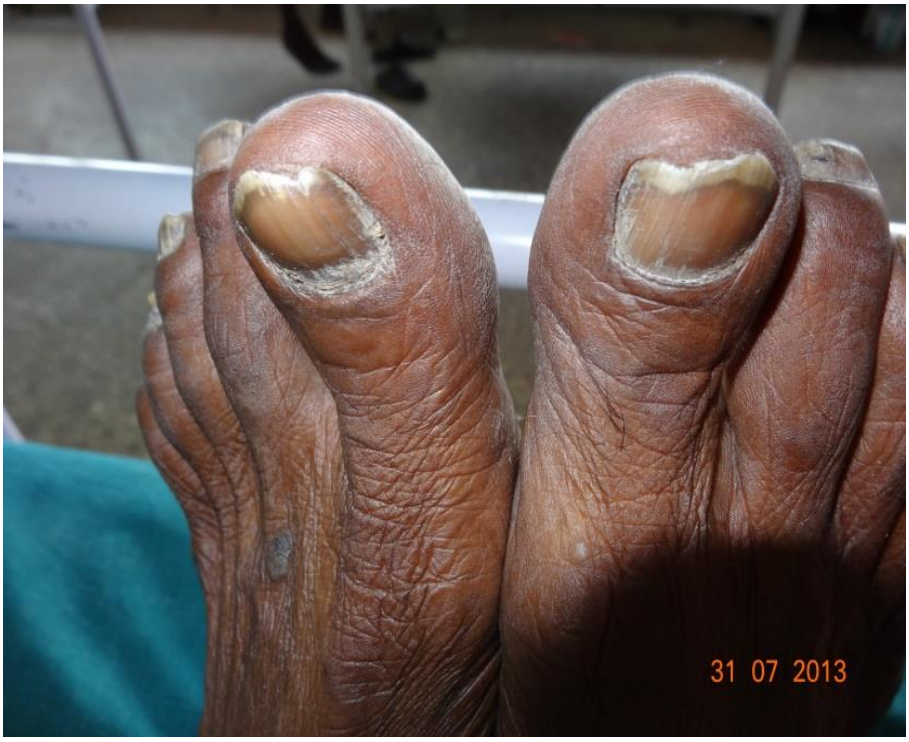
KOEBNERIZATION



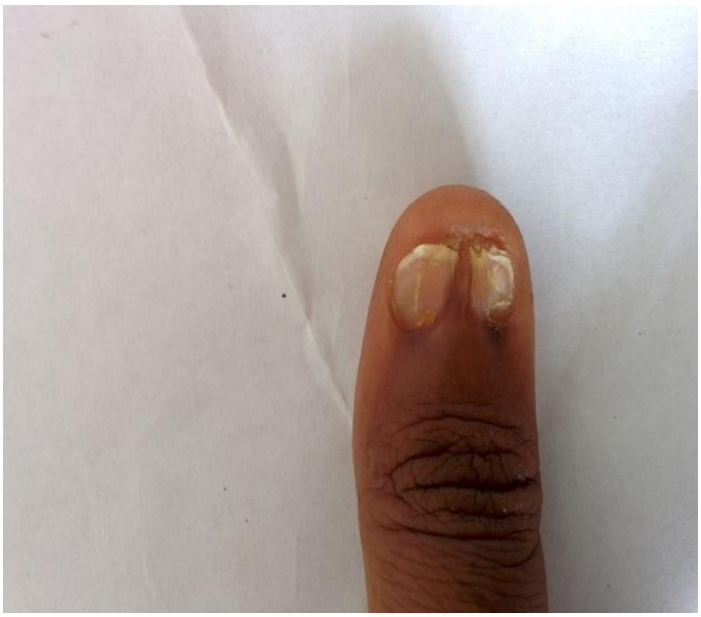


PALMS AND SOLES INVOLVEMENT

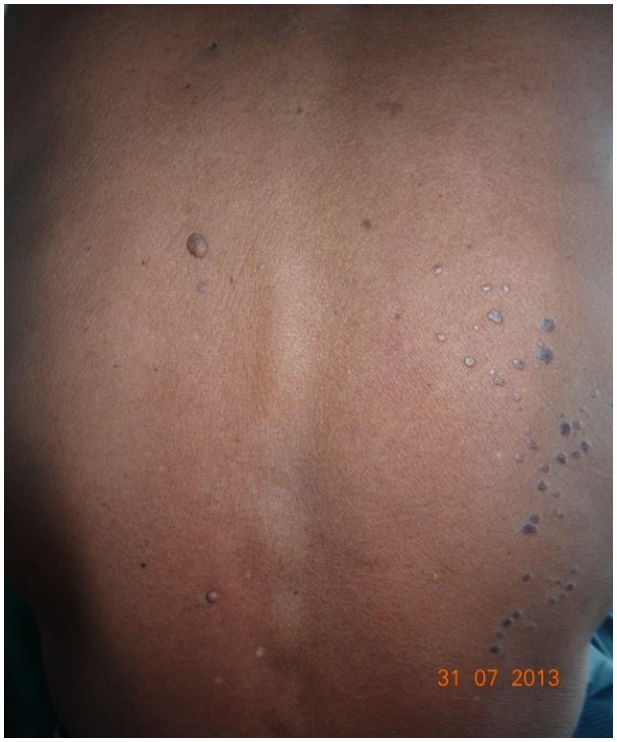




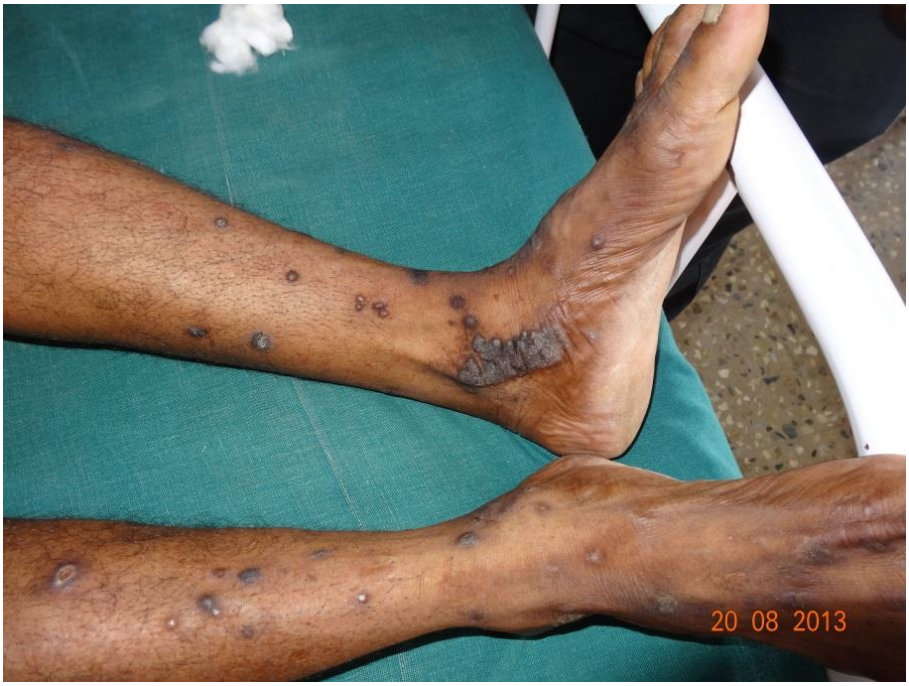
NAIL INVOLVEMENT

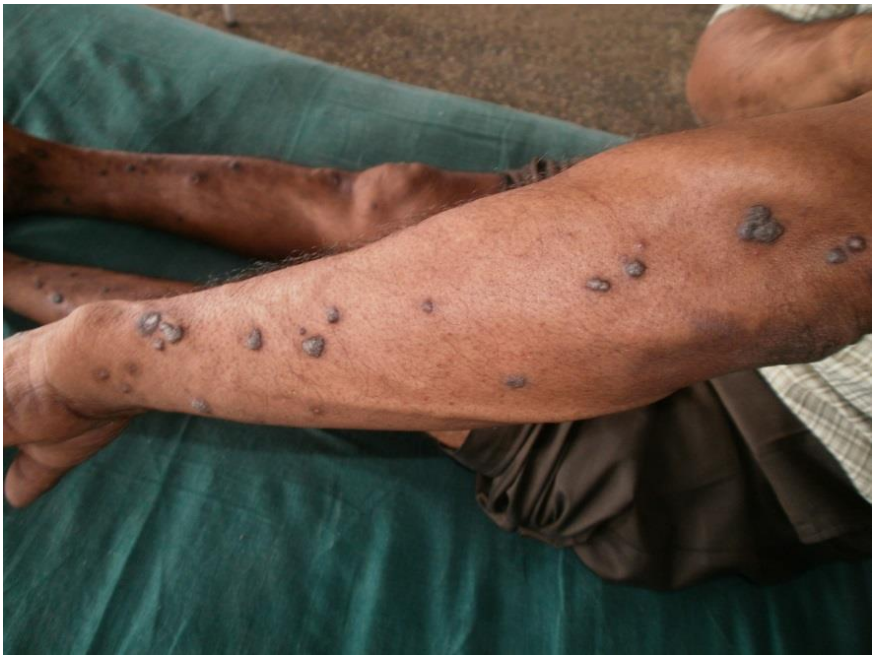


PTERYGIUM

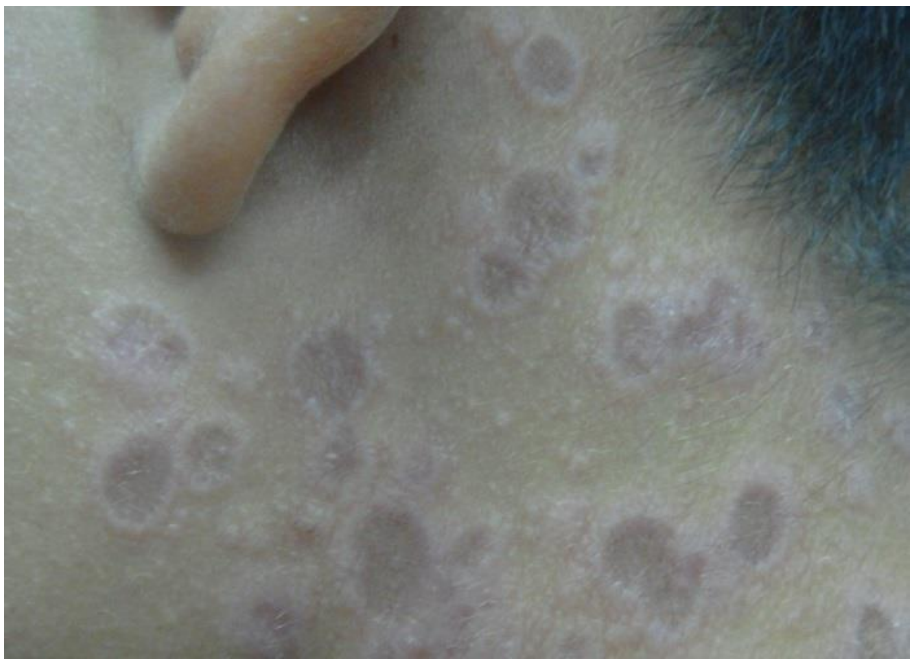


LINEAR LICHEN PLANUS

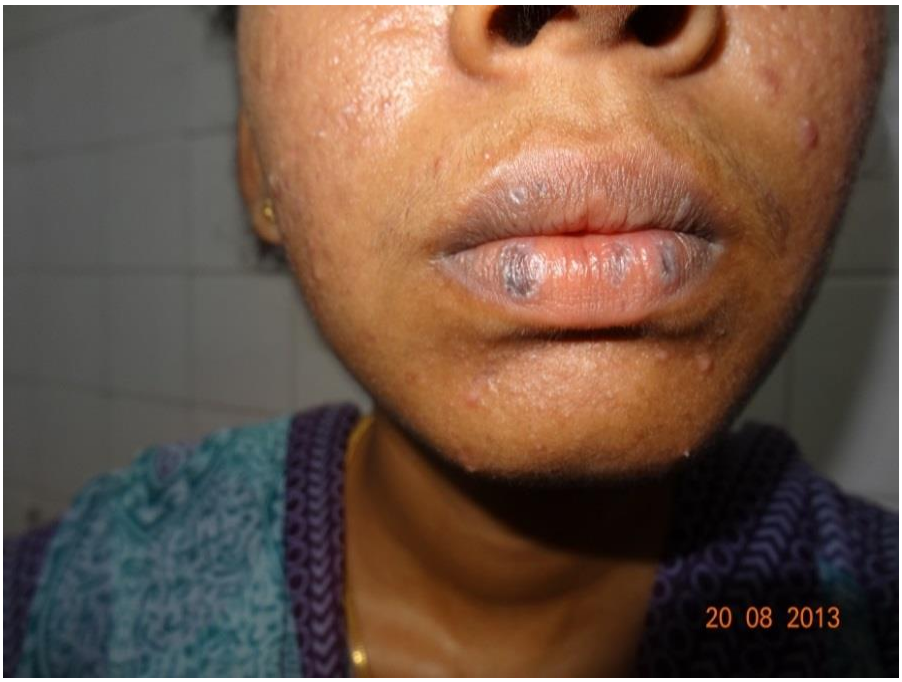




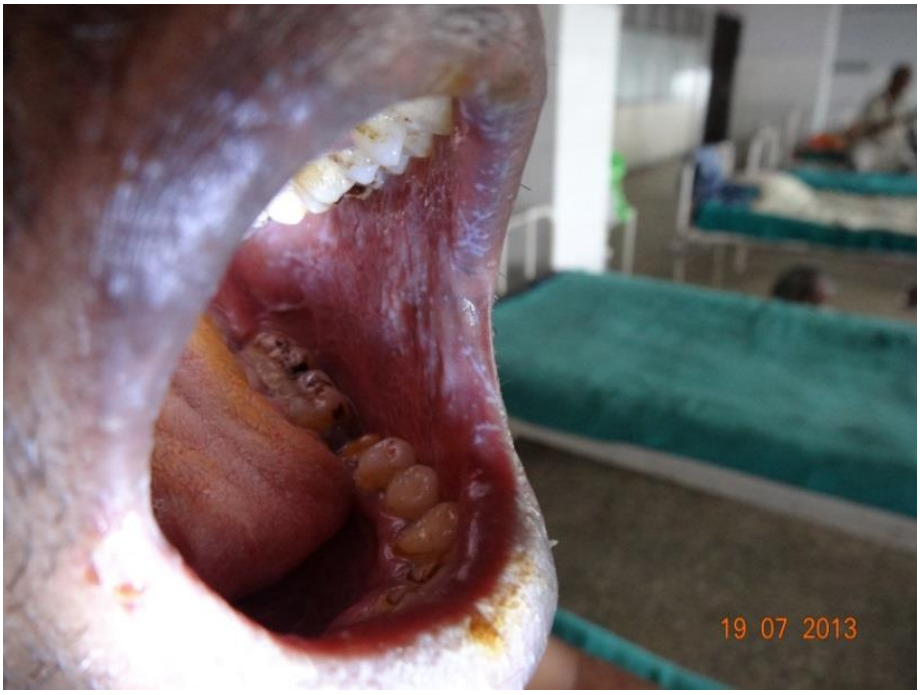
HYPERTROPHIC LICHEN PLANUS



ACTINIC LICHEN PLANUS



ORAL LICHEN PLANUS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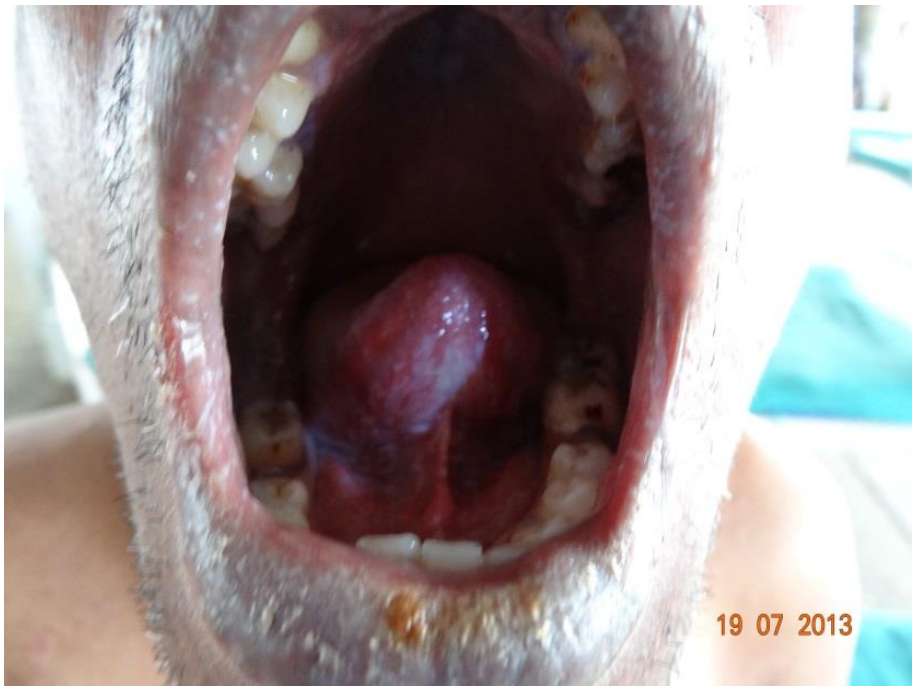
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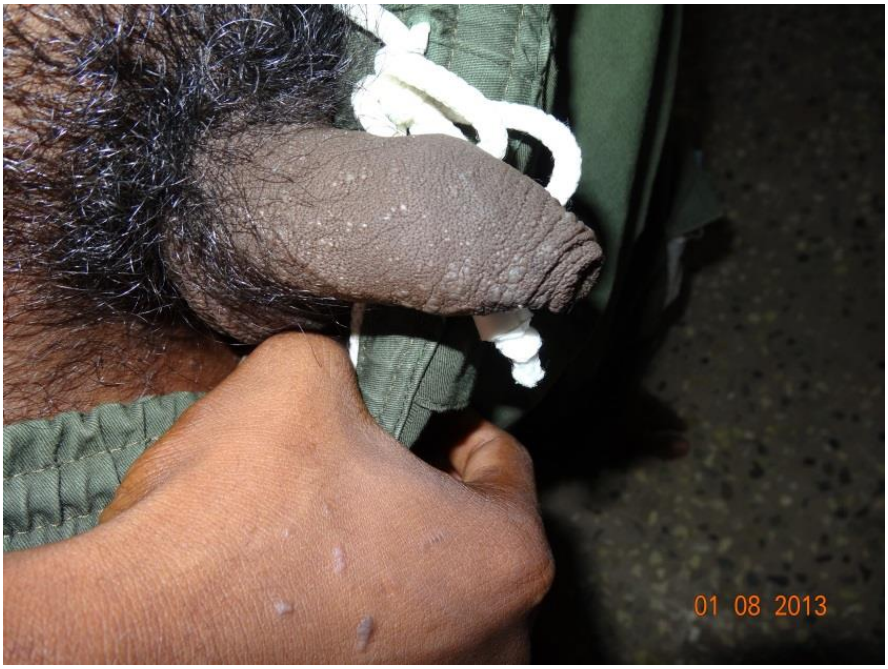
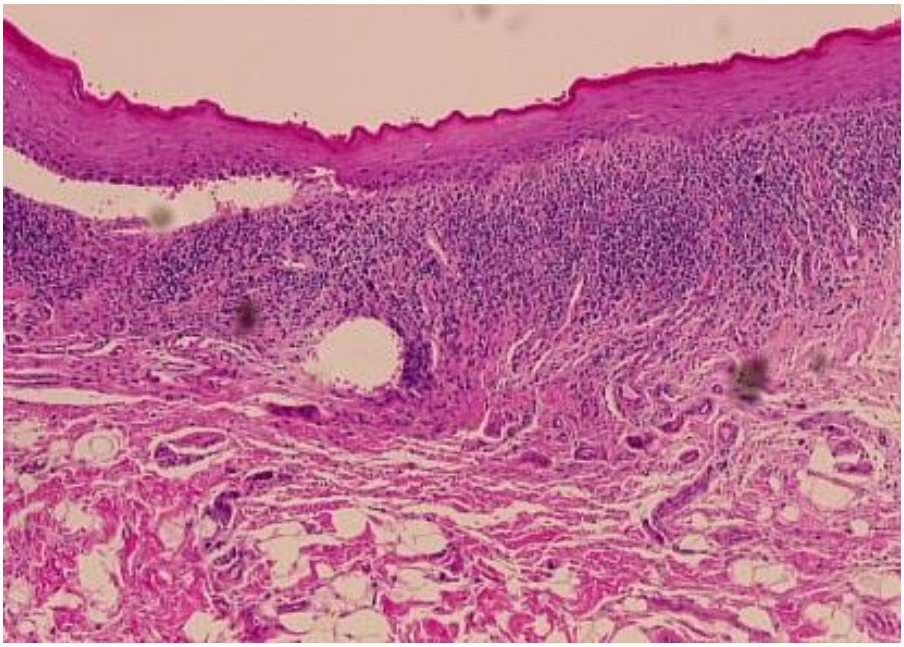
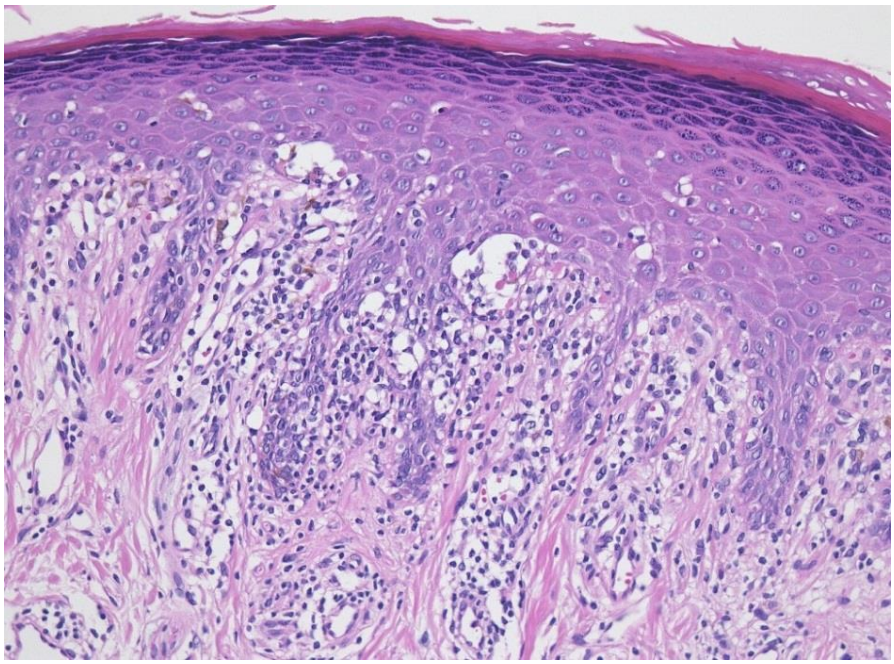


GENITAL INVOLVEMENT





HISTOPATHOLOGY

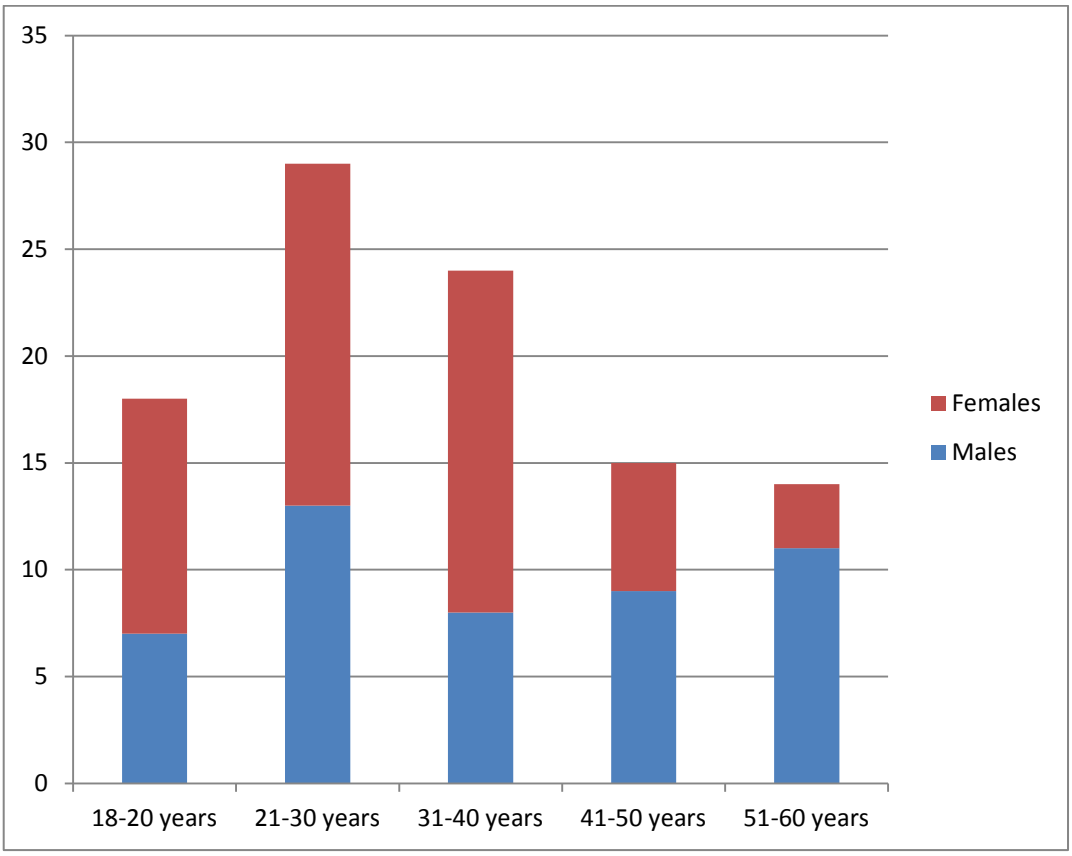
RESULTS

AGE DISTRIBUTION

Age (Years)	No. of cases	Percentage
18-20	Males- 7 Females- 11	18
21-30	Males- 13 Females- 16	29
31-40	Males- 8 Females- 16	24
41-50	Males- 9 Females- 6	15
51-60	Males- 11 Females- 3	14
Total	**100**	**100**

In the present study, most of the cases were in the age group 21-30 years and minimal number was seen at extremes of age group.

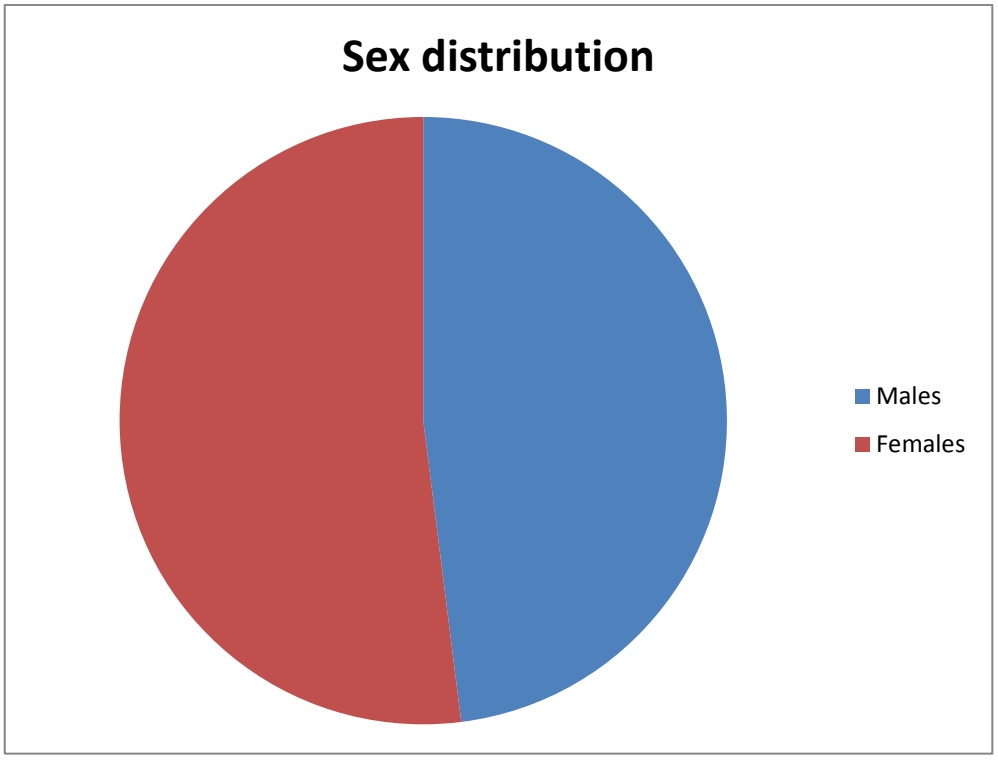
AGE DISTRIBUTION



SEX DISTRIBUTION

Sex	No. of cases	Percentage
Male	48	48
Female	52	52
Total	**100**	**100**

There was slight female preponderance. (M:F = 1:1.08)

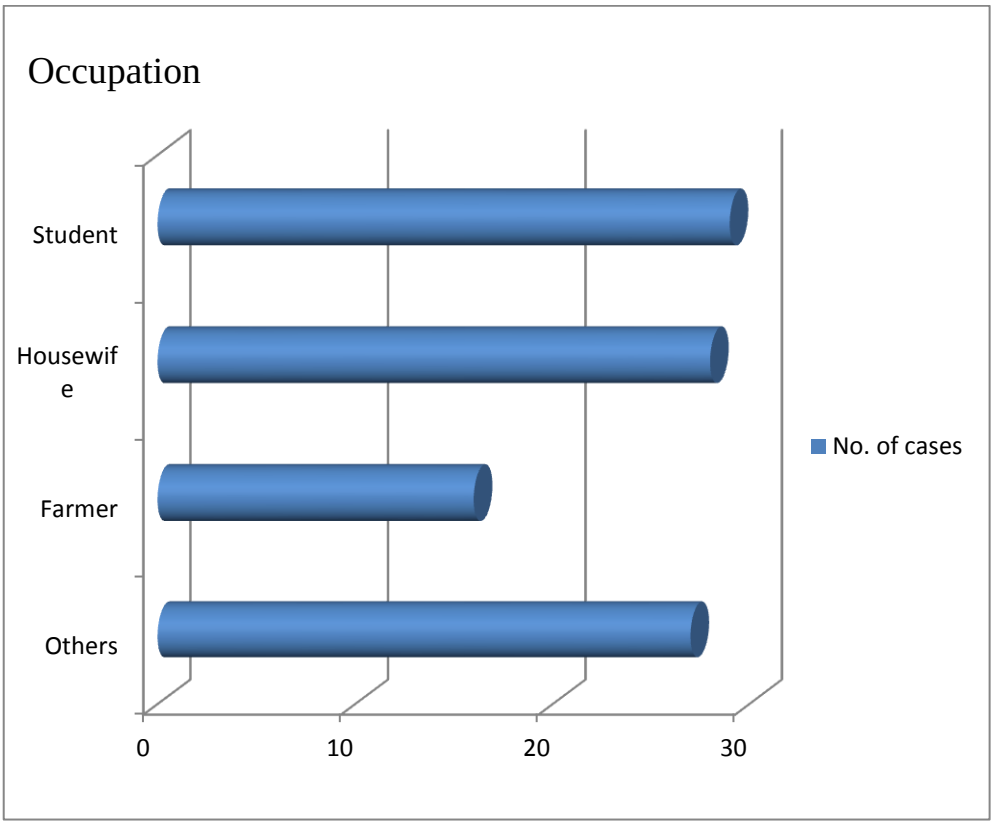

Sex distribution
Males
Females

OCCUPATION

Occupation	No. of patients	Percentage
Housewife	28	28
Student	29	29
Farmer/ Labourer	16	16
Others	27	27
Total	**100**	**100**

In our study, most of the patients were house-wives (Female group), students (Younger age group) and farmers/ labourers (Elderly patients). Remaining cases were working in different fields, including driver, constable, teacher and nurse.

OCCUPATION

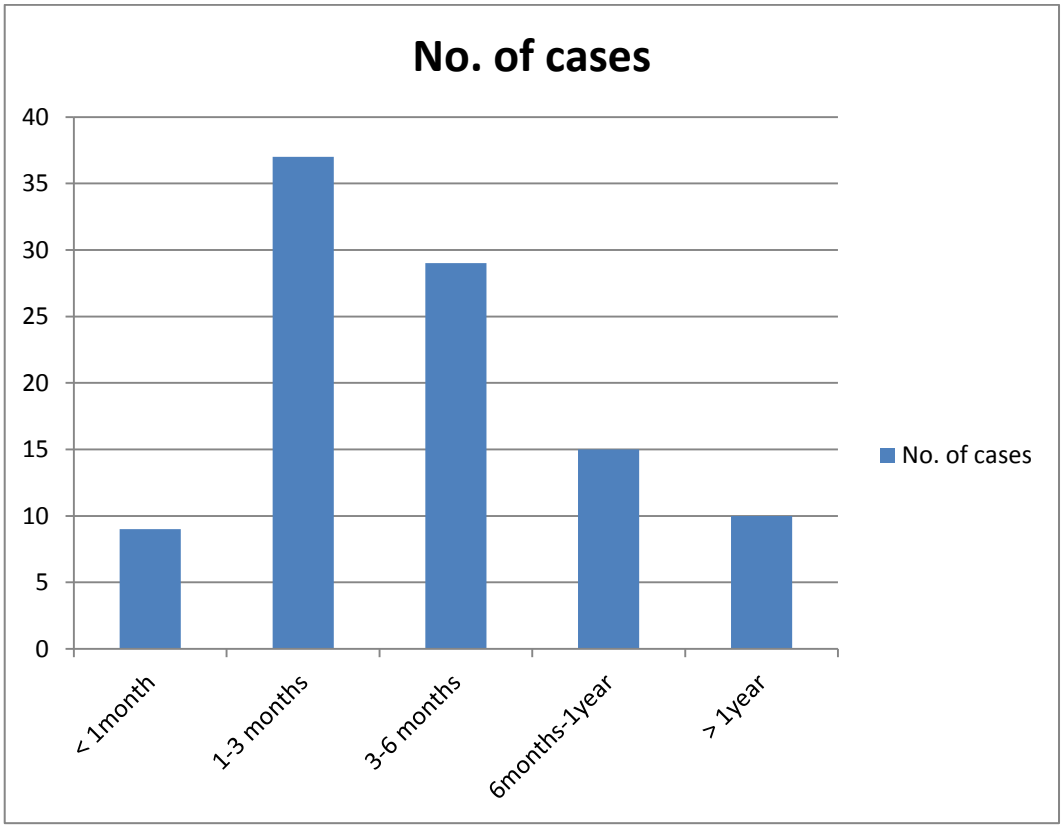

Occupation
Student
Housewife
Farmer
Others
0
10
20
30
No. of cases

DURATION OF DISEASE

Duration	No. of cases	Percentage
<1 month	9	9
1-3 months	37	37
3-6 months	29	29
6months- 1year	15	15
>1 year	10	10
Total	**100**	**100**

Maximum duration of illness was 2 years, but most of patients were having the disease since 1-3 months (37%).

DURATION OF DISEASE

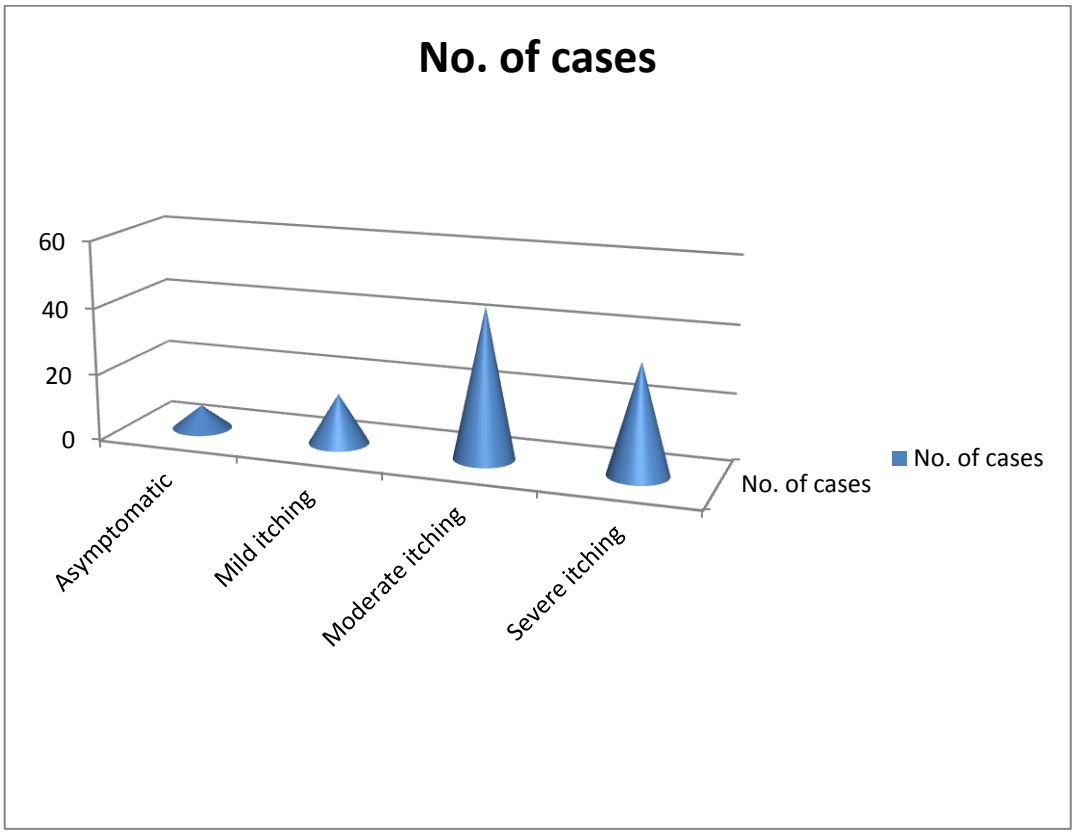


SYMPTOMS

Symptoms	No. of cases	Percentage
Asymptomatic	7	7
Mild itching	15	15
Moderate itching	45	45
Severe itching	33	33
Total	**100**	**100**

In study, only 7 cases were found to be asymptomatic. On the other hand, 78 patients had moderate to severe itching.

SYMPTOMS

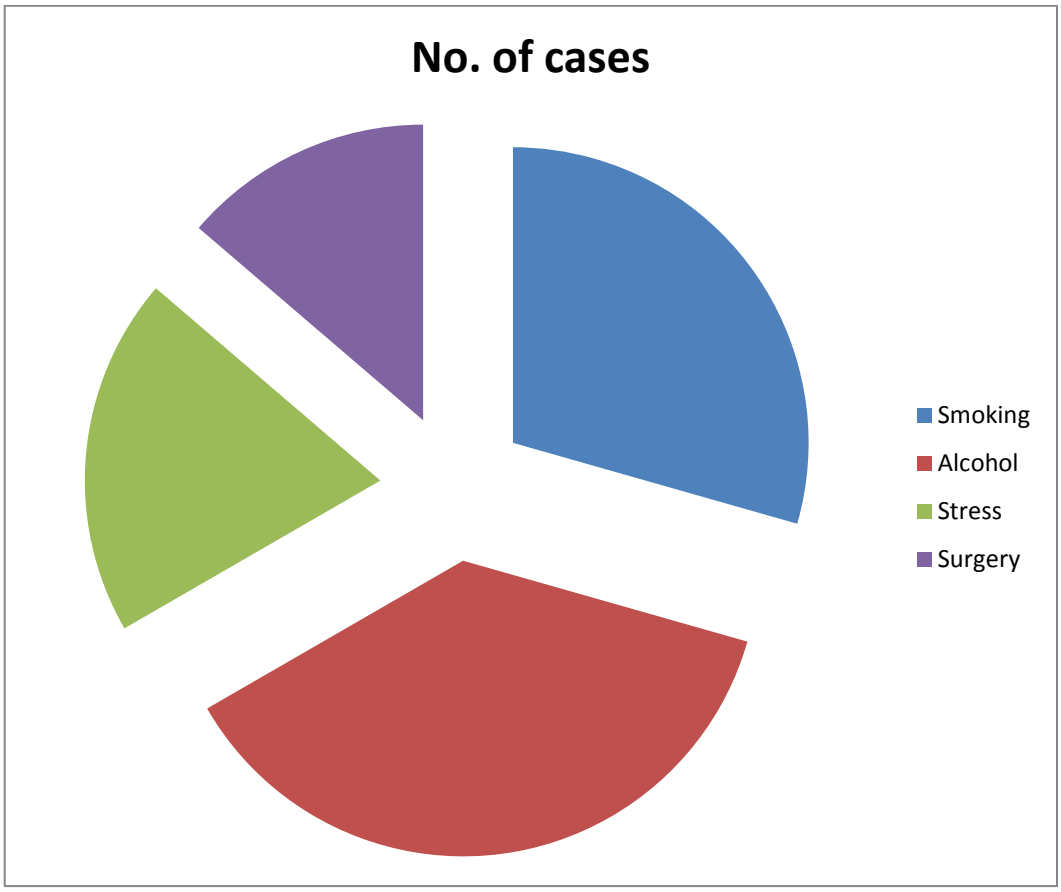

No. of cases
60
40
20
0
Asymptomatic
Mild itching
Moderate itching
Severe itching
No. of cases
No. of cases

RISK FACTORS

Risk factor	No. of cases	Percentage
Smoking	15	15
Alcohol	19	19
Stress	10	10
Surgery	7	7

19 lichen planus patients were alcoholic and 15 of them were smokers. Out of these 34 cases, 8 were smoker as well as alcoholic. 10 patients gave history of emotional stress and 7 cases had undergone a surgery in the past.

RISK FACTORS

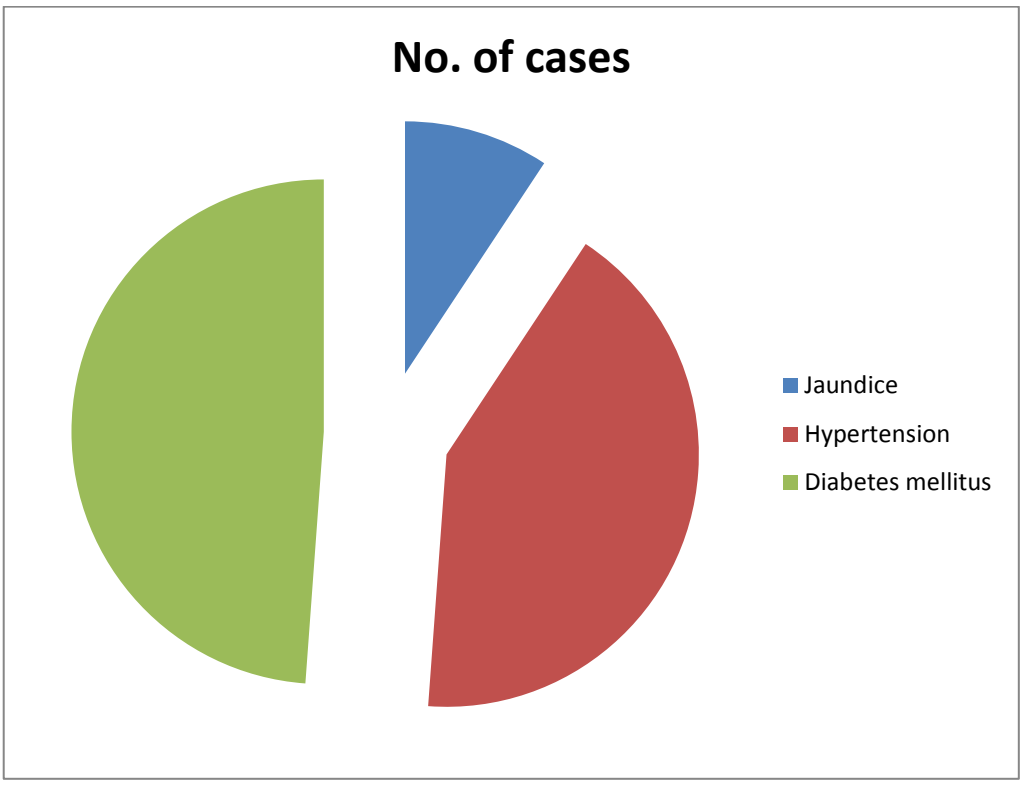


PREVIOUS MEDICAL HISTORY

History	No. of cases	Percentage
Jaundice	4	4
Hypertension	18	18
Diabetes Mellitus	21	21

21 patients were diabetic and 18 were hypertensive. 4 patients had jaundice in the past.

PREVIOUS MEDICAL HISTORY

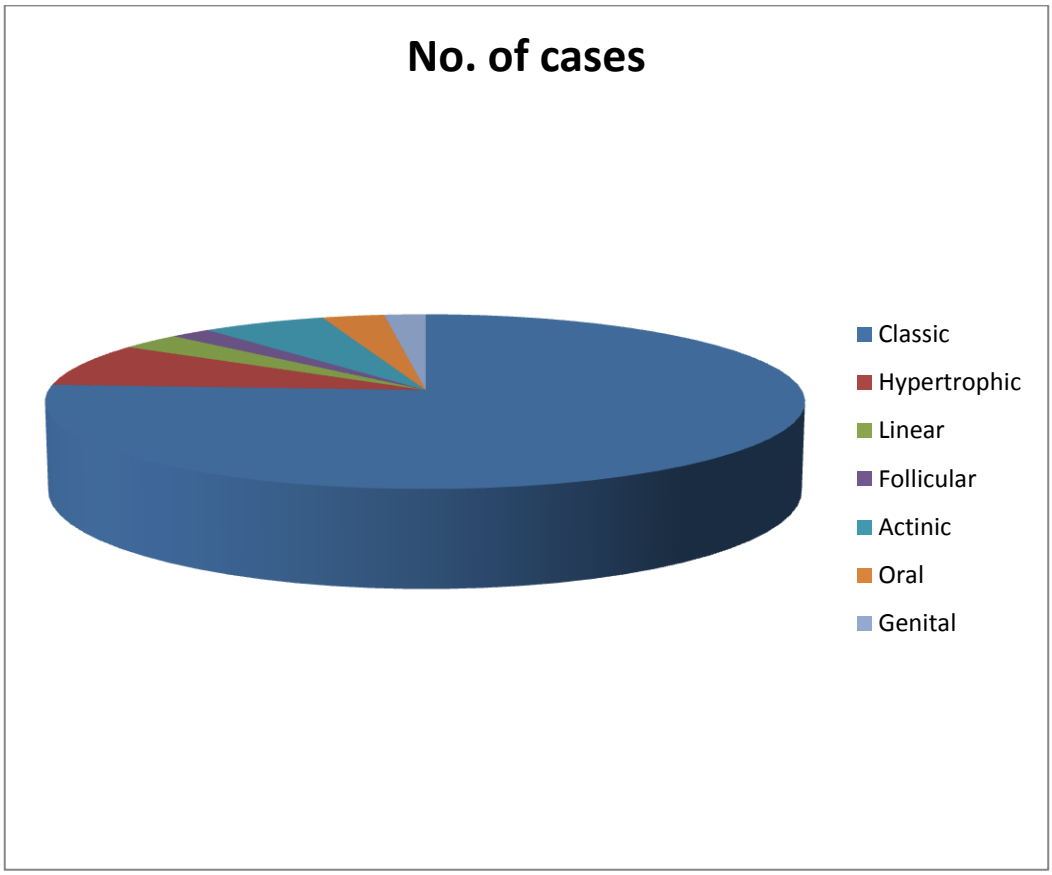


CLINICAL VARIANTS

Variant	No. of cases	Percentage
Classic	76	76
Hypertrophic	8	8
Linear	3	3
Follicular	2	2
Actinic	6	6
Oral	3	3
Genital	2	2
Total	**100**	**100**

Classical lichen planus was the most common clinical form of disease encountered in our study (76%). Hypertrophic lichen planus was seen in 8 patients and the least common variants were follicular and genital lichen planus, with 2 cases each.

CLINICAL VARIANTS



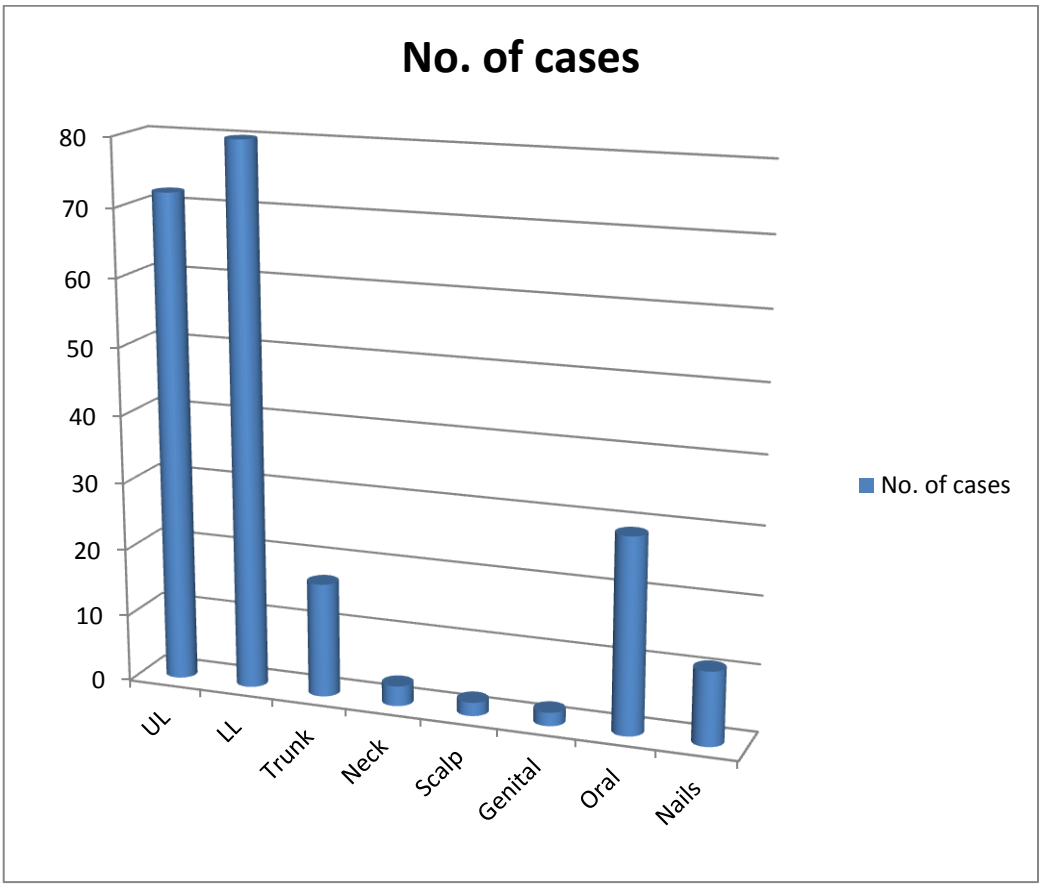
SITES OF INVOLVEMENT

Site	No. of cases	Percentage
Upper limb	72	72
Lower limb	80	80
Trunk	17	17
Neck	3	3
Scalp	2	2
Genital	2	2
Oral	29	29
Nails	11	11

In present study, most commonly, upper and lower limbs were affected. Trunk was involved in 17 cases, nails in 11 cases and oral mucosa in 29 patients.

Only 2 cases showed scalp and genital involvement, each.

SITES OF INVOLVEMENT



ASSOCIATION WITH HCV ANTIBODIES

	Study Group	**Control Group**
No. of cases	100	100
Seropositive cases	0	2

Out of 100 voluntary blood donors, two were HCV seropositive, but none of the lichen planus patients tested seropositive for HCV antibodies.

DISCUSSION

Prevalence

The present study was conducted over a period of one year (July 2013 to June 2014), during which 40,107 new patients attended Skin OPD at Govt. Stanley Medical College & Hospital. Out of these, 100 patients (>18 years and <60 years of age), diagnosed clinically as lichen planus were taken up for study. So, prevalence of lichen planus is about 0.25%.

The prevalence reported worldwide[6] is <1%.Other studies include 0.28% by Anbar[76] and 0.38% by Bhattacharya[14] (India).

Age distribution

In present study, most of the cases were in age group 21-40 years (53%). In the study by Kachhawa et al, 47% cases were in this age group.[78]

Sex distribution

Slight female preponderance was noted in our study.(52%)

Predilection for male sex has been reported by Kachhawa et al[78], but female preponderance was shown in study by Boyd et al.[6]

Occupation

Most of the patients in or study were house-wives (28%), students (29%) and farmers/ labourers (16%).

Naldi et al[79] study showed predominance of manual workers (46%).

Duration of disease

Maximum duration of illness in our study was 2 years, and 37% of patients were having the disease since 1-3 months.

This is in accordance with the study by Sehgal et al, in which most of cases were having disease since 2-3months.[11]

Symptoms

78 patients had moderate to severe itching, 15 had mild itching, and 7 cases were asymptomatic.

According to previous studies, moderate to severe itching has been reported in 95% cases (Sehgal et al)[11] and 73% cases (Kachhawa et al)[78]. But, Fine et al concluded that severity of itching varies with extent of involvement.

Risk factors

In present study, 19 lichen planus patients were alcoholic and 15 of them were smokers. Out of these 34 cases, 8 were both smoker and alcoholic. 10 patients gave history of emotional stress and 7 cases had undergone a surgery in the past.

Naldi et al had reported smoking in 36% cases and alcohol as risk factor in 67% cases.[79]

Previous medical history

In our study, 21 patients were diabetic, 18 were hypertensive and 4 patients had jaundice in the past.

This is supported by studies of Kachhawa et al[78] (Hypertension in 12% cases) and Naldi et al[79] (Diabetes in 5% cases). But is in contrast to the study by Anjana et al[102], where no association was seen with diabetes or hypertension.

Clinical variants

Classic lichen planus was the most common clinical form of disease encountered in our study (76% cases). Hypertrophic lichen planus was seen in 8 patients and the least common variants were follicular and genital lichen planus, with 2 cases each.

Sites of involvement

Our study showed upper and lower limbs (72-80%) as the most common sites of involvement in lichen planus. Trunk was involved in 17% cases, nails in 11% cases and oral mucosa in 29% patients. Only 2 cases showed scalp and genital involvement, each. The result is like that of study by Kachhawa et al[78] (Lower limb involvement in 62% cases). Study by Ebrahimi also showed oral involvement in 29% of patients having cutaneous lichen planus.[77]

Anbar et al[76] reported involvement of both skin and mucosa in 65% cases and only mucosal lesions in 15-35% cases. In other studies, involvement of skin, both skin and mucosa, and mucosa alone was seen in 98%, 68% and 7% cases (Stojanovic et al)[81], 71%, 20% and 12% cases (Sehgal et al)[11], respectively.

Koebner's phenomenon

17% of subjects in present study showed Koebner's phenomenon. This is similar to the result of studies by Fine et al[80] and Boyd et al[6].

Nail changes

In our study, 11% patients had nail changes. Kachhawa et al[78] found nails to be involved in 6.4% cases. But in study by Sehgal et al[11], none of the cases had nail involvement.

Correlation with HCV

S.No.	Study	Place	Year	Lichen planus cases associated with anti-HCV antibodies
1.	Tanei et al[82]	Japan	1995	37.8%
2.	Sanchez-Perez et al[83]	Spain	1996	20%
3.	Imhof et al[84]	Germany	1996	16%
4.	Narayan et al[85]	India	1997	2.66%
5.	Zahra Ghodsi et al[86]	Iran	1998	4.8%
6.	Chuang et al[87]	USA	1999	55%
7.	Tucker et al[88]	England	1999	0
8.	Kirtak et al[89]	Turkey	2000	6.8%
9.	Daramola et al[90]	Nigeria	2000	15.8%
10.	Asaad Tonsi et al[91]	Makkah	2000	26.3%
11.	Leslie et al[92]	USA	2001	17%
12.	Prabhu et al[95]	India (Calicut)	2002	0
13.	Garg et al[100]	Nepal	2002	0
14.	Lodi et al[93]	Italy	2004	19.1%
15.	Bokor-Bratic[94]	Serbia	2004	0
16.	Cunha et al[96]	Brazil	2005	1.5%
17.	Ghaderi et al[97]	Iran	2006	4.1%
18.	Das et al[98]	India (Kolkata)	2006	1.92%
19.	Yarom et al[99]	Israel	2006	1.5%
20.	Stojanovic et al[81]	Slovenia	2008	1.2%

CONCLUSION

The study shows that lichen planus commonly affects young adults, with almost equal male-female ratio. Prevalence of lichen planus is 0.25%.

Most common age group affected is 21-40 years.

Slight female preponderance is seen (M:F = 1:1.08).

Maximum duration is 2 years. But most of patients (37%) have disease since 1-3 months.

Moderate to severe itching is seen in 78% cases. Only 7% cases are asymptomatic.

Alcohol (19%) and smoking (15%) are the most common risk factors.

Diabetes and hypertension are associated in 21% and 18% patients, respectively.

Most common clinical variant is classic type of lichen planus (76%), followed by hypertrophic type (8%).

The most common sites involved are the extremities, with lower limb in 80% cases and upper limb in 72% cases.

Along with cutaneous involvement, 26% of the cases show oral changes. But 3% show only oral lesions (Reticular type) without any cutaneous lesions.

11% patients have nail changes.

Koebner's phenomenon is seen in 17% patients.

2% of controls (voluntary blood donors) showed HCV seropositivity, but none of the lichen planus patients showed positive test for anti-HCV antibodies.

The present study shows no association between lichen planus and hepatitis C infection. Based on this result, it can be concluded that anti-HCV antibody testing is not necessarily required in lichen planus patients having no risk factors for HCV infection in this geographic region.

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ANNEXURES

PROFORMA
(ANNEXURE 1)

NAME:

AGE:

SEX:

OCCUPATION:

ADDRESS:

CHIEF COMPLAINTS:

HISTORY & DURATION OF PRESENT ILLNESS:

PAST MEDICAL HISTORY:

RISK FACTORS:

EXAMINATION:

SITE:

CLINICAL VARIANT:

WICKHAM STRAIE:

KOEBNER PHENOMENON:

NAIL CHANGES:

ORAL INVOLVEMENT:

DIAGNOSIS:

INVESTIGATIONS:

CBC: HB:

TC:

DC:

ESR:

PLATELET:

BLOOD GLUCOSE:

LFT: S. BIL:

SGOT:

SGPT:

ALP:

STP:

S. ALB:

RFT: S. UREA:

S. CREATININE:

HCV SEROLOGY:

CONSENT FORM

(ANNEXURE 2)

Mr/Miss/Mrs:

Age/Sex:

Address:

Phone:

I undersigned Mr/Miss/Mrs._____ have been explained regarding above said study in my regional language.

I have been informed that this study will be done by Dr. Nishant Gupta.

I further state that I have carefully read and understood all the information provided in this form and with full conscious mind, I hereby give my consent to be involved in this study.

I also give consent to take my clinical photograph required for the study purpose.

Signature/Right Thumb Impression of patient:

Signature/Thumb impression of the parent/guardian (In minors):

Witness:

Name: Signature:

Date:

INSTITUTIONAL ETHICAL COMMITTEE, STANLEY MEDICAL COLLEGE, CHENNAI-1

Title of the Work : Study of association between lichen planus and Hepatitis – C virus infection

Principal Investigator : Dr.Nishant Gupta

Designation : PG in MD(Derm)

Department : Department of Dermatology
Government Stanley Medical College,
Chennai-1

The request for an approval from the Institutional Ethical Committee (IEC) was considered on the IEC meeting held on 08.07.2013 at the Council Hall, Stanley Medical College, Chennai-1 at 2PM

The members of the Committee, the secretary and the Chairman are pleased to approve the proposed work mentioned above, submitted by the principal investigator.

The Principal investigator and their team are directed to adhere to the guidelines given below:

1. You should inform the IEC in case of changes in study procedure, site investigator investigation or guide or any other changes.
2. You should not deviate from the area of the work for which you applied for ethical clearance.
3. You should inform the IEC immediately, in case of any adverse events or serious adverse reaction.
4. You should abide to the rules and regulation of the institution(s).
5. You should complete the work within the specified period and if any extension of time is required, you should apply for permission again and do the work.
6. You should submit the summary of the work to the ethical committee on completion of the work.

22/8/13

MEMBER SECRETARY,
IEC, SMC, CHENNAI

KEY TO MASTER CHART

M- Male

F- Female

D- Diabetes mellitus

H- Hypertension

Sm- Smoker

St- Emotional stress

Sg- Surgery in the past

Al- Alcoholic

J- Past history of jaundice

UL- Upper limb

LL- Lower limb

T- Trunk

N- Neck

HT- Hypertrophic lichen planus

MASTER CHART

MASTER CHART

S. No.	Name	Age	Sex	Occupation	Duration	Risk Factors	Site	WS	KP	Clinical Variant	Nail changes	Oral involvement	Anti- HCV Antibody
1	Renuga	38	F	Housewife	4months	D	UL,LL	-	-	Classic	-	+	-
2	Devaki	29	F	Student	2months	-	UL,LL	-	+	Classic	-	-	-
3	Uma	18	F	Student	1month	J	LL	-	-	Classic	-	-	-
4	Thangaraj	30	M	Driver	1month	St,Al	UL,LL	-	-	Classic	-	-	-
5	Vasugi	35	F	Housewife	3months	-	LL	-	-	HT	-	-	-
6	Ganesh	42	M	Driver	4months	Sm,Al	UL,LL,T	-	-	Classic	-	-	-
7	Devi	26	F	Housewife	2months	-	UL,LL	-	+	Classic	-	-	-
8	Jayanthi	56	F	Housewife	10months	D,H	UL,LL,T	+	-	Classic	+	+	-
9	Ruban	55	M	Farmer	1year	Sm,Al,D	UL,LL	-	-	Classic	+	-	-
10	Nirmala	28	F	Housewife	1month	-	LL	-	+	Classic	-	-	-
11	Hemchandran	35	M	Business	5months	St,Al	UL,LL	-	+	Classic	-	-	-
12	Devendran	40	M	Clerk	6months	Al	UL,LL	-	-	Classic	-	+	-
13	Selvarani	18	F	Student	1month	-	LL	-	+	Linear	-	-	-
14	Sarath	19	M	Student	1month	-	UL,LL	-	-	Classic	-	-	-
15	Lalitha	28	F	Housewife	3months	-	LL	-	-	Classic	-	-	-
16	Jamaal	38	M	Labourer	4months	Sm,Al	UL,LL	-	-	Classic	-	-	-
17	Paneerselvam	42	M	Clerk	8months	Sm,H	UL,LL	-	-	Classic	-	-	-
18	Selvaraj	49	M	Business	9months	Al, D	UL,LL	-	-	Classic	-	+	-
19	Nagesh	45	M	Farmer	5months	St,Al	UL,LL	-	-	Classic	-	-	-
20	Kousalya	30	F	Teacher	1month	-	UL,N	-	-	Actinic	-	-	-
21	Balraj	46	M	Constable	3months	Al,D	UL,LL	-	-	Classic	-	-	-
22	Thambiraj	21	M	Student	1month	-	T	-	+	Linear	-	-	-
23	Ileyas	36	M	Job	2months	Sg, D	UL,LL	-	-	Classic	-	-	-

24	Venkatesan	60	M	Farmer	2years	Al,H	LL,T	-	-	HT	+	+	-
25	Vignesh	21	M	Student	20days	-	UL	-	-	Classic	-	-	-

MASTER CHART (Contd.)

S.No.	Name	Age	Sex	Occupation	Duration	Risk Factors	Site	WS	KP	Clinical Variant	Nail changes	Oral involvement	Anti- HCV Antibody
26	Rakib	20	M	Student	1month	-	LL	-	-	Classic	-	-	-
27	Bhavani	23	F	Student	2months	-	UL	-	+	Actinic	-	-	-
28	Paavai	60	F	Labourer	1.5years	Sm,D	UL,LL	-	-	HT	+	+	-
29	Pradalaya	18	F	Student	1month	-	UL,LL	-	-	Classic	-	-	-
30	Jailaxmi	20	F	Student	20days	-	LL	-	-	Classic	-	-	-
31	Gangan	60	M	Ex-constable	2years	Sm,D	UL,LL	-	-	Classic	-	-	-
32	Gomati	40	F	Housewife	7months	H	UL,LL	-	+	Classic	-	+	-
33	Selvi	30	F	Housewife	2months	-	UL,LL	-	-	Classic	-	-	-
34	Babu	46	M	Clerk	6months	Sg, H	UL,Scalp	-	-	Follicular	-	+	-
35	Ravi	28	M	Business	2months	-	LL	-	-	Classic	-	-	-
36	Raj	28	M	Job	4months	-	LL,Penis	-	+	Genital	-	-	-
37	Venkatesh	60	M	Business	1year	Sm,Al,St,D	UL,LL	+	-	Classic	-	+	-
38	Srinivasan	37	M	Labourer	6months	-	UL,LL	-	-	Classic	-	+	-
39	Arumugam	50	M	Farmer	1.5years	Al,D	LL,T	-	-	HT	-	+	-
40	Abdul	29	M	Job	2months	St	UL	-	-	Actinic	-	-	-
41	Kamatchi	19	F	Student	1month	-	LL	-	-	Classic	-	-	-
42	Selvi	23	F	Student	4months	-	UL,LL	-	-	Classic	-	-	-
43	Radha	22	F	Student	20days	J	UL	-	+	Classic	-	-	-
44	Nagarani	40	F	Housewife	9months	Sg, H	UL,LL	+	-	Classic	+	+	-
45	Abinesh	21	M	Student	1month	-	LL	-	-	Classic	-	-	-
46	Praveen	18	M	Student	15days	J	LL	-	-	Classic	-	-	-

47	Vimala	30	F	Housewife	5months	-	UL,LL	-	-	Classic	-	+	-
48	Karthiga	22	F	Student	3months	-	UL,LL	-	+	Classic	-	-	-
49	Panduranga	56	M	Labourer	2years	Sm, D	LL,T	-	-	HT	+	+	-
50	Sharmila	38	F	Housewife	1year	D	UL,LL	-	-	Classic	+	+	-

MASTER CHART (Contd.)

S. No.	Name	Age	Sex	Occupation	Duration	Risk Factors	Site	WS	KP	Clinical Variant	Nail changes	Oral involvement	Anti- HCV Antibody
51	Seshini	18	F	Student	1month	-	UL,LL	-	-	Classic	-	-	-
52	Madhan	19	M	Student	15days	-	LL,Penis	-	+	Genital	-	-	-
53	Kamalama	46	F	Housewife	1.5years	Sg, D	UL,LL,T	+	-	Classic	-	+	-
54	Deepan	21	M	Job	1month	-	UL,N	-	-	Actinic	-	-	-
55	Ravi	48	M	Driver	6months	St,H	Oral	-	-	Oral	-	+	-
56	Dinesh	19	M	Student	2months	-	UL	-	-	Classic	-	-	-
57	Amvardeen	49	M	Farmer	7months	Sm,Al,H	UL,LL	-	-	Classic	-	-	-
58	Dhanam	48	F	Housewife	8months	-	UL,LL,T	-	-	HT	+	+	-
59	Tamizhselvi	48	F	Housewife	6months	D	UL,LL,T	-	-	Classic	-	-	-
60	Hemavathy	39	F	Housewife	6months	-	Oral	-	-	Oral	-	+	-
61	Devakumar	32	M	Job	3months	St,Sm	UL,LL	-	+	Classic	-	-	-
62	Thangalingam	55	M	Farmer	2years	Al,H	UL,LL	-	-	Classic	+	+	-
63	Kanchal	35	F	Housewife	3months	D	LL	-	-	Classic	-	-	-
64	Priya	19	F	Student	10days	-	UL,N	-	-	Actinic	-	-	-
65	Jayanthi	22	F	Student	2months	-	T	-	-	Linear	-	-	-
66	Vinita	19	F	Student	1month	J	UL,LL	-	-	Classic	-	-	-
67	Rajalaxmi	20	F	Student	20days	-	UL	-	-	Classic	-	-	-
68	Velangani	28	F	Housewife	6months	-	UL,LL	+	-	Classic	-	-	-
69	Roopchandran	30	M	Business	5months	St,H	UL,LL	-	-	Classic	-	-	-

70	Imtiaz	20	M	Student	2months	-	LL	-	-	Classic	-	-	-
71	Manoharan	55	M	Farmer	2years	Sm,H	UL,LL	-	-	Classic	-	-	-
72	Sakthivel	60	M	Farmer	1year	Al, D,H	UL,LL,T	-	-	Classic	-	+	-
73	Prabhavathy	18	F	Student	20days	-	UL	-	-	Classic	-	-	-
74	Raja	21	M	Student	6months	-	UL,LL	-	-	Classic	-	-	-
75	Lakshmi	38	F	Housewife	1year	D	UL,LL	-	-	Classic	+	+	-

MASTER CHART (Contd.)

S. No.	Name	Age	Sex	Occupation	Duration	Risk Factors	Site	WS	KP	Clinical Variant	Nail changes	Oral involvement	Anti- HCV Antibody
76	Kamladevi	40	F	Housewife	5months	Sg	UL,LL	-	-	Classic	-	-	-
77	Ahmadnesha	48	F	Housewife	4months	H	UL,LL	-	-	Classic	-	+	-
78	Albert	24	M	Business	4months	Sm,St	UL	-	-	Actinic	-	-	-
79	Naveen	18	M	Student	15days	-	UL	-	+	Classic	-	-	-
80	Palani	59	M	Labourer	1.5years	Sm,Al,D,H	UL,LL,T	+	-	Classic	+	+	-
81	Madhavan	33	M	Driver	6months	Sm,Al	Scalp	-	+	Follicular	-	-	-
82	Balkish	25	F	Clerk	2months	-	LL	-	-	Classic	-	-	-
83	Gayathri	24	F	Student	3months	-	UL,LL	-	-	Classic	-	-	-
84	Lavanya	19	F	Student	1month	-	LL	-	+	Classic	-	-	-
85	Vijaylaxmi	37	F	Constable	8months	-	UL,LL	-	-	Classic	-	+	-
86	Vijaya	35	F	Housewife	6months	-	UL,LL,T	-	-	Classic	-	-	-
87	Shanthi	60	F	Housewife	2years	D,H, Sg	UL,LL,T	-	-	HT	-	+	-
88	Abdul	21	M	Constable	1month	-	LL	-	-	Classic	-	-	-
89	Rukmani	36	F	Nurse	1month	D	UL,LL	-	-	Classic	-	-	-
90	Sumathi	35	F	Housewife	4months	-	Oral	-	-	Oral	-	+	-
91	Shanthi	50	F	Housewife	6months	-	UL,LL	-	-	Classic	-	-	-
92	Dhanpal	57	M	Conductor	1year	Sm,Al,H	LL	-	-	HT	-	-	-

93	Rani	33	F	Housewife	5months	-	UL,LL	-	-	Classic	-	-	-
94	Vijaylaxmi	38	F	Housewife	1year	St,H	UL,LL	-	-	Classic	-	-	-
95	Ramamurthy	30	M	Clerk	4months	-	UL,LL	-	+	Classic	-	-	-
96	Dulkanam	50	F	Housewife	6months	Sg,H	UL,LL	-	-	Classic	-	+	-
97	Kalpana	29	F	Housewife	2months	-	UL,LL	-	-	Classic	-	-	-
98	Nithya	35	F	Labourer	4months	-	UL,LL	-	-	Classic	-	-	-
99	Rathnavelu	32	M	Labourer	6months	-	UL,LL,T	-	-	Classic	-	-	-
100	Moorthy	55	M	Labourer	2years	Al,D	UL,LL,T	-	-	Classic	-	+	-