DERMOSCOPIC ASSESSMENT OF CUTANEOUS SMALL VESSEL VASCULITIS AND CORRELATION WITH CLINICAL AND HISTOPATHOLOGICAL FINDINGS A CROSS SECTIONAL STUDY.

By

Dr. KAVYADEEPA R.M.

Dissertation submitted to

BLDE (Deemed to be University) Vijayapur, Karnataka

In partial fulfillment of the requirements for the degree of

DOCTOR OF MEDICINE IN

DERMATOLOGY, VENEROLOGY AND LEPROSY

Under the guidance of

Dr.KESHAVMURTHY .ADYA

PROFESSOR

DERMATOLOGY, VENEROLOGY AND LEPROSY

BLDE (Deemed to be University)

SHRI B.M.PATIL MEDICAL COLLEGE

HOSPITAL & RESEARCH CENTRE, VIJAYAPUR

KARNATAKA

2020

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MD

IN

DERMATOLOGY, VENEROLOGY AND LEPROSY

LIST OF ABBREVIATIONS

HSP -Henoch Schonlein Purpura

DIF -Direct Immunofluorescence

CSVV-Cutaneous Small Vessel Vasculitis

Nlr- Neutrophil-To-Lymphocyte Ratio

LCV- Leukocytoclastic Vasculitis

EED-Erythema Elevatum Diutinum

PAN - Polyarteritis Nodosa

MPA- Microscopic Polyangiitis

WG- Wegener's Granulomatosis

KD - Kawasaki Disease

C-Pan- Cutaneous Pan

UV- Urticarial Vasculitis

NUV- Normocomplementemic Vasculitis

HUV- Hypocomplementemic Vasculitis

PAN- Polyarteritis Nodosa

CSS- Churg-Strauss Syndrome

GCA - Giant Cell Arteritis

SVV- Small Vessel Vasculitis

ANCA- Anti-Neutrophil Cytoplasmic Antibody

EULAR/PRES - European League Against Rheumatism/Paediatric Rheumatology European Society

DIF -Direct Immunofluorescence

HPE- Histopathological Examination

M:F Ratio – Male:Female Ratio

ABSTRACT

Background: Cutaneous vasculitis encompasses a wide array of diseases characterised by inflammation of the cutaneous blood vessels and surrounding skin tissues. The use of dermoscopy in cutaneous small vessel vasculitis (CSVV), which is a noninvasive diagnostic tool that aids and confirms the clinical diagnosis, has not been investigated. Hence we are undertaking this study.

Objective: This study aimed to establish the dermoscopic criteria in the diagnosis of Cutaneous vasculitis and to correlate dermoscopic features with histopathological findings and NLR and systemic involvement in Cutaneous vasculitis and

Methods: This was a hospital-based prospective cross-sectional study of 30 patients clinically diagnosed with Cutaneous small vessel vasculitis, irrespective of age, between 2020 and 2022.

Results: The study consisted of 30 patients with a mean age of 34.60 ±15.44 years. Males outnumbered females by a ratio of 1.3:1. Optimum cut-off of NLR predicting systemic involvement was found to be 3.615 with sensitivity and specificity of 60% and 93.33% respectively. A statistically significant association was found between NLR and systemic involvement (p value -0.001) was derived. A moderately positive correlation between NLR and the duration of the cutaneous lesions was found (r=0.598, p value 0.000). The red background was the most frequent dermoscopy finding in established lesions of cutaneous vasculitis lesions seen in all the 30 patients (100.0%), followed in descending order by white structureless areas and yellowish areas in 19 patients each (63.33%), red globules in 18 patients (60.0%), and red dots in 16 patients (53.3%). Perifollicular scaling seen in 12 patients (40.0%), follicular keratotic plugs in 11 patients (36.7%), and violaceous patches in 2 patients (6.7%) were other less frequent observations. Dermoscopy in early/evolving lesions (lesions that had been present for less than 2

days) revealed dull red background as the most common finding in all the 30 patients (100.0%) followed by red globules in 8 patients (26.70%) and red dots in 4 patients (13.30%). In terms of dermoscopy-histopathological connection, red globules (p value- 0.011) but not red dots (p value -0.07) were indicative of RBC extravasation. The sparse and dense perivascular infiltrates were represented by white structureless areas (p value 0.023) and yellowish areas (p value 0.007) respectively. On histopathology, a red background did not statistically correlate with dilated vessels (p value 0.5). Red background was the most prevalent dermoscopy finding in 10 individuals with NLR >3.615, followed in descending order by white structureless patches, red globules, red dots, and yellowish areas. Additionally, there was a statistically significant correlation between NLR and the dermoscopy finding of white structureless areas (p value - 0.049) but not with others.

Conclusion: Although dermoscopy cannot completely replace histopathology, it is a valuable method for diagnosing cutaneous small vessel vasculitis and confirming a clinical diagnosis. A particular dermoscopy finding like white structureless areas in our study, may indicate systemic involvement and be linked to a higher NLR value. This suggests that dermoscopy may predict systemic involvement in the CSVV in a noninvasive manner.

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INTRODUCTION

Vasculitides are a group of disorders that manifest in diverse ways and are characterised primarily by inflammation of the blood vessel wall with the involvement of any organ system[1]. Cutaneous vasculitis encompasses a wide array of diseases characterised by inflammation of the cutaneous blood vessels and surrounding skin tissues[2].

It is either idiopathic or induced by infections, drugs, underlying malignancies, or connective tissue disorders, with cutaneous involvement being the most common[3]. It is characterised by inflammation predominantly composed of neutrophils mainly limited to the superficial blood vessel walls. Cutaneous vasculitis may involve the blood vessels alone or be a secondary manifestation of an underlying systemic pathology[2].

"The estimated global incidence of cutaneous vasculitis ranges from 15.4 to 29.4 per million, affecting individuals of all ages.[4] While both genders are affected; equally, the disease's prevalence increases with age at diagnosis, affecting adults more commonly than children[5].

Although Henoch Schonlein purpura (HSP) is known to be one of the more common types of vasculitis in India, epidemiological data on the relative frequency of various types of vasculitis in India is limited. Since managing suspected vasculitis necessitates a thorough search for any treatable underlying cause, its epidemiological and etiological associations must always be thoroughly interpreted[3].

Based on the size and location of the vessels involved, they can cause myriad clinical manifestations[5]. The type of cutaneous lesions is related to the depth of affected vessels. Small superficial vessel involvement causes mostly urticarial but relatively persistent plaques, papules, and palpable purpura. Ulcers, nodules, or livedo are caused by vessel involvement in the dermo hypodermic junction or hypodermis[6]. Confirming vasculitis requires histopathological evidence

of vascular inflammation, whereas direct immunofluorescence (DIF) study helps further categorise the condition. The histopathological and DIF study's diagnostic yield depends on the timing of the biopsy. The fact that essential histological information coupled with DIF and etiological association enables a precise diagnosis of vasculitis syndromes[4], paving the way to the most efficacious therapeutic approach, envisages the need for a similar correlating study. Dermoscopic evaluation of patients with cutaneous small vessel vasculitis (CSVV) facilitates earlier and non-invasive diagnosis before confirmation with biopsy. To the best of our knowledge, the primary study involving dermoscopy in cutaneous vasculitis is done only in urticarial vasculitis and not on other types of cutaneous small vessel vasculitis. Hence we are undertaking this study to establish the dermoscopic diagnostic criteria for cutaneous small vessel vasculitis and correlate the findings with clinical, laboratory, and histopathological findings. The neutrophil-to-lymphocyte ratio (NLR) is a non-invasive, relatively inexpensive, and easily accessible laboratory parameter that incorporates two constituents of the immune system: the innate immune response, which is chiefly mediated by neutrophils, and adaptive immunity, which is influenced by lymphocytes and has a superior predictive ability over other inflammatory parameters[7]. It is an effective inflammatory biomarker for predicting systemic involvement in IgA vasculitis.[8] Since increased NLR is associated with systemic involvement, we intend to correlate the dermoscopic findings with NLR to determine whether any dermoscopic results will predict internal involvement.

AIMS & OBJECTIVES OF THE STUDY:

1. Dermoscopic analysis of cutaneous lesions of vasculitis & correlation with histopathological changes

2. Correlation of dermoscopic findings with Neutrophilic lymphocyte ratio (NLR) reflecting systemic invovment.

3. Correlation of NLR with the duration of the cutaneous manifestation

REVIEW OF LITERATURE

Vasculitis is a clinicopathologically defined process characterised by inflammation and necrosis of blood vessels that can affect any body organ system[9].

Cutaneous vasculitis refers to a wide array of diseases that primarily affect the blood vessels and surrounding skin tissues, resulting in altered microcirculation, ischemia, and damage[10].

The condition can affect any blood vessel, but post-capillary venules are the most usually encountered[11].

Skin lesions can present as a component of vasculitis, which can also affect internal organs, with cutaneous involvement being the first sign of disease in some instances[12].

HISTORY:

The Latin word 'purpura' may have derived from the Greek word 'Porphyra,' a colour produced by several varieties of sea snails in the 'muciridae' family[13]

Purpura was initially used to describe infectious diseases like hemorrhagic fevers. Later, the English dermatologist Robert William extensively about the condition in his classic work on cutaneous diseases (1808), which included descriptions of purpura associated with Henoch-Schönlein[14,15].

He also described purpura's greater propensity for lower extremities, its occurrence as groups of lesions, and its association with various systemic diseases[15].

Johann Lukas Schönlein, his pupil Eduard Heinrich Henoch, and afterwards William Osler described a wide range of purpura and small-vessel vasculitis-related signs and symptoms, including arthritis, abdominal pain, peripheral neuropathy, pulmonary haemorrhage, and nephritis [16-19].

Zeek *et al*. linked purpura to leukocytoclastic vasculitis (LCV) in 1948 and 1952. This type of vasculitis affecting the small vessels was labelled hypersensitivity angiitis[20-21].

Henry Radcliff Crocker (1845-1909), an English dermatologist, evaluated a six-year-old male child with discrete, tender, purplish red nodules over his knees, gluteal region, fingers, and elbows in 1893. He entitled this condition as erythema elevatumdiutinum (EED)[15].

Later that year, in 1929, John Besancon and Fred Weidman described the condition as a type of vasculitis[22].

In 1866, Rudolf Maier and Adolf Kussmaul described a 27-year-old patient with fever, cough, weight loss, abdominal pain, paresthesias, polyneuropathy, and proteinuria. The condition was initially known as periarteritis nodosa but was later renamed polyarteritis nodosa (PAN)[23].

In Germany, Friedrich Wohlwill elaborated on microscopic polyangiitis (MPA) and differentiated it from polyarteritis nodosa[24].

Heinz Klinger, a medical student, was the first to describe Wegener's granulomatosis (WG), a vasculitis of both small and medium vessels. Later, Friedrich Wegener, a pathologist, observed many manifestations in 11 patients, including sniffles, destructive lesions of the nose and throat, upper airways, spleen, and kidneys.

He recognised the combination of vasculitis and granuloma formation as pathological changes[25,26].

EPIDEMIOLOGY:

"The annual cutaneous vasculitis incidence varies from 15.4 to 29.4 cases per million"[3]. The condition affects individuals of all age groups, common among female patients over males and adults outnumbering children[4].

Henoch-Schonlein purpura (HSP) is common among children but not uncommon in adults[7], with an average annual incidence of 3.0- 26.7 cases per million children [27], accounting for approximately 10% of vasculitis and being the most frequent cause of vasculitis in children (90%)[28].

The incidence rate of HSP in adults is 1.0-1.5 cases per million, while the overall annual incidence is 14 cases per million people [29].

Data on the prevalence of cutaneous vasculitis in the Indian population is scarce.

Table 1: Type of vasculitis with predominant age and gender[27]

TYPE OF VASCULITIS	**AGE GROUP**	**SEX (M:F)**
Henoch Schonlein purpura (HSP)	Children	M=F
Kawasaki disease (KD)	Children	M>F
Cutaneous PAN (c-PAN)	Children	
Urticarial vasculitis (UV)	Young adult	
Normocomplementemic vasculitis (NUV)	30-40 years	F>M
Hypoocomplementemic vasculitis (HUV)	-	Almost exclusive in females
Nodular vasculitis	-	F> M
Behcet's disease	Young adult	M=F

Takayasu's arteritis	<40years	F>M
Wegener's granulomatosis (WG)	Middle age	M>F
Polyarteritis nodosa (PAN)	Middle age	M>F
Churg-strauss syndrome (CSS)	Middle age	M>F
Giant cell arteritis (GCA)	Elderly	F>M

CLASSIFICATION:

TABLE 2: 2012 International Chapel Hill Consensus Conference on the nomenclature of Vasculitides: [30]

LARGE VESSEL VASCULITIS:
Takayasu arteritis (TAK) Giant cell arteritis (GCA)
MEDIUM CELL VASCULITIS:
Polyarteritis nodosa (PAN) Kawasaki disease
SMALL VESSEL VASCULITIS: (SVV)
Anti-neutrophil cytoplasmic antibody (ANCA) – associated vasculitis: a) Microscopic polyangiitis (MPA) b) Granulomatosis with polyangiitis

c) Wegener's granulomatosis d) Eosinophilic granulomatosis with polyangiitis (Churg Strauss)
IMMUNE COMPLEX SVV: **a)** Antiglomerular basement membrane disease (anti GBM) **b)** Cryoglobulinemic vasculitis **c)** IgA vasculitis (Henoch-Schonlein purpura) **d)** Hypocomplementemic urticarial vasculitis (HUV)
VARIABLE VESSEL VASCULITIS: (VVV) Behcet's disease Cogan's syndrome
SINGLE ORGAN VASCULITIS: Cutaneous leukocytoclastic angiitis Cutaneous arteritis Central nervous system vasculitis Isolated aortitis Others
VASCULITIS ASSOCIATED WITH SYSTEMIC DISEASES: Lupus vasculitis Rheumatoid vasculitis Sarcoid vasculitis Others
VASCULITIS ASSOCIATED WITH PROBABLE AETIOLOGY: Hepatitis C virus-associated cryoglobulinemic vasculitis

Hepatitis B virus-associated vasculitis
Syphilis associated aortitis
Drug-associated immune complex vasculitis
Drug associated ANCA associated vasculitis
Cancer-associated vasculitis

ETIOLOGY:

In approximately 50% of cases, cutaneous vasculitis runs a self-limited course limited to the skin with no apparent cause, triggering factor, or underlying systemic disease. It is referred to as idiopathic cutaneous leukocytoclastic vasculitis (LCV)[31].

Table 2 describes the other causes, such as recent infection (15-20%), inflammatory or autoimmune connective diseases (15-20%), drug ingestion (10-15%), and malignancy (2-5%). According to Khetan *et al*., the most common culprit agents were 18 drugs, with "nonsteroidal anti-inflammatory drugs (NSAIDs) being the most commonly associated drugs," [32] followed by antibiotics.

Infections and drugs are the most causative factors, according to Baigrie *et al*. [33], after idiopathic aetiology.

Blanco *et al*.[34] stated that infections and connective tissue disorders were the most common etiological agents.

Upper respiratory tract streptococcal infections are the most common infectious triggers[35]. In drug-induced vasculitis, the onset of symptoms is noticed to be 1-3 weeks after the commencement of the drug[35].

Despite IgA vasculitis being immune complex-mediated, few associations such as genetic causes, drugs, infections, food allergies, insect bites, cold weather, and trauma have all been proposed, though not conclusively proven[36].

Cryoglobulinemic vasculitis is a systemic vasculitis caused by an immune complex deposition affecting small to medium-sized vessels. Cryoglobulinemia is classified into three subtypes: monoclonal (type I), "mixed" (monoclonal and polyclonal) (type II), and polyclonal (type III). Type I is associated with haematological disorders, whereas vasculitis is only noted in cryoglobulinemia types II and III. Type II ("mixed") has been linked to autoimmune connective tissue diseases, particularly rheumatoid arthritis, followed by Sjögren's syndrome and systemic sclerosis in a minority of the patients. In contrast, hepatitis C virus (HCV) is known to be the underlying disorder in over 80% of patients[37].

PAN is classified into two subtypes: systemic and cutaneous. Systemic PAN has been associated with hepatitis B infection. Hepatitis C, cytomegalovirus, human immunodeficiency virus, parvovirus B19, and human T-lymphotropic virus are other infectious associations[38]. Streptococcal infections have been associated with cutaneous PAN in paediatric populations [39].

Table 3: Common causes of cutaneous vasculitis [27,35]

1. Infection	Cutaneous -Streptococcus, Staphylococcus aureus, Mycobacterium leprae, Candida albicans, Herpes simplex, Plasmodium, Schistosoma [27] Systemic- Hepatitis B and C virus [27]

	Human immunodeficiency virus [35]
2. Drugs	NSAIDs Antibiotics (Penicillins, cephalosporins, sulfonamides, tetracyclines, erythromycin, clindamycin, vancomycin, minocycline) PAS, Insulin, Thiazide, Tamoxifen, Oral contraceptives, Allopurinol, Hydralazine
3. Inflammatory condition	Inflammatory bowel disease (Crohn's disease, ulcerative colitis) Cryoglobulinemia Antineutrophilic cytoplasmic antibody (ANCA) associated vasculitis Behcet's disease
4. Connective tissue diseases	Lupus erythematosus Dermatomyositis Rheumatoid arthritis Sjogren's syndrome
5. Malignancy	Haematological: Chronic myelomonocytic leukaemia, lymphoid malignancy Solid organ: Head and neck, breast, renal, bronchogenic, colonic, prostatic

6. Miscellaneous	Vaccines, serum products, insecticides, petroleum, gluten, UV light

Flowchart 1: Pathogenesis of cutaneous vasculitis[40]:

Antigenic triggers (Infections, drugs, tumours)

↓

Production of antibodies

↓

Circulating Immune complex formation and deposition in and around the blood vessel wall

↓

Complement cascade activation and generation of C3a and C5a (anaphylatoxins)

↓

Degranulation of mast cells and production of cytokines and chemokines

↓

Expression of adhesion molecules

↓

- Increased vascular permeability
- Neutrophil chemotaxis
- Further deposition of immune complexes

⇩

Degranulation and destruction of neutrophils (leukocytoclasia)

⇩

Liberation of proteolytic enzymes (collagenase, elastase)

- Destruction of the vessel
- Formation of platelet thrombi

Ischemia, haemorrhage and necrosis of tissues involved

Clinical signs and symptoms

CLINICAL FEATURES:

There are numerous cutaneous manifestations of vasculitis, which are attributed to vessels that are primarily involved. The most common cutaneous manifestation of cutaneous vasculitis is palpable purpura, which can range in size from 1 millimetre to a few centimetres[35]. Palpability indicates the presence of inflammatory cell infiltrate[41]. They are initially erythematous macules, evolve into papules, nodules, vesicles or bullae, pustules, annular lesions, or necrotic ulcers, and then heal with post-inflammatory hyperpigmentation. They are distributed symmetrically over stasis-prone regions, typically the lower extremities, including the lower legs and ankles[42] . "Involvement of the upper extremities, trunk, head, and neck is uncommon and frequently indicates more severe illness or concurrent systemic vasculitis"[4] In cutaneous vasculitis linked to connective tissue disorders, Raynaud's phenomenon and peripheral cyanosis are frequent[4].

In Wegener's granulomatosis (WG), chronic mucosal ulcers of the mouth and nose are typical. A pathognomonic sign of WG is strawberry gingival hyperplasia (hyperplastic gingivitis with

petechiae). Prolonged recurrent pansinusitis may be the first sign of WG before other organ involvements become apparent. Persistent nasal polyps are seen in Churg Strauss syndrome[27]. Table 4 illustrates that cutaneous involvement in vasculitis affects small and medium-sized arteries.

TABLE 4:

Clinical presentation based on the predominant vessel involved [1,40,4]

Size of the blood vessel	Cutaneous features
Small vessel	Purpuric macules and purpura, urticarial plaques, nodules, hemorrhagic vesicles and bullae
Medium vessel	Subcutaneous deep nodules, livedoreticularis, infarction, deep ulcers, gangrene
Large vessel	Claudication of limbs, absence of pulses, asymmetric blood pressure, aortic dilation, bruit[4]

"Vasculitis resulting from exposure to an inciting factor, such as a medication or an infection, occurs after 7 to 10 days, whereas a latency of weeks to years may occur between the appearance of symptoms and signs of systemic disease following the onset of cutaneous vasculitis[1].

Three patterns of disease evolution in cutaneous vasculitis[4] :

1. "A single acute, self-limited episode (resolved in < 6 months) of vasculitis often associated with a drug or infectious trigger[3]".

2. “A relapsing disease with symptom-free periods usually found in patients with HSP and associated vasculitis”.

3. “A chronic, unremitting disease often associated with cryoglobulinemia, hypergammaglobulinemia and malignancy”.

For several weeks, new lesion formation may persist. Although 10% of individuals will experience recurrence of the lesions, they subside within a few weeks or months[40].

According to Khetan *et al*.[32], palpable purpura, which was seen in 43 out of 61 (70.5%) patients, was the most common cutaneous lesion. “Clinical evidence of deep-seated nodules, ulcers, or gangrene was detected in 14 (22.9%) patients “[32]. Thirty-two (52.4%) of the patients also had involvement of faces, trunks, or upper limbs [32].

Palpable purpurae were the most frequent cutaneous manifestation in 43 (86%) patients, according to Gupta *et al*[43]. The most common sites of purpurae involved were the legs and ankles, followed by the thighs, buttocks, forearm, belly, back, and chest[43].

IgA VASCULITIS / HENOCH- SCHONLEIN PURPURA (HSP)

IgA vasculitis is an immune-complex vasculitis characterised by the deposition of IgA1 immune deposits in the wall of cutaneous vessels. It affects children and adults, with a peak occurrence between the ages of 40-60years.

Definition of HSP by “European League Against Rheumatism/Paediatric Rheumatology European Society (EULAR/PRES)”[44]

Mandatory criterion à palpable purpura

+

Presence of at least 1 of the following manifestations:

(1) Abdominal pain, diffuse in nature; (2) Biopsy showing predominant IgA deposition; (3) arthralgia/arthritis; (4) renal involvement (proteinuria and/or hematuria)

Purpura, colicky pain abdomen & arthritis are classical findings. A characteristic rash that appears in crops persists for an average duration of 3 weeks. The characteristic rash, which typically develops in crops and lasts an average of 3 weeks, is the condition's defining feature. It commonly affects the gluteal region and upper thighs in children and over feet, ankles, and legs in adults.[45] Relapses and long-term complications are more common in affected adults compared to children[46].

The most significant cause of mortality in IgA vasculitis is renal pathology, which can appear up to 3 months after the rash first appears and can last for up to 6 months. In 2-5% of patients, end-stage renal failure may develop[45].

Table 5: Systemic involvement in vasculitis:[27,40,47]

Constitutional	Fever, chills, weight loss, fatigue
Musculoskeletal	Arthralgia /arthritis (non-erosive in nature) Myalgia, weakness
Gastrointestinal	Pain abdomen, nausea, vomiting, gastrointestinal haemorrhage, melena, hematemesis, intussusception, acute appendicitis, bowel infarction, and ileal stricture.
Renal	Microscopic hematuria, proteinuria,

	Pedal oedema Membranoproliferative glomerulonephritis (MPGN)
Respiratory	Dyspnea, cough, hemoptysis, wheezing.
Cardiac	Angina, palpitations Pericardial rub, pericardial oedema, Congestive cardiac failure
Neurological	Paresthesia, weakness, numbness Abnormal reflexes, wrist and foot drop
Mucosal	Xerostomia /xerophthalmia Nasal/ oral ulcers Sinus/ nasal congestion

TABLE 6: OTHER SINGLE ORGAN (SKIN) SMALL-VESSEL VASCULITIDES[40,47]

SUBTYPE	**EPIDEMIOLOGY**	**CUTANEOUS INVOLVEMENT**
Urticarial vasculitis	Women > men It may be associated with	Erythematous indurated wheals with purpura, macular erythema, livedo

	connective tissue disorders and hematologic malignancies.	reticularis, angioedema, nodules and bullae Lesions last for five days.
Erythema elevatumdiutinum	Rare Entity Common in the 4^{th} to 7^{th} decade	Red-purple or yellow papules, plaques or nodules over joints and gluteal region
Acute hemorrhagic oedema of infancy	Children < 2 years of age	Edematous petechiae and ecchymoses, painful in nature, oedema of the face, targetoid lesions with bullae and necrosis. Lesions can be recurrent and chronic.
Eosinophilic vasculitis	Idiopathic	Purpuric papules and plaques, pruritic and recurrent in nature, angioedema
Granuloma faciale	Common in the 4^{th} to 6^{th} decade	Smooth red to greyish brown nodules and plaques with

		telangiectasia and prominent follicular orifices over face

TABLE 7: OTHER SMALL VESSEL IMMUNE COMPLEX ASSOCIATED VASCULITIDES[40,47]

Cryoglobulinemic vasculitis	Type 1 -Monoclonal IgM > IgG Associated with lymphoproliferative disorders and plasma cell dyscrasias	Meltzer's triad – purpura, arthralgia and weakness. Erythematous macules, nodules, ecchymoses Extracutaneous features- sensory neuropathy Mononeuritis multiplex Renal – Membranoproliferative glomerulonephritis
	Type 2- Monoclonal IgM (>IgG) against polyclonal IgG Type 3 – Polyclonal IgM against polyclonal IgG Associated with Hepatitis C > B, HIV, Rheumatoid arthritis, and lymphoproliferative	

	disorders.	
Hypocomplementaemic urticarial vasculitis	Predominant in women of 3rd decade Associated with SLE	Erythematous wheals with induration with purpurae, nodules, livedoreticularis and bullae Glomerulonephritis, arthritis, pain abdomen, chronic obstructive pulmonary disease, episcleritis, uveitis, conjunctivitis
Antiglomerular basement membrane vasculitis disease/Good pasture syndrome	Seen in both children and adults (3rd and 7th decades)	Erythematous macules over the instep of the foot Hemoptysis, fatigue, dyspnoea and cough

TABLE 8: SMALL VESSEL ANCA- ASSOCIATED VASCULITIS[40,47]

Microscopic polyangiitis	Common after 6th decade	Palpable purpura over stasis-prone areas, oral cavity ulcers, splinter haemorrhages, livedo reticularis

		Glomerulonephritis and pulmonary haemorrhage, sensorimotor neuropathy
Granulomatosis with polyangiitis / Wegener's granulomatosis	Both children and adults	Palpable purpura over dependant areas, infarcts over digits, papules, vesicles and nodules Oral cavity ulcers Upper respiratory tract involvement- otitis, epistaxis, rhinorrhea, sinusitis Lower respiratory tract involvement- cough, breathlessness, chest pain, cavities on chest x-ray.
Eosinophilic granulomatosis with polyangiitis / Churg Strauss syndrome	Most common between 15-70 years	First phase – Bronchial asthma, nasal polyps and allergic rhinitis Second phase- Tissue and peripheral eosinophilia Third phase – Vasculitis characterised by palpable

		purpura, papules, infiltrated nodules, livedo reticularis

A preliminary clinical diagnosis of cutaneous vasculitis is made with the patient's history and physical examination confirmed with histopathology, direct immunofluorescence, and relevant laboratory testing.

Investigations required for a diagnosis to be confirmed

SKIN BIOPSY:

Evidence of microscopic vascular inflammation is confirmatory for the clinicopathological diagnosis of vasculitis[49]. Biopsy from the lesional skin separately should be optimally taken for both histopathological examination and direct immunofluorescence (DIF)[1].

HISTOPATHOLOGICAL EXAMINATION:

A deep punch/incision biopsy from a fresh lesion less than 48 hr old is ideal[40]. In the case of CSVV, early lesions from the uppermost portion of the limb are chosen[27]. The main characteristics of CSVV include segmental vascular wall inflammation in an angiocentric pattern, endothelial swelling, leucocytoclasia, fibrinoid necrosis and extravasation of erythrocytes[40]. Lesions younger or older than the designated time frame may have a predominance of lymphocytic infiltration and lack of leucocytoclasis and fibrinoid necrosis[27]. In a study by Nandeesh *et al*., biopsies were done between less than 72 hours (3 days) and 6 months after the onset of lesions. Leukocytoclastic vasculitis was the most common histopathological finding in 130 of 198 cases (66%), preceded by lymphocytic vasculitis in 35

patients (18%).35 51 out of 53 patients (96%) showed small vessel involvement, while just 2 (4%) had medium vessel involvement, according to Khetan *et al*[31].

DIRECT IMMUNOFLUORESCENCE STUDY:

Both the timing of the biopsy and the presence of extracutaneous characteristics have a significant influence on DIF positivity[28]. Sample for DIF should be chosen from the most proximal, fresh, non-infarcted lesion of less than 6 hours in duration[27].Biopsy from stasis-prone area viz lower leg may demonstrate nonspecific fluorescence due to hydrostatic extravasation of immune complex[27]. The immunofluorescence finding correlates inversely with the age of the biopsied lesion. Within the first 48 hours, 100% of biopsies will be positive for immunoglobulins, 70% will be positive between 48 and 72 hours, and no immunoglobulins will be detected after 72 hours; however, complement can still be demonstrable in more than 50% of vasculitic lesions after 72 hours[4].

IgM, C3, and fibrin are the most common immune deposits within the blood vessels. Although not specific, IgA deposits in the vessel wall differentiate HSP from other types of cutaneous small vessel vasculitis. Histopathological examination of a skin biopsy is confirmatory, while DIF examination adds to this and aids in the classification of vasculitis[27].

In a study by Khushboo *et al*., DIF was positive in 60% (119/198) of the cases, with vascular IgA deposition being the most common, followed by C3. DIF confirmed the clinical diagnosis of Henoch-Schonlein purpura in 61.5% (40/65) of the cases, and there was a variable nonspecific deposition of C3 and IgM in 42% of the other cases[50]. DIF was positive in 39% (n = 77) of cases, with C3 positive in 26% (n = 52) and IgA positive in 23% (n = 46) in a study done by Nandeesh *et al*[35]. In a retrospective study by Takatu *et al*. on 282 patients, DIF was observed to be overall

positive in 235 (70.21%) patients, and C3 was the most common deposit found." IgA deposition was seen at a relatively young age[45].

LABORATORY EVALUATION:

"The main targets of laboratory assessment are to search for an underlying cause, to exclude internal organ involvement[40].

NLR, an indicator of systemic inflammation, has been used as a valuable tool for diagnosing and predicting the prognosis of multiple conditions[51]. It is a stable blood parameter less affected by conditions like dehydration, overhydration, and laboratory techniques[52.] Atopic dermatitis, allergic rhinitis and bronchial asthma are among the conditions associated with elevated NLR levels[52]. High NLR values have been linked to non-allergic diseases such as various malignancy states, neurological disorders (Parkinson's disease, multiple sclerosis), acute coronary syndrome, atherosclerosis and myocardial infarction, in addition to being an indicator of systemic inflammation[52]. The blood neutrophil-to-lymphocyte ratio (NLR) is a potential prognostic indicator of clinical outcome or internal organ involvement in diseases with an inflammatory component, such as HSP. It can be used to identify individuals at risk of developing extracutaneous manifestations as well as speculate their severity of systemic involvement[7]". It is calculated by dividing the absolute values of neutrophils by the absolute values of lymphocytes[53]. "Because inflammation is a major predictor of the severity of autoimmune diseases and NLR is a marker of inflammation severity, the ratio can be useful in predicting the severity of immune complex-mediated inflammatory conditions like HSP"[53].

The diagnosis of IgA vasculitis is mainly based on history and clinical findings.

In addition to an elevated serum IgA level, other common laboratory abnormalities in IgA vasculitis include elevated white blood cells, eosinophilia and megakaryocyte counts, and

erythrocyte sedimentation rate[53]. Electrolyte disturbances can occur due to the involvement of the gastrointestinal tract. Renal involvement may occur up to three months after the onset of the rash, necessitating urinalysis as well as creatinine levels and blood urea nitrogen monthly in the presence of persistent haematuria[53].

Occult or gross blood in the stool can be an early sign of gastrointestinal involvement. A positive Guaiac test indicates the presence of occult blood in the stool.

Table 9: Laboratory evaluation in patients with cutaneous vasculitis [4,54]

Type of evaluation	**Laboratory tests**
Baseline	"Complete blood count with differential counts[54]" Urinalysis "Serum creatinine, urea and electrolytes[54."] "Liver function test[54]"

Additional	Anti-streptolysin O titers Erythrocyte sedimentation rate, C-reactive protein Serum complement levels (C3, C4, total) Antinuclear antibody "Hepatitis B and C serology[54]" "Human immunodeficiency virus antibody[54]" Stool Guaiac test

	Antineutrophil cytoplasmic antibodies Cryoglobulins Rheumatoid factor Chest radiography Serum monoclonal protein study (protein electrophoresis and immunofixation) Other tests for specific organ involvement, malignancy, etc.

"Gayret *et al*. concluded in their retrospective study that the NLR was significantly increased in patients with HSP"[53]. "Makay *et al*.[55] observed that NLR was significantly higher in HSP in pediatric patients with gastrointestinal bleeding than in those who did not have gastrointestinal bleeding, with 2.82 being the optimal cut-off NLR for predicting gastrointestinal bleeding"[55]. Park *et al*. noticed a higher NLR in adult HSP patients presenting with gastrointestinal bleeding than in those who did not, and the optimal cut-off value was estimated to be 3.90 "[56].

"Nagy *et al*.[7] postulated a significant association between pretreatment NLR and gastrointestinal or renal manifestations of the disease, with 3.34 being the optimal NLR cut-off value for predicting systemic involvement".

TREATMENT

Since most cases of isolated cutaneous vasculitis are self-limiting and resolve spontaneously within 3 to 4 weeks, most patients do not require systemic treatment. Systemic therapy may be indicated for those with severe, persistent, refractory or chronic and relapsing vasculitis and should be modified to the severity of the disease[57]. Table 10 features management of cutaneous vasculitis.

Table 10: Treatment options for cutaneous vasculitis.[4,49,58,59,60]

Category		**Treatment**
General measures		"Remove inciting agent or triggering agent (Infection, drug)[49]."
		"Complete bed rest[49]"
		Elevation of dependent areas
		Compression hosiery to minimise stasis
		Avoid smoking, tight-fitting clothing and exposure to cold.

		Symptom alleviation: NSAIDs to address joint pain and Antihistamines for pruritus
Mild, limited skin involvement		"Colchicine 0.6 mg 2 times daily (CLA, HSP, UV)49"
		Dapsone 50-150mg (CLA, HSP, UV)
		Pentoxyphylline 400mg 3 times daily (CPAN)
Moderate to severe skin involvement (above waist lesion)		Systemic steroid: Injectable /Oral.
		Azathioprine 1-2mg/kg/day
		Methotrexate 15-20mg/ week
		Cyclosporine 2.5-4mg/kg/day
Nodules, vesiculobullous, ulceronecrotic lesions)		Cyclophosphamide 100mg-2gm/day
		Mycophenolate mofetil 0.5-2g/day (HUV, WG, MPA)

Systemic vasculitis		Prednisolone 1-1.5mg/kg ± cyclophosphamide/azathioprine/mycophenolate mofetil
		Pulsed IV methylprednisolone 1g/day for three days then prednisolone 1-1.5mg /kg/day
Recalcitrant (not responding to the above-mentioned treatment)		"Hydroxychloroquine (400 mg daily; only for urticarial vasculitis)[59]."
		"Intravenous immunoglobulin (2 g/kg monthly, divided over 2–4 days)[59]."
		"Rituximab (375mg / m^2 per week for four weeks or two doses, 1g each two weeks apart[60]) Rituximab 0.5-1 gm 6th monthly to maintain remission and avoid relapses.[60]
		"Cyclosporine (2.5–5 mg/kg daily, in divided doses; short-term use in severe disease)[59]."

NSAIDs are commonly used to treat arthritis and do not usually exacerbate the purpura. Ibuprofen is the treatment of choice for the initial management of mild to moderate arthritis, with flurbiprofen, ketoprofen, and naproxen available as alternatives[61]. Immunosuppressants mitigate inflammation by inhibiting polymorphonuclear leucocyte migration and reducing the increased capillary permeability. Corticosteroids are recommended in cases of nephritis or subcutaneous oedema since these are potent anti-inflammatory agents[61].

Indications of usage of corticosteroids include:[61]

- Severe Abdominal pain, severe in nature
- Haemorrhage in the gastrointestinal tract
- Persistent nephrotic syndrome
- More than 50% of glomeruli showing crescents
- Neurological involvement
- Pulmonary haemorrhage
- Severe scrotal edema

The duration of treatment for cutaneous small vessel vasculitis is not known. A particular therapy may take several weeks to achieve desirable improvement. In general, tapering after cutaneous vasculitis has been in remission for 3-6 months is reasonable, but there is a lack of data to assist decision-making[57]. The severity of renal involvement directly influences the long-term prognosis of IgA vasculitis[61]. To prevent the progression of the disease, nephropathy is treated with conservative measures such as restriction of salt, correction of fluid and electrolyte imbalance, glucocorticoids, azathioprine, cyclophosphamide, or antihypertensives and plasmapheresis if appropriate[61].

"According to the 2012 Kidney Disease Improving Global Outcomes (KDIGO) guidelines, children with proteinuria greater than 0.5g should be treated with Angiotensin II receptor antagonists for 3 to 6 months"[61]. In patients with biopsy showing >50% crescentic glomeruli and rapidly deteriorating renal status irrespective of nephrotic syndrome, a combination of pulsed IV methylprednisolone with cyclophosphamide is used. Plasmapheresis will be supplemented to the treatment regimen if plasma creatinine exceeds 500 micromol/l as it retards the progression of renal involvement[61]. Surgical intervention is appropriate in treating severe bowel ischemia[61]. "Renal transplantation is indicated in severe renal deterioration refractory to medical therapy "[61]. "Pediatric population presenting with microscopic hematuria, or proteinuria should be evaluated at an interval of 3 to 6 months since hypertension or hypertension can develop up to 10 years after the disease onset.""Kidney transplantation is the treatment modality of choice for HSP patients with nephritis that has transitioned to end-stage kidney disease"[61]. Based on a review of the literature on cutaneous vasculitis, "the comprehensive approach of patients with suspected vasculitis entails detailed history taking, assessing probable inciting factors, appropriate medical history and thorough clinical examination with histopathological and DIF confirmation to arrive at a definitive diagnosis and classification of vasculitis"[32].

In addition, "literature supports the role of NLR as a predictive biomarker of systemic involvement in adult HSP patients," allowing for early intervention and prevention of systemic vasculitis complications.

DERMOSCOPY

The term "Dermatoscopy" was coined by German dermatologist Johann Saphier in 1920. Later, Goldman introduced the word "dermoscopy." Dermoscopy is also known as dermatoscopy,

epiluminecsence microscopy, skin surface microscopy, and incident light microscopy. Stolz and Braun- Falco pioneered the first dermoscope in 1989[62].

The dermoscope is a portable, non-invasive diagnostic equipment that magnifies both the fine surface details of skin lesions and a few skin substratal structures that are invisible to the naked eye and even to a magnifying lens[63]. It bridges microscopic dermatopathology and macroscopic clinical dermatology[64].

Dermoscopic evaluation of patients with small vessel cutaneous vasculitis facilitates earlier and non-invasive diagnosis before confirmation with biopsy. To date, the major study utilising dermoscopy in vasculitis is only done in urticarial vasculitis and not on other types of cutaneous small vessel vasculitis. Thus we intend to undertake this study to establish the dermoscopic diagnostic criteria for cutaneous small vessel vasculitis.

Dermoscopy also has additional benefits over histopathology, which includes[65]:

. It is simple and time-saving

. It is an outpatient-based non-invasive investigation that enables quicker evaluation of skin lesions.

. It aids the investigator in focusing on the lesion

. It can be used in follow-up visits after treatment

. Provides a place to store photographs for comparison and analysis in the future.

PRINCIPLE:

Dermoscopic visualisation's fundamental technique entails employing lenses to magnify skin lesions and varying light sources to illuminate them[66]. Any light beam that travels through skin typically is refracted, diffracted, reflected, or absorbed depending upon the type of skin (Figure 1)[67].

Light is reflected by dry, scaly skin, penetrating deeper through smooth, oily skin, increasing the transparency of the skin's subsurface. In the case of contact technique dermoscopy, the latter principle is utilised by observing the skin lesion after the application of coupling fluids such as oil (immersion oil, mineral oil), an antiseptic solution, water, glycerin, and gels[68].

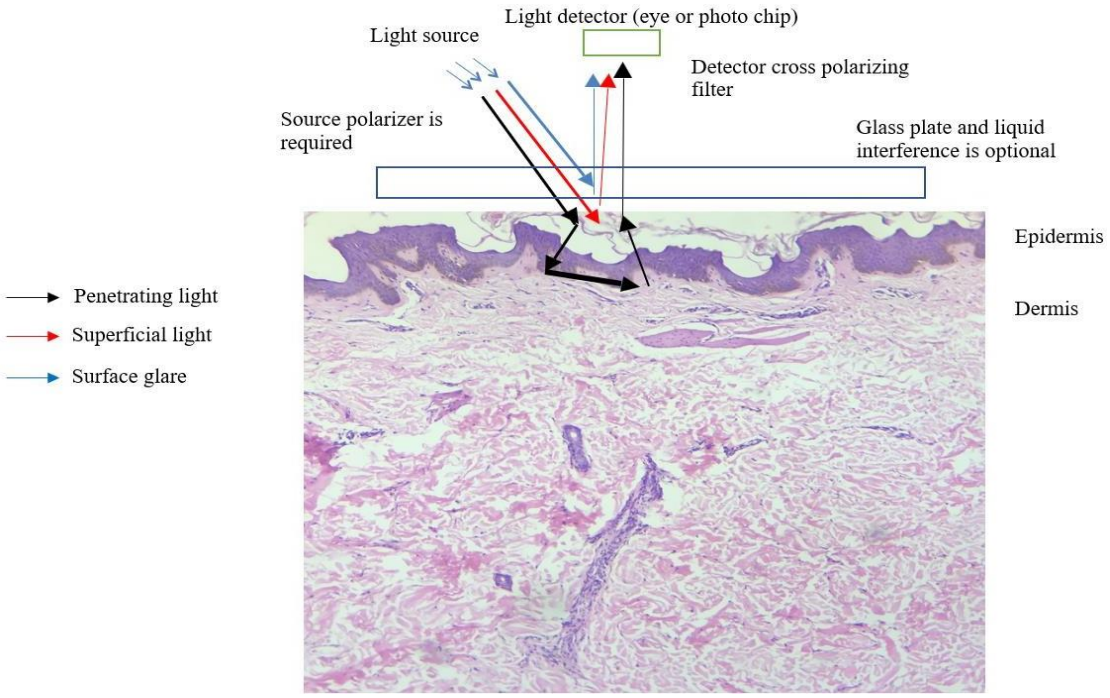


Figure 1: Optics of Polarized and non-polarized dermoscopy

COMPONENTS OF DERMOSCOPE:[63]

A. *Achromatic lens*: Most dermoscopes have a 10X magnification. However, a video-dermoscope can attain magnifications of up to 1000X.

B. *In-built illumination system:* Compared to traditional halogen lights, which emit yellow light, light-emitting diodes (LEDs) are the standard sources for high-intensity white light utilising 70% less energy.

C. *Power supply:* This portable equipment is battery-powered or has rechargeable handles

D. *Contact plate*: The components of the contact technique dermoscopy are large contact plates (20 mm in diameter) and small contact plates (8 mm in diameter). 2% glutaraldehyde or methylated spirit can be used to sterilise the multi-located silicone glass used in the contact plates. The purpose can also be achieved by boiling or autoclaving for five minutes at 134^0 C. These plates come in both graded and non-graduated varieties, some of which have scales.

E. *Display system*: Unlike the video-dermoscope, which can be connected to a computer or other displays or even have its own screen, the hand-held dermoscope has a see-through viewing window.

F. *Inbuilt photography system*: Except for the hand-held dermoscope, these now constitute a vital part of a dermoscope. The camera could be an integrated video camera, an attachable conventional or digital camera, or both. In the former situations, supporting software is implemented for image capture, storage, retrieval, and even analysis.

TYPES OF DERMOSCOPE: [63]

Marghoob *et al*. reviewed different dermoscope models and classified them into the following categories.

A. *Dermoscopes without image capturing facility:* These are portable, otoscope-like equipment without an internal camera or other means of image capturing. The use of an adaptor, however, allows the attachment of cameras to certain of these devices.

Based on the principle that the depth of penetration of light is proportional to wavelength, it constitutes four different colouredpolarised light, namely white, blue (surface pigmentation), yellow (superficial vessels), and red (deep pigment and vessels), to enable for better appreciation of skin structures.

B. *Dermoscopes with image capturing facility:* These devices either consist of a connected camera for taking pictures or have an integrated image capture system. With this technique, entire-body photography (body mapping) is also possible. Some have distinct lenses that may be attached to traditional or digital cameras. Photos that are 10X magnified can be taken both clinically and microscopically. A higher-resolution camera is attached to the handpiece of a video dermoscope, and the image is displayed on a computer screen. This device can also be used to record brief videos.

C. *Dermoscopes with image capture facility and analytical capability*: These equipment are mostly utilised for diagnostic workup of pigmented lesions in nations with high melanoma incidence. Images of the patient that have been maintained can be compared to recent ones. Any significant alteration to the lesion results in a change in colour signals. The malignancy potential of melanocytic nevus can be determined using an artificial neural network method.

DERMOSCOPY TECHNIQUE:

Both contact and non-contact methods can be employed to use the dermoscope. Dermoscopyutilising the contact technique applies a glass plate or contact plate to the surface of the lesion with an interface fluid and illuminates it with non-polarized light (NPL). When employing polarised light, a non-contact approach, there is no contact

with the surface of the skin, which has the extra benefit of preventing nosocomial infections[69].

Polarised light offers better visualisation of deeper components in the skin, whereas NPL allows for improved visualisation of more superficial structures[70].

Because the dermoscope enables picturisation in a horizontal view of the skin, the vessels that run parallel to the skin's surface are depicted as lines, while those that run perpendicular are represented as loops. Due to the non-contact technique's inability to compress the vascular systems, vessels can be seen more clearly[71].

IMMERSION FLUID

The immersion oil linkage is the most ideal one for dermoscopic assessment[63].

Categorisation of immersion or linkage fluid into four groups:

i) Oils

ii) Water-based gels

iii) Water and

iv) Disinfectant solutions

The characteristics of an optimal immersion liquid are:[63]

i Inexpensive and readily available

ii Enhances the structural characteristics of skin lesions without affecting their colour.

iii Non-volatile

iv Should produce fewer air bubbles

v Can be used in specific areas like periorbital skin

vi Shouldn't produce an excessive amount of bright or matte light.

Immersion oil is a better choice for an immersion fluid in visualizing the pigment network. Ultrasound gel or immersion oil can be employed for structural elements other than pigment networks. Ultrasound gel is a preferable option to immersion oil for dermoscopic inspection of non-pigmented skin lesions because it is less expensive and easier to wipe from the skin than immersion oil, which contains chemicals that are teratogenic, embryotoxic and carcinogenic like dibutyl phthalate and chlorinated paraffin.

A 70% alcoholic formulation provides the best outcomes regarding image quality, minimizing air bubbles, and improved patient tolerance because it has a less unpleasant odour, according to a study by Gewirtzmanet *et al*.[72] Alcohol is more effective in inflammatory dermatoses and may reduce the spread of infections. Glass, when placed over skin coated in linkage fluid (as in contact plates), greatly increases the transillumination of the skin lesion since its refractive index (1.52) is approximately identical to the skin refractive index (1.55). Dermoscopy of solid curved areas can be performed with the help of ultrasound gel, especially in the periphery of the nail plate[73].

It is also suitable for evaluating the eyelids, mucosa, genitalia, and nail bed[63]. By utilising gel, the total curved area of the nail can be visible because unlike liquids, which escape out, viscose gel fills up and stays in the space between the surface to be observed and the contact plate[63].

Major categories of dermoscopic criterion

Each disease can be distinguished dermoscopically by one or two characteristic criteria. A structure that is more prominent than other coexisting features in a lesion's greater portion is

referred to as a "predominant" criterion. Scales, vasculature, and structures related to hair follicles are frequently observed structures in inflammatory skin conditions. The most significant factors to evaluate while doing a dermoscopy are

1A. SCALES COLOUR

i) *White*: The most common scale colour seen in primary and secondary follicular keratotic diseases, as well as other conditions, including papulosquamous and erythematosquamous skin disorders.

ii) *Yellow*: Extravasation of serum results in yellow crusts, and serum combined with keratin results in yellow scales. This feature corresponds to spongiosis on histopathological examination.

iii) *Brown*: Scales that are brown in colour result from pigmented parakeratosis seen in a number of dermatoses. Exogenous pigmentation may also lead to brown scaling.

1B. **SCALES DISTRIBUTION**

i) *Patchy*: Scale distribution is asymmetric and random. Numerous conditions exhibit this.

ii) *Diffuse*: Scales spanning the entire lesion’s surface. Since it can be found in many hyperkeratotic dermatoses, a diffuse scale cannot be used to arrive at a diagnosis.

iii) *Central*: The centre of the lesion is highlighted by scales in this instance. Despite being extremely common in psoriasis, this scaling pattern cannot be considered distinct.

iv) *Peripheral*: Scales are mainly found on the edges, with central clearing. Although it can also be a feature of other illnesses like tinea corporis, it is a hallmark of pityriasis rosea.

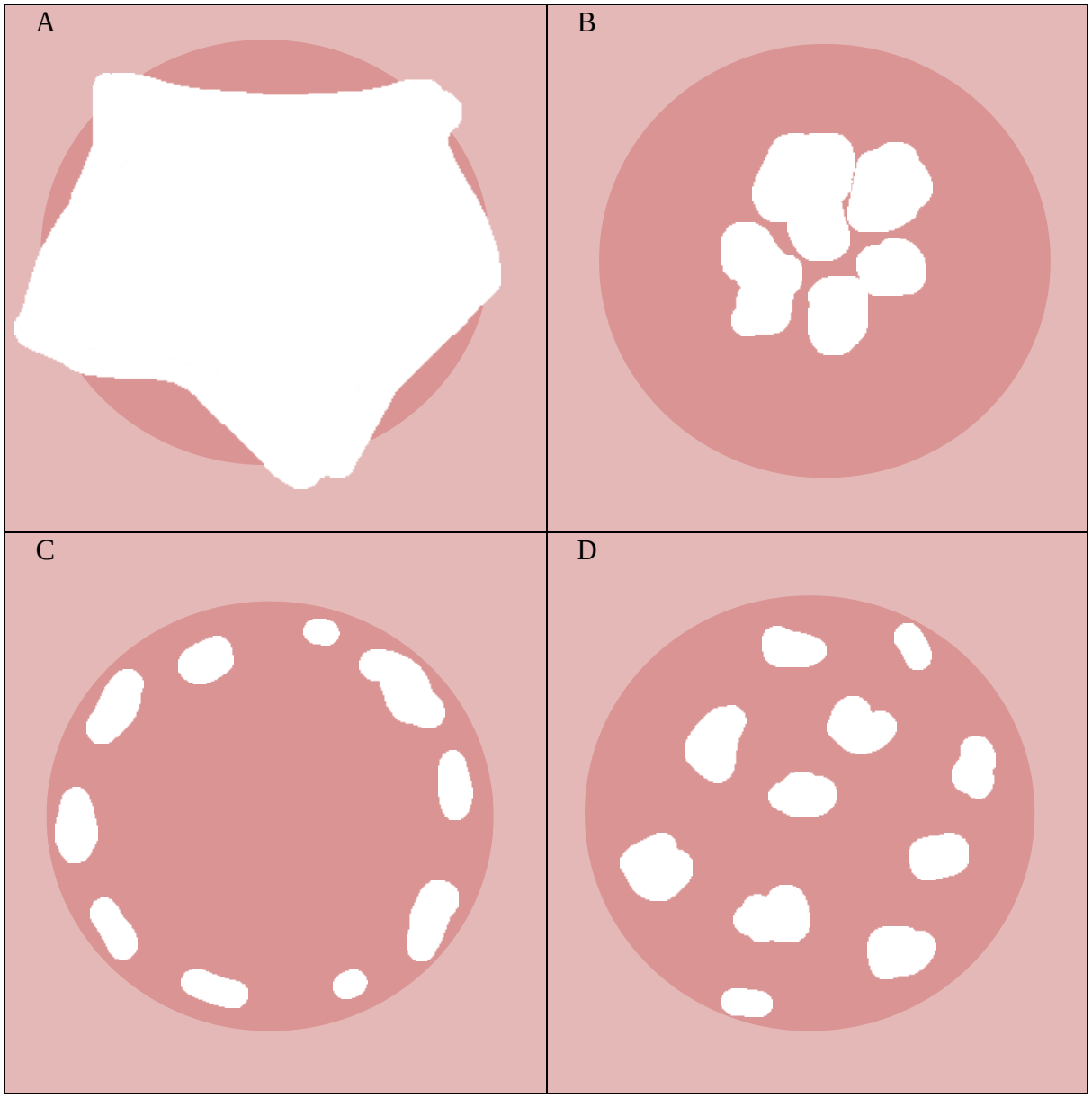


Figure 2 : Scales distribution: A)Diffuse B)Central C)Periphery D) Patchy

2. FOLLICULAR CRITERIA[74]

i. *Follicular red dots*: This indicates vasodilation and perifollicular inflammation. They can also be seen in follicular mucinosis but typically in discoid lupus erythematosus.

ii. *Follicular plugs:* Filling the follicular ostia are keratin plugs that are white or yellow in hue. It is a dermoscopic sign of discoid lupus erythematosus in its early stages, although it is also observed in other conditions, such as follicular keratosis disorders.

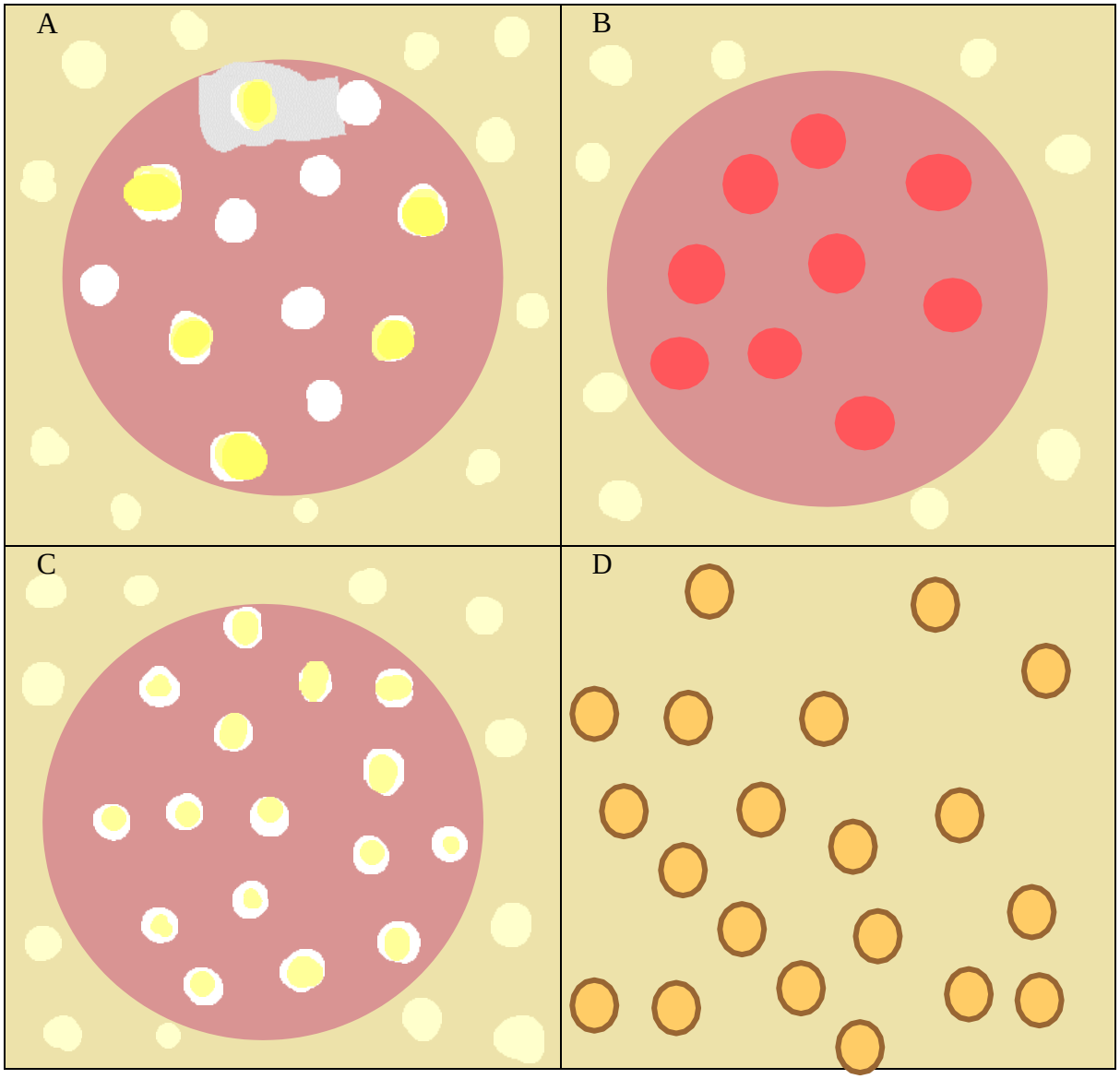
iii. *Perifollicular white colour*: Each hair follicle and/or the spaces between hair follicles are surrounded by a white circle. It may be attributed to epidermal hyperplasia (such as hypertrophic lichen planus), perifollicular depigmentation seen in vitiligo, or perifollicular fibrosis (such as DLE)

iv. *Perifollicular pigmentation*: Pigment is primarily concentrated or prominent around the hair follicles. It is the first indication of repigmentation in vitiligo and is also visible in some alopecias

Figure 3: Follicular criteria: A) Follicular plugs B) Follicular red dots C)Perifollicular white colour D)Perifollicular pigmentation

3. Vessels

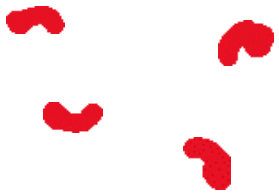
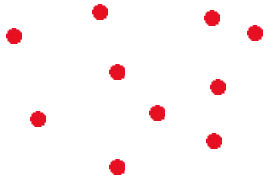
Vessels situated in the dermis are usually pink and look out of focus. This is due to the result of dispersion of light through the connective tissue in the dermis. In contrast, those situated

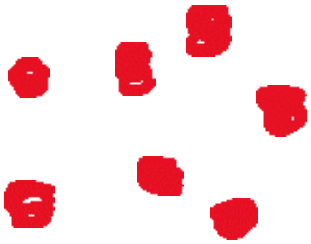
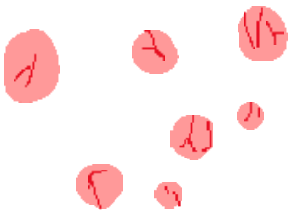


closer to the surface (directly beneath the epidermis) are brilliant red and well-defined[75].

Vessel morphology and distribution are illustrated in Table 11a and 11b, respectively.

Pattern of the vessel	Description	Diagram
Telangiectasias / Arborising vessels	Vessels with a large diameter that branches into small secondary vessels	
Hairpin shaped vessels	Vessels that loop back on themselves and are visible when they are oblique to the lesion's surface; They are encircled by a hypopigmented halo in keratinizing tumours.	
Crown vessels	Peripheral arteries with few branches that don't traverse through the centre of the lesion	

Comma shaped vessels	Curved, linear thick lines with little branches and may have one end that is thicker than the other.	
Dotted vessels	Regularly spaced small red dots that are closely adjacent to one another.	

Glomerular vessels	Large-caliber, clustered red dots resembling the kidney's glomerular system are created by dilated capillaries.	
Corkscrew vessels	Linear irregular spiral shaped.	
Milky red areas/ globules	Atypical linear vessel-containing pinkish-reddish oval or polygonal regions	

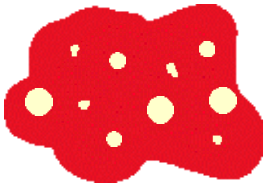
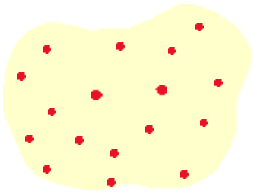
Strawberry pattern	Heterogenous white areas with structureless erythematous areas form a type of pseudo network.	
Linear irregular	Straight vessels differing in shape and size	
Polymorphous vessels	The same lesion might have various vascular morphologies.	

Table 11a: Vessel morphology

VESSEL PATTERN	DESCRIPTION	DIAGRAM
Regular	Even distribution of vessels throughout the lesion	
String of pearls	Dotted vessels placed in a string of pearls-like patterns along a linear pattern	

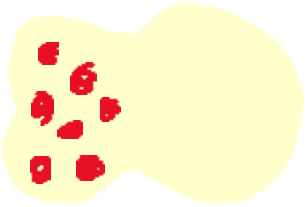
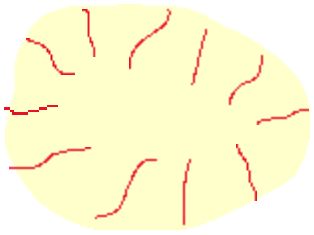
Clustered	The tendency of a group to concentrate in a lesional area	
Radial	Vessels at the periphery of the lesion not traversing the centre	
Branching	Large vessels that branch into smaller vessels	
Irregular	Vascular polymorphism with no discernible pattern	
Rope ladder pattern	Short, slightly dilated loops arising from the periphery of the scar and cross it completely.	

Table 11b: Vessel distribution pattern

There exists little evidence regarding the dermoscopic pattern of vasculitides.

In a study conducted by Garcia B *et al.*[76] to develop a clinical-dermoscopic model for the differential diagnosis of 27 urticarial vasculitis (UV) and 108 spontaneous urticaria (CSU) cases, Purpuric patches/globules were highly discriminative, being present in most of the UV patients (n

= 19, 70.4%), but only in a minority of CSU patients (n = 11; 10.2%) whereas red linear vessels were seen in the majority of both CSU and UV patients (85% and 74%, respectively)

In a randomised control trial study by Madarkar *et al.*[77] in assessing the Importance of dermoscopy in differentiating common urticaria and urticarial vasculitis, it was shown that dermoscopy in 9 individuals who had been clinically diagnosed with urticarial vasculitis showed purpuric spots in 8 (40%) and purpuric globules in 5 (25%).

In a case series by Lopez *et al.* [78] to assess the dermoscopy role in the screening of common urticaria and urticarial vasculitis, lesions of urticarial vasculitis demonstrated purpuric dots or globules in a patchy orange-brown background on dermoscopy. These structures were associated with extravasation and degradation of erythrocytes.

Henoch-Schonlein purpura has been shown to dermoscopically reveal irregularly shaped red patches with blurred borders[79].

Dermoscopic evaluation of patients with cutaneous small vasculitis facilitates earlier and non-invasive diagnosis before confirmation with biopsy. Currently, the major study involving dermoscopy in vasculitis is done only in urticarial vasculitis and not on other types of cutaneous small vessel vasculitis. Hence we are undertaking this study to establish the dermoscopic diagnostic criteria for cutaneous small vessel vasculitis and to categorise based on the duration of the disease. And also to correlate dermoscopic features with NLR, and clinical and histopathological changes. Lastly, to assess if dermoscopic characteristics can predict systemic involvement.

METHODOLOGY

SOURCE OF DATA

Patients presented to the Dermatology OPD at Shri B.M. Patil Medical College Hospital and Research Centre, VIJAYAPURA.

Period of study:

The study was conducted during the period of January 2021 to June 2022.

Study design:

A hospital based cross-sectional study.

Sample size:

With anticipated Proportion of leukocytoclastic vasculitis as 85% [14], the study required a sample size of 50 with 95% level of confidence and 10% absolute precision.

Formula used

$$n=\frac{z^2\ p*q}{d^2}$$

Where Z= Z statistic at α level of significance

d^2= Absolute error

P= Proportion rate

q= 100-p

METHOD OF COLLECTION OF DATA:

Inclusion criteria:

1. All the patients presenting with clinical features of cutaneous small vessel vasculitis defined by palpable purpura, papules, plaques, nodules, vesicles, bullae, ulcers and other cutaneous findings like urticarial, livedo reticularis irrespective of age, sex, duration and treatment at Shri BM Patil Medical College, VIJAYAPURA.

Exclusion criteria:

1. Patients with clinical features not conforming to the abovementioned definition of cutaneous small vessel vasculitis.
2. Patients who do not give consent.

Methodology:

Detailed history and clinical examination was recorded in the proforma. After obtaining consent, patient's lesion was examined with a hand-held dermoscope (DermLite™ DL3, 3Gen Inc., San Juan Capistrano, CA, USA) under polarized mode and images were captured using a sony digital camera attached to the dermoscope. The dermoscopic findings was recorded in terms as per the standard dermoscopic pattern analysis

Investigations:

CBC (NLR)

Urine analysis

Throat swab

Stool for occult blood

Skin biopsy was done and sent for HPE and DIF from the established lesion as early lesion might not show all the characteristic features. Finally, we correlated the dermoscopic and histopathological findings and statistical assessment will be done.

Following parameters will be assessed

1. Dermoscopic analysis of cutaneous lesions of vasculitis
2. Correlation of dermoscopy features with histopathological changes.
3. Correlation of dermoscopic findings with NLR reflecting systemic involvement
4. Correlation of NLR with duration

Statistical Analysis:

- The data obtained was entered in a Microsoft Excel sheet, and statistical analysis was performed using statistical package for the social sciences (Version 20).
- Results were presented as Mean (Median) ±SD, counts and percentages and diagrams.
- Pearson/Spearman's Correlation was used to find the correlation between quantitative variables.
- Association of categorical variables was be computed using Chi square test.

  , $p<0.05$ was considered statistically significant. All statistical tests performed were two tailed.

ETHICAL CLEARANCE

Institutional ethical commitee clearance was undertaken for the study

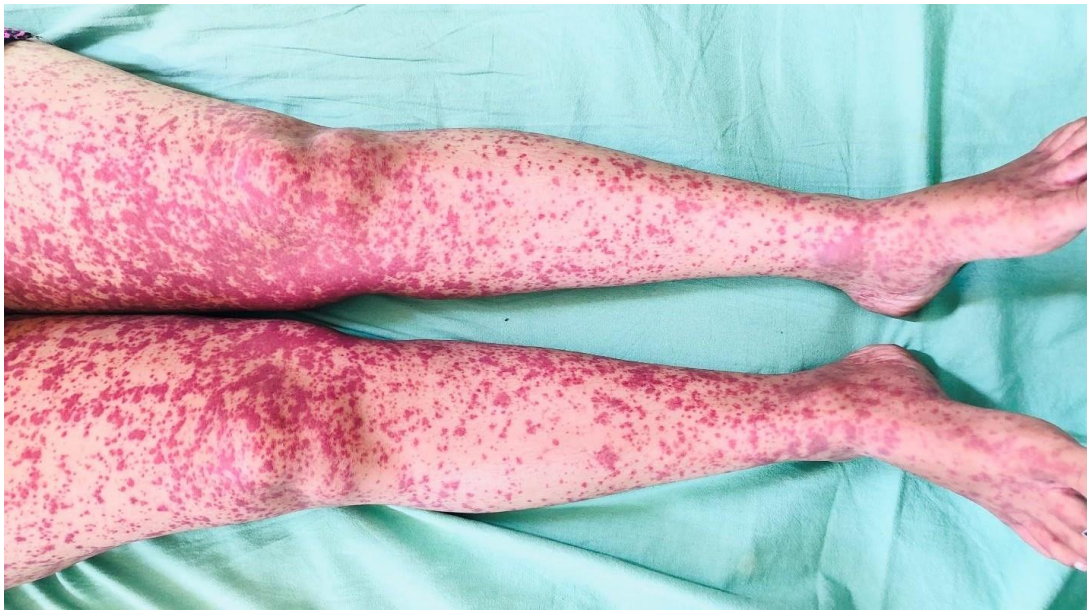


Figure 4: Multiple palpable petechiae and purpurae over bilateral lower extremities

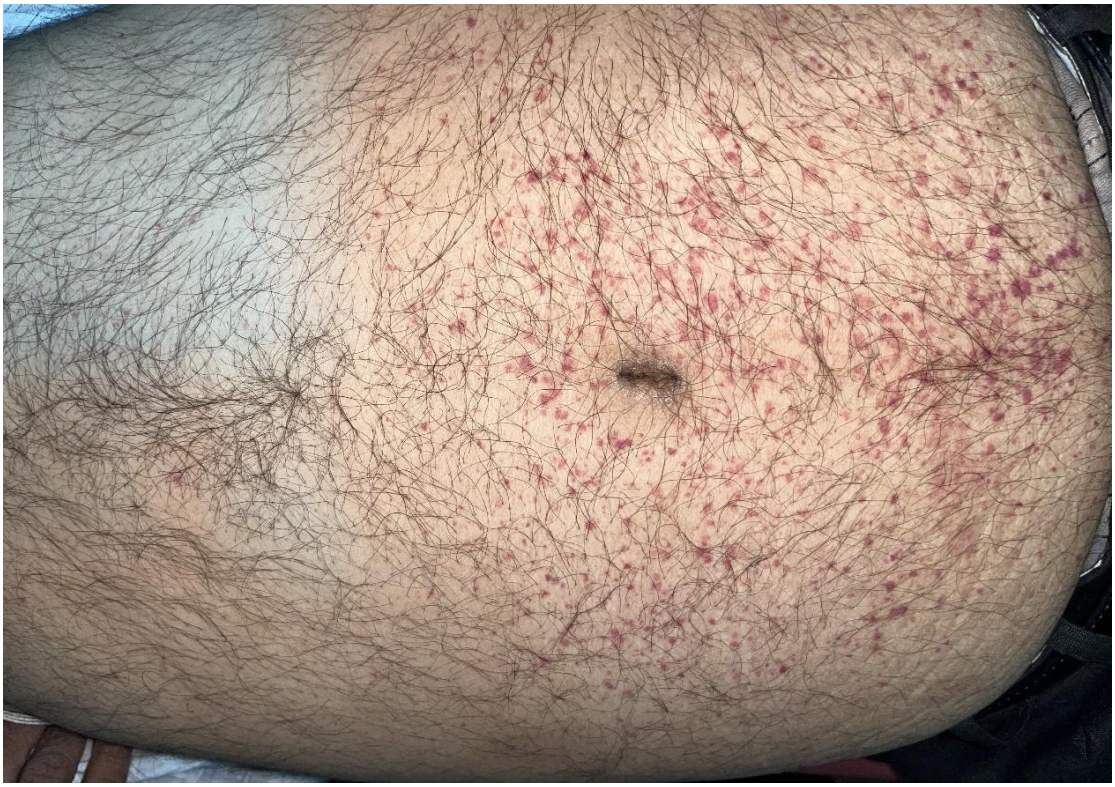


Figure 5: Palpable purpurae over abdomen over the waist line

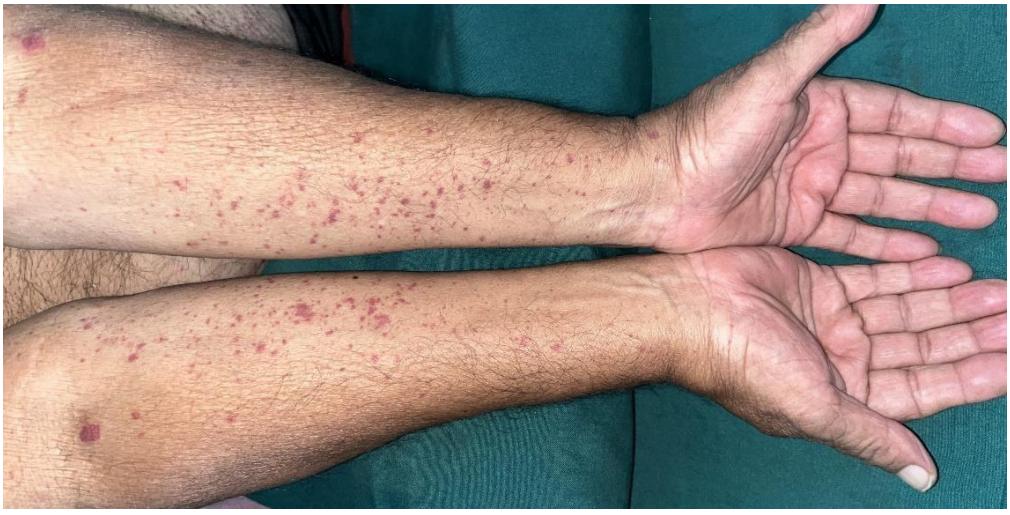


Figure 6: Petechiae and purpurae over bilateral upper extremities

RESULTS

A hospital based cross-sectional study was conducted from January 2021 to June 2022.

A total of 30 patients with cutaneous vasculitis were included in the study

DISTRIBUTION OF CASES

Based on DIF findings, out of 30 patients with a diagnosis of vasculitis,14(46.70%) and 16 (53.30%) were found to have cutaneous small vessel vasculitis and HSP, respectively. (Figure 7 and Table 12) presents distribution of cases of cutaneous vasculitis included in the study)

Table 12: Distribution of cases based on DIF findings

Diagnosis	Frequency	Percent
HSP	16	53.3%
CSVV	14	46.7%
Total	30	100.0%

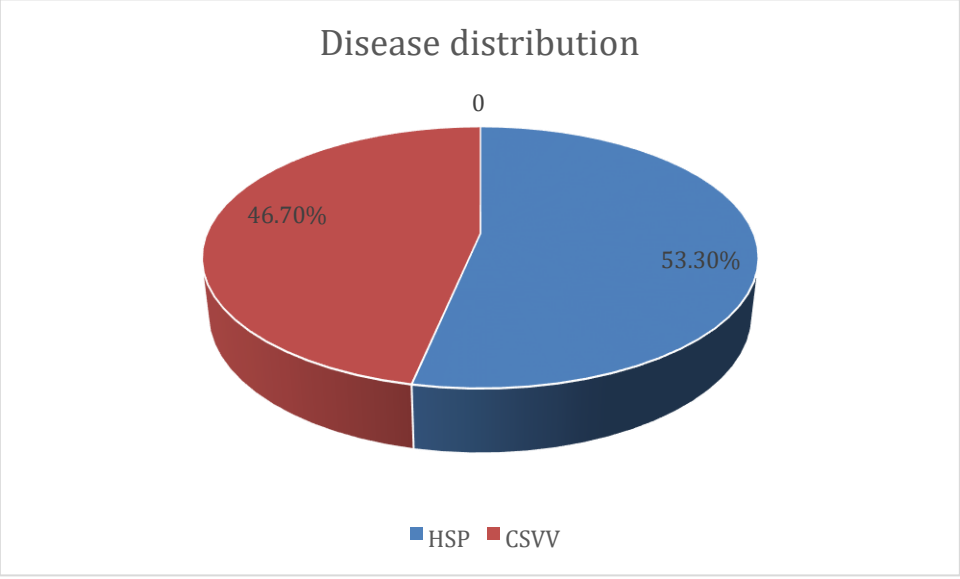


Figure 7: Distribution of cases based on DIF findings

AGE DISTRIBUTION:

The age of the patients enrolled in the study ranged from 10 years to 80 years with a mean age of 34.60 ±15.44 years. Table 13 and Figure8present the age distribution of the patients included in the study. Population in the age group between 20 to 30 years constituted the majority of the study population with a maximum of 8 (26.7%) patients followed by 6 (20.0%) in the age group 40 - 50 years followed by age group less than 20 years, 30-39 years, 50-59 years with 5 each (16.7%) patients, and 1 (3.3.4%) lies in the age group above 70years.

Table 13: Age (years) distribution

Parameters	No. of patients	Percentage
< 20	5	16.7%
20 – 29	8	26.7%
30 - 39	5	16.7%
40 - 49	6	20.0%
50 - 59	5	16.7%
70 - 80	1	3.3%
Total	30	100.0%

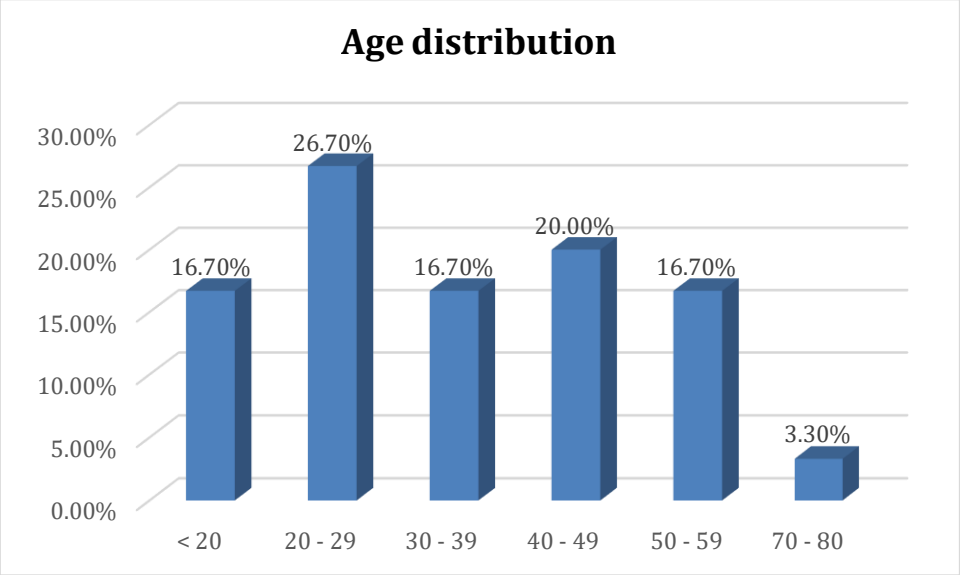


Figure 8: Age distribution in Cutaneous vasculitis patients

GENDER DISTRIBUTION:

Among 30 patients, 17 (56.7%) were males and 13 (43.3%) were females.

Table 14 and Figure 9 presents the gender distribution of the patients with cutaneous vasculitis included in the study.

Table14: Gender distribution in study population

Parameters	No. of patients	Percentage
Female	13	43.3%
Male	17	56.7%
Total	30	100.0%

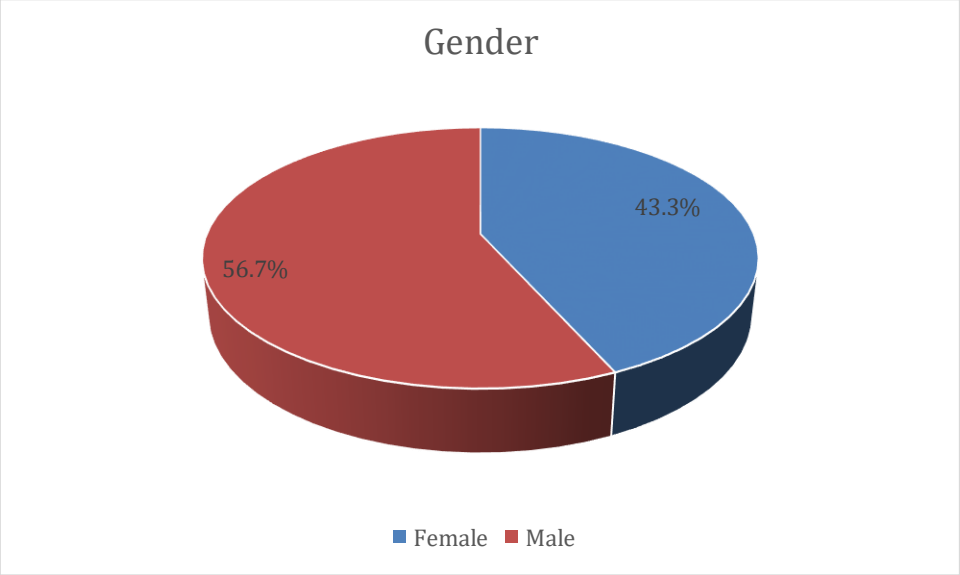


Figure9: Distribution of patients based on gender

Duration of lesions:

The mean duration of study population was 10.5 ±6.9days. The duration of lesions were found to be less than or equal to 7days (1week) in the majority of the cases which consisted of 22 (73.3%) whereas patients with lesions presenting for more than 7days in duration were 8 (26.67%) .Table 15 and Figure 10 represents the duration of lesions of cutaneous vasculitis included in the study.

Table 15: Duration of the lesions

Duration	Frequency	Percent
</=7days	22	73.33%
>7days	8	26.67%
Total	30	100.0%

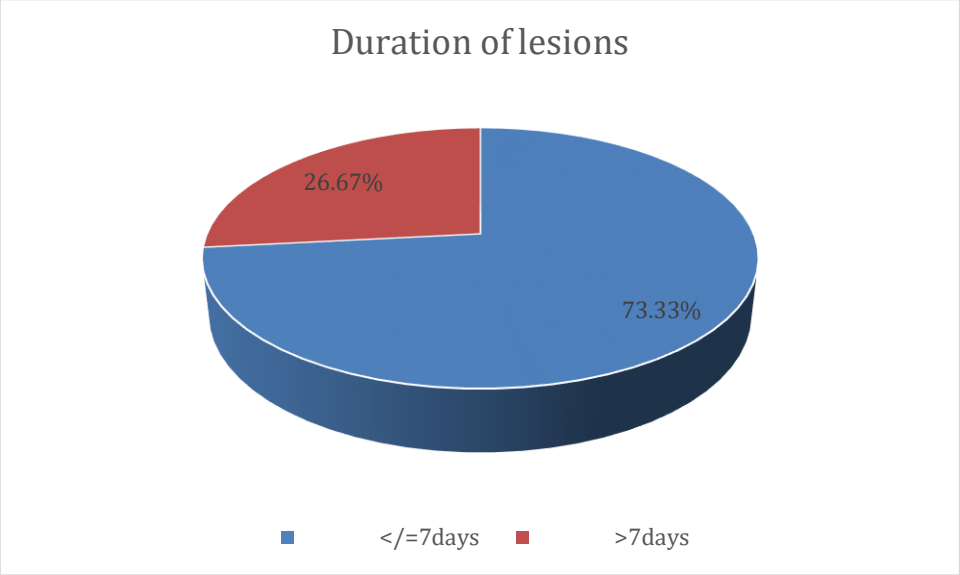


Figure 10: Duration of lesions

Prior Infection:

History of cutaneous lesions preceded by infections were noted in 9 patients (30%). Table 16 and Figure 11 represents the cutaneous vasculitis patients included in the study with nidus of infection prior to onset of lesions

Table 16: History of infection prior to cutaneous lesions

Prior infection	Frequency	Percent
Absent	21	70.0%
Present	9	30.0%
Total	30	100.0%

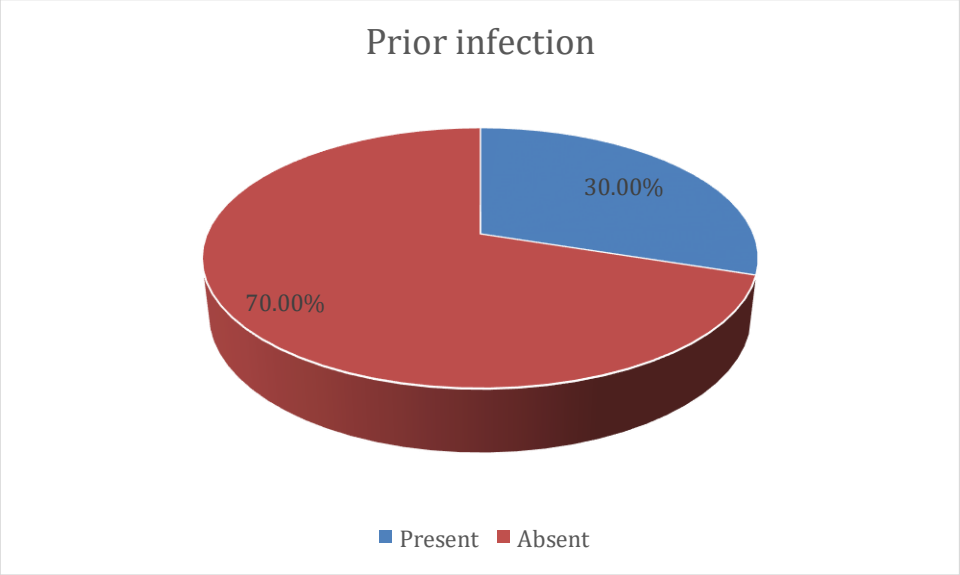


Figure 11: History of infection prior to cutaneous presentation

Drug intake:

History of drug intake prior to onset of lesions were seen in 2 patients of total 30 patients (6.7%). Table 17 and Figure 12 represents the patients with cutaneous vasculitis included in the study with history of drug intake prior to onset of lesions.

Table 17: Patients with history of drug intake prior to clinical features

Drug intake	Frequency	Percent
Absent	28	93.3%
Present	2	6.7%
Total	30	100.0%

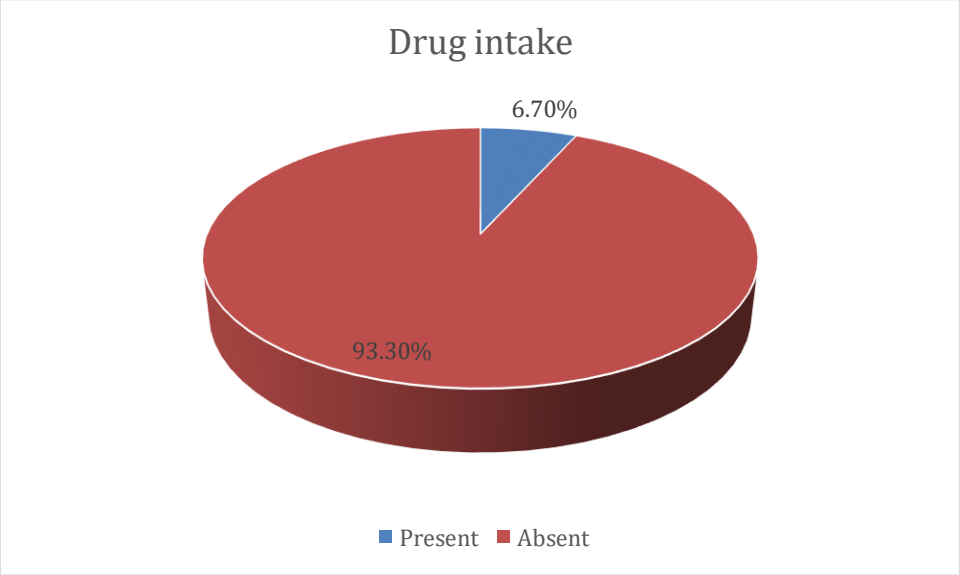


Figure 12: Patients with history of drug intake prior to clinical presentation

Recurrence:

History of recurrence of lesions was noted in 7 patients in a total of 30 patients (23.3%). Table 19 and Figure 13 represents the patients with cutaneous vasculitis included in the study with history of recurrence of lesions.

Table 18: Recurrence of cutaneous lesions

Recurrence	Frequency	Percent
Absent	23	76.7%
Present	7	23.3%
Total	30	100.0%

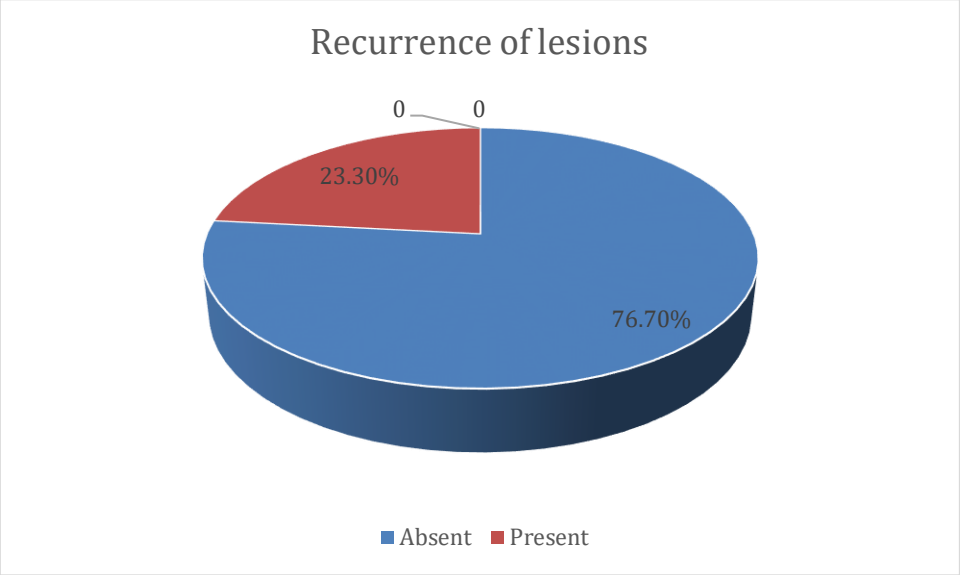


Figure 13: Patients wIth history of recurrence of the lesions

CORRELATION BETWEEN NLR AND DURATION OF THE LESIONS

There was a moderate correlation found between NLR and duration of the lesions depicted in Figure 14.

The duration of the lesions in cutaneous vasculitis showed moderate correlation with NLR (r = 0.598, P value =0.000); longer the duration of lesions greater the NLR value.

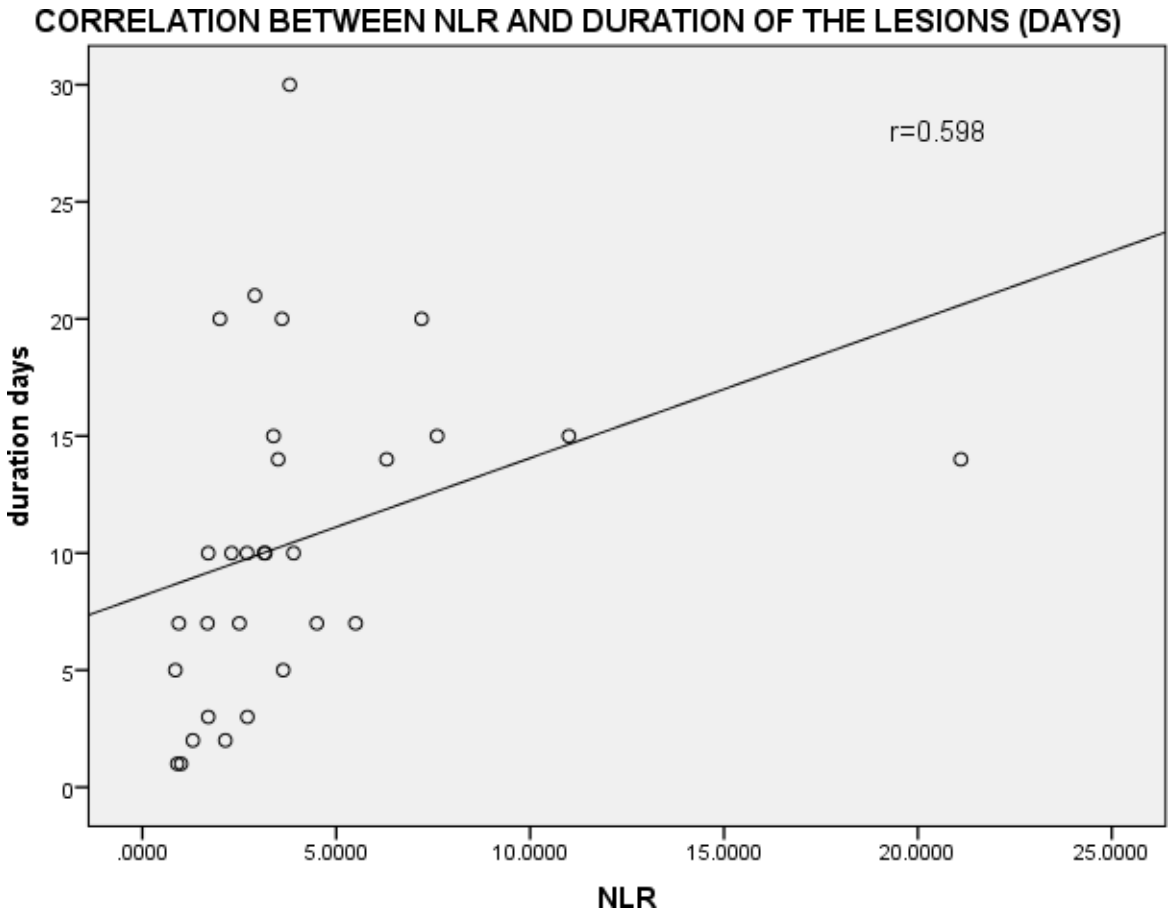


Figure 14:Correlation between NLR and duration of the lesions

ROC Curve

"In the Receiver Operating Characteristics (ROC) curve for combined systemic involvement (both renal and gastrointestinal tract), the area under ROC (AUROC) of NLR is 77.6% (95% of Confidence Interval = 60.5% - 94.6%) and the optimal cut-off value is 3.615." "Using this cut-off value, the sensitivity and specificity are 60% and 93.33% respectively." as can be depicted in Figure 15 making NLR a better prognostic indicator for systemic involvement in Cutaneous vasculitis.

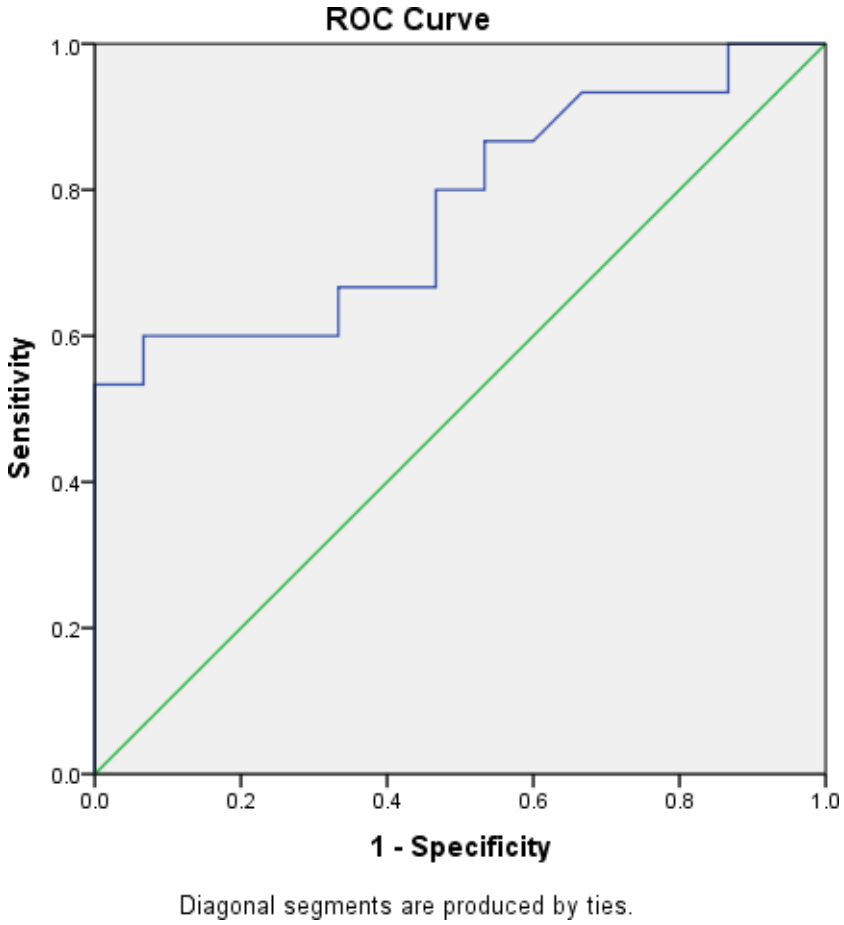


Figure 15: ROC curve of NLR as prognostic indicator of systemic involvement in Cutaneous vasculitis

Area Under the Curve

Test Result Variable(s): NLR

Area	Std. Error	Asymptotic Sig.	Asymptotic 95% Confidence Interval	
			Lower Bound	Upper Bound
.776	.087	.010	.605	.946

NLR value was found to be less than/equal to 3.615 in 20 patients (66.67%) and more than 3.615 in 10 patients (33.33%) represented in Table 19 and Figure 16.

Table 19: NLR value of patients with cutaneous vasculitis

NLR	Frequency	Percent
≤3.615	20	66.67%
>3.615	10	33.33%
Total	30	100.0%

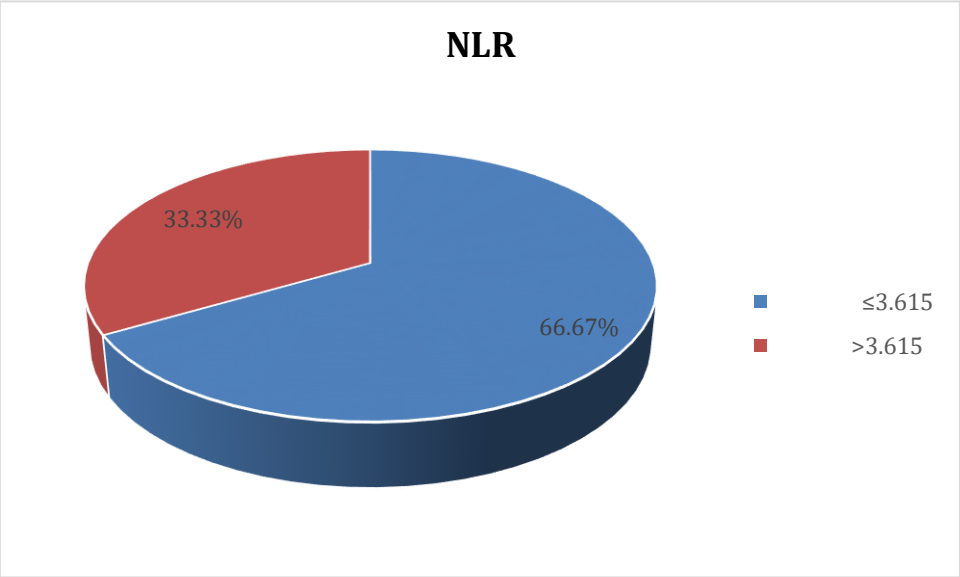


Figure 16: NLR value in study population based on cut-off of 3.615

Systemic involvement:

Systemic involvement in the form of renal (hematuria and /or proteinuria) and gastrointestinal manifestations was present in 16 patients (50%) depicted in Table 20 and Figure 17), among which 14 (87.50%) had renal involvement and 2 (12.50%) had gastrointestinal involvement (Figure 18)

Table 20: Patients with Systemic involvement

Systemic involvement	Frequency	Percent
Present	16	53.33%
Absent	14	46.67%
Total	30	100.0%

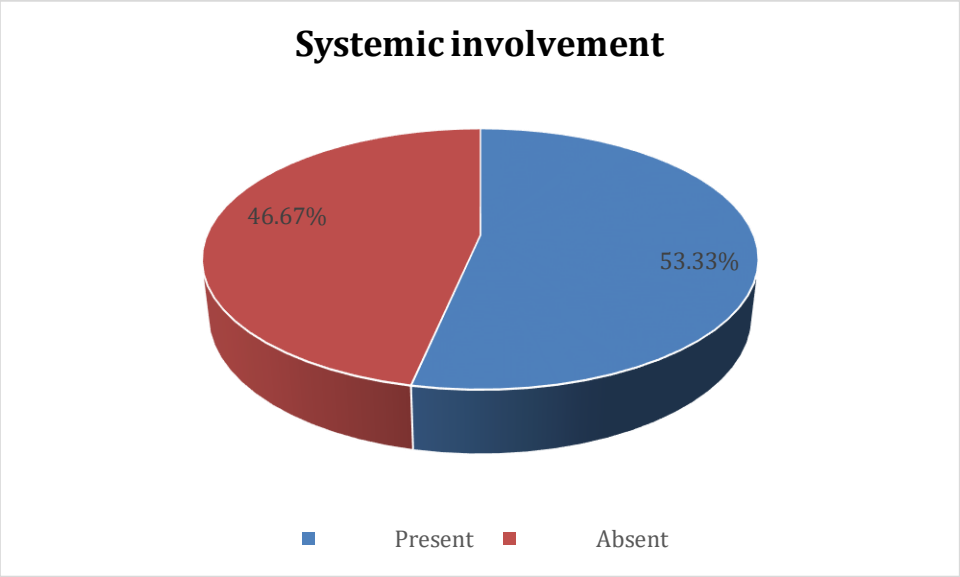


Figure 17: Study population with systemic involvement

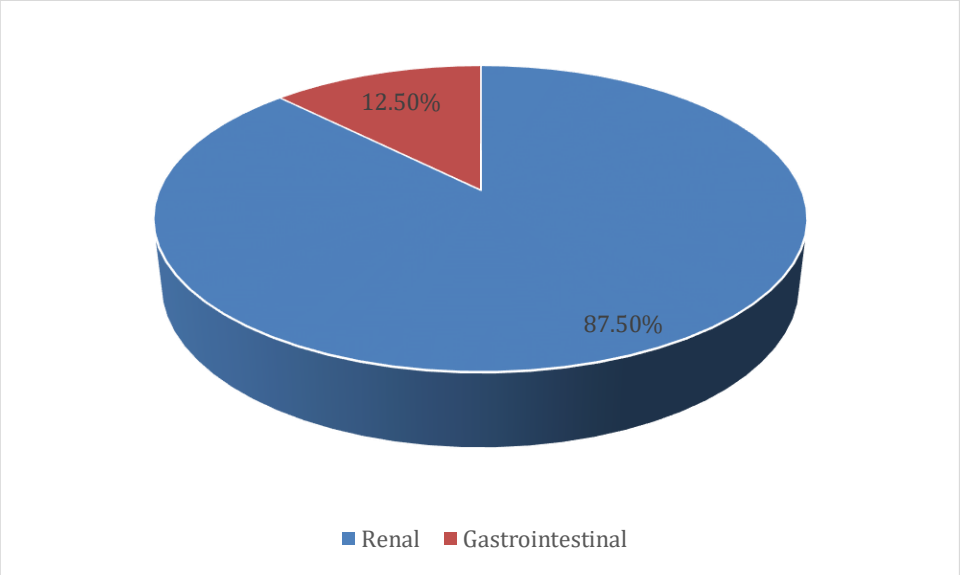


Figure 18: Categorization of systemic involvement based on renal and gastrointestinal tract involvement in 16 patients with systemic involvement

Association between NLR and systemic involvement

There was a statistically significant association between NLR and systemic involvement signifying NLR increases in the case of systemic involvement in patients with CSVV shown in Table 21.

Table 21: Association between NLR and systemic involvement

Systemic involvement	NLR			Chi square test	P value
	< 3.615	≥3.615	Total		
Absent	14	0	14	13.125	**0.001**
%	70%	0%	46.667%		
Present	6	10	16		
%	30%	100.0%	53.333%		
Total	20	10	30		
%	100.0%	100.0%	100.0%		
Statistically significant					

DERMOSCOPY FINDINGS:

Early/Evolving lesions were those that had appeared within 48hoursof patient's presentation to us. The remainder were regarded as old lesions.

Dermoscopy of established lesions:

Dermoscopy in established lesions includes features like red background was seen in 28 (93.3%), yellowish areas and white structureless areas in 19 (63.33%), red globules in 18 (60%), red dots

in 16 (53.3%), perifollicular scaling in 12 (40%), follicular keratotic plugs in 11 (36.7%) and Violaceous patches in 2 (6.7%) patients.

Table 22 and Figure 19 represent the frequency of individual dermoscopy findings in old lesions

Table 22: Dermoscopy findings of established lesions

Dermoscopy of established lesions	Frequency	Percent
Red dots	16	53.3%
Red globules	18	60.0%
Yellowish areas	19	63.33%
Red background	28	93.3%
White structureless areas	19	63.33%
Perifollicular scaling	12	40.0%
Follicular keratotic plugs	11	36.7%
Violaceous patches	2	6.7%

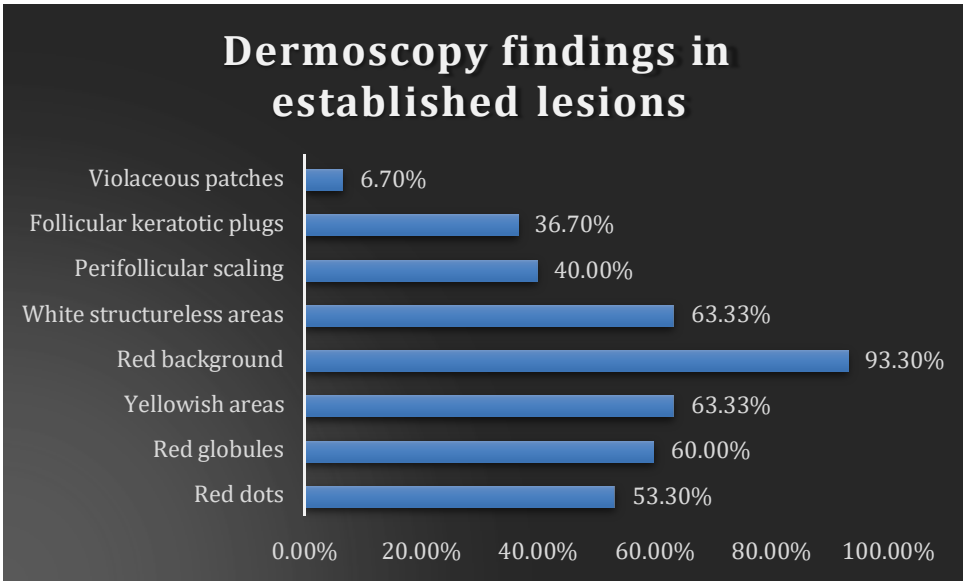


Figure 19: Dermoscopy findings of established lesions

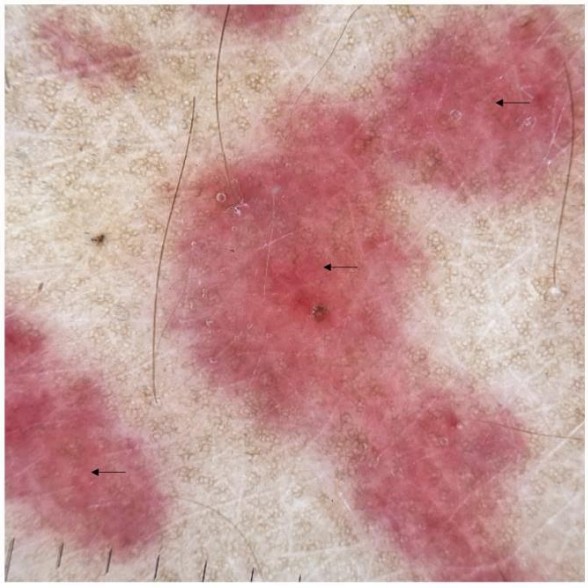


Figure 20 : Dermoscopy showing diffuse red background

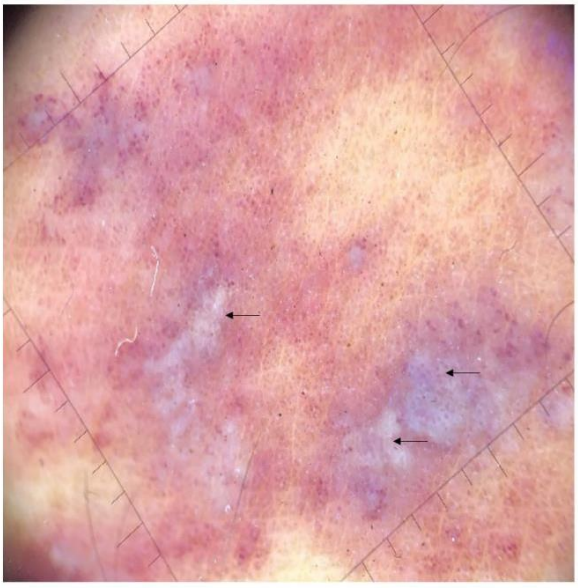


Figure 21 : Dermoscopy showing white structureless areas

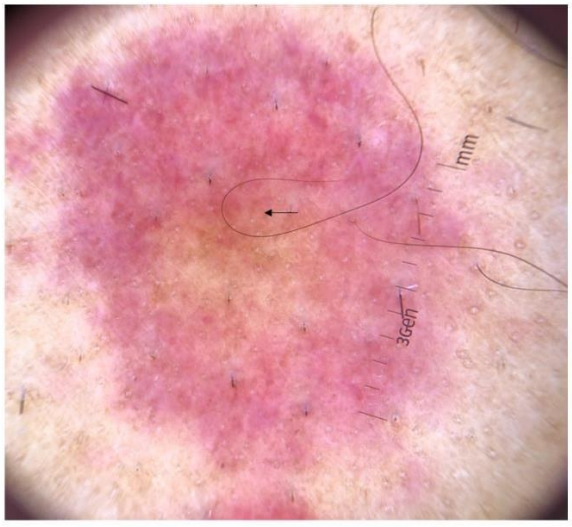


Figure 22 : Dermoscopy showing yellowish areas

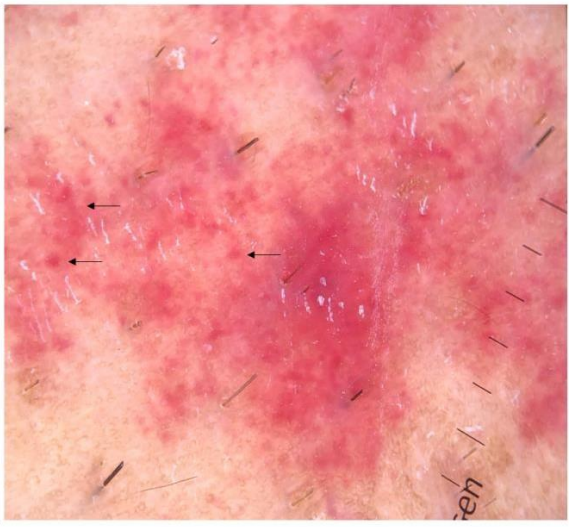


Figure 23 : Dermoscopy showing red globules

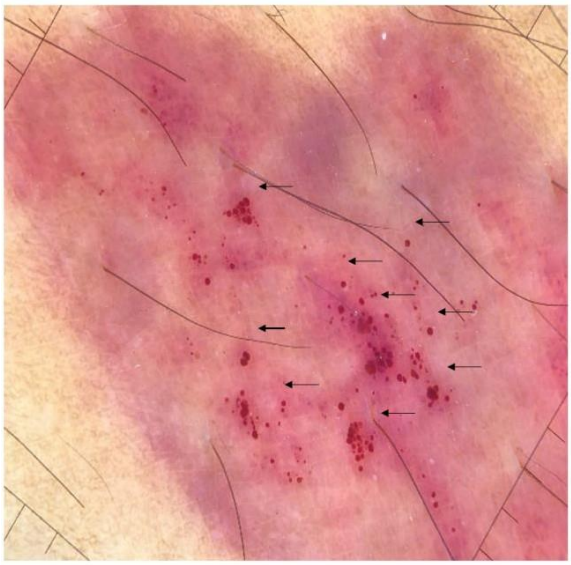


Figure 24 : Dermoscopy showing red dots

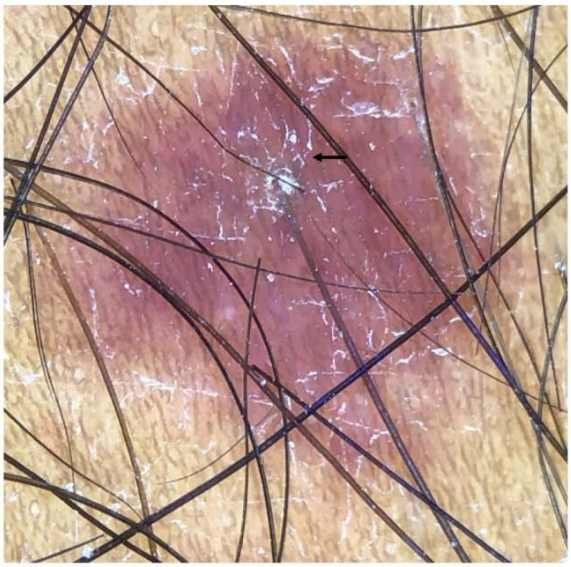


Figure 25 : Dermoscopy showing perifollicular scaling

Figure 26 : Dermoscopy showing follicular keratotic plug

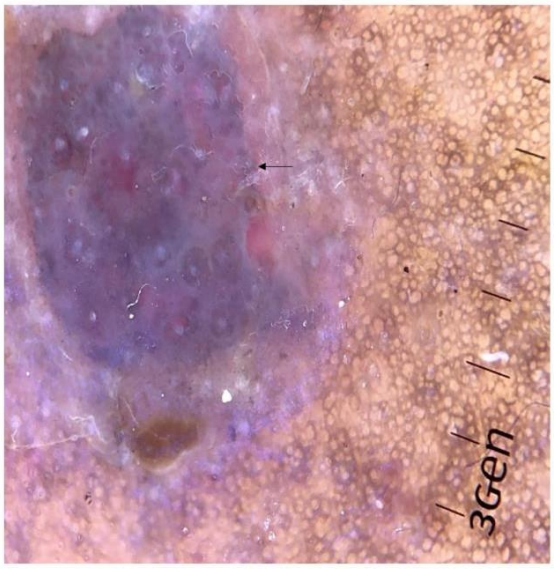


Figure 27 : Dermoscopy showing violaceous patches

Dermoscopy of early/evolving lesions:

Out of 30 patients, dermoscopy showed presence of dull red background in all the 30 patients (100.0%) followed by red globules in 8 (26.7%) and red dots in 4 (13.3%) patients.

Table 23and Figure 28 displays the frequency of each dermoscopy finding in early/evolving lesions

Table 23: Dermoscopy findings of early/evolving lesions

Dermoscopy finding	Frequency	Percent
Dull red background	30	100.0%
Red globules	8	26.70%
Red dots	4	13.30%

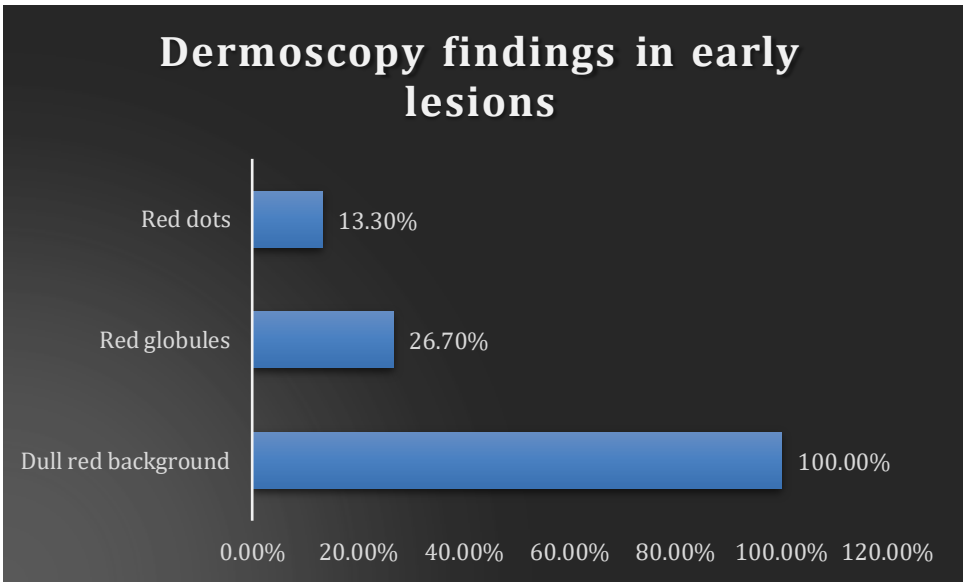


Figure 28: Dermoscopy findings in early lesions

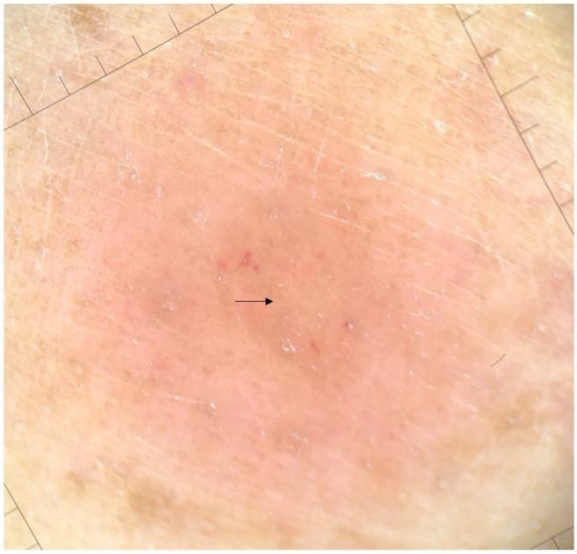


Figure 29 : Dermoscopy showing dull red areas

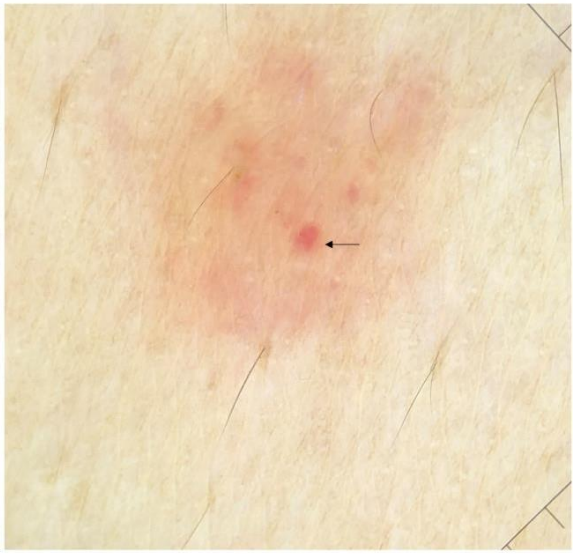


Figure 30 : Dermoscopy showing red globules

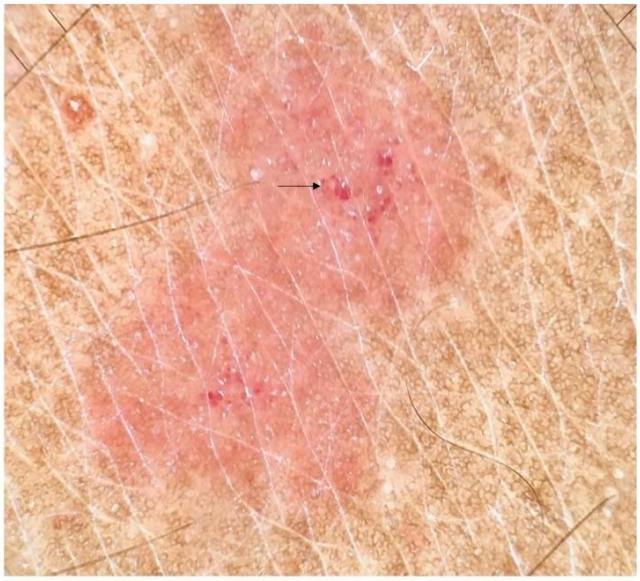


Figure 31 : Dermoscopy showing red dots

Histopathology:

The histopathological findings noted were perivascular infiltrate in all 30 (100.0%) patients out of which sparse and dense infiltrate was found in 17 (56.67%) and 13 (43.33%) patients respectively.Dilatation of vessels was noted in 21 (70%) patients. Leucocytoclasia was seen in

27 (90.0%) patients. Extravasation of RBCs were found in 16 (53.3%) patients. Fibrin deposition was noted in 15 (50.00%)patients.

Table 24 represent the presence of histopathological findings of cutaneous vasculitis included in the study.

Table 24: Findings on histopathology

Histopathology finding		**Frequency**	**Percent**
Perivascular infiltrate	Sparse (17)	30	100.0%
	Dense (13)		
Leucocytoclasia		27	90.0%
Extravasation of RBCs		16	53.3%
Fibrin deposition		15	50.0%
Dilatation of vessels		21	70.0%

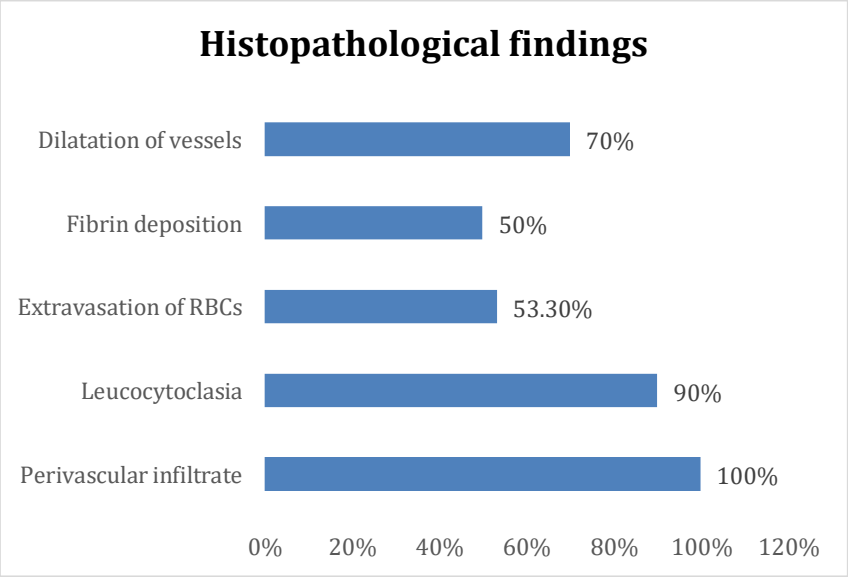


Figure 32: Histopathological findings in the study population

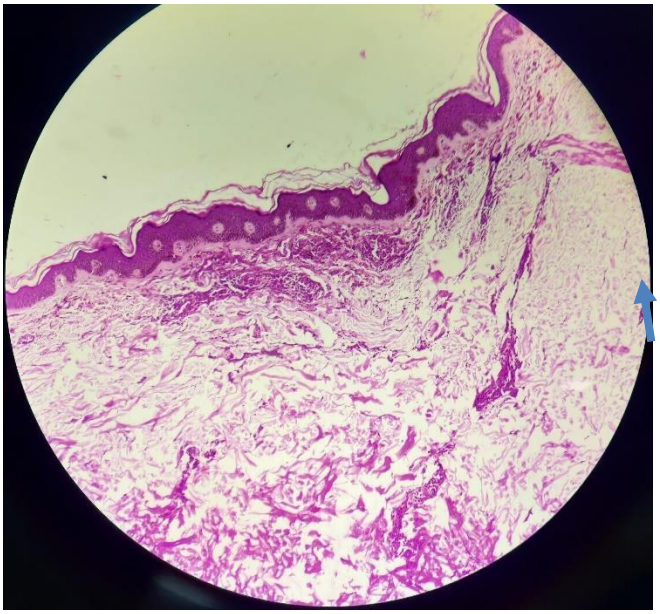


Figure 33: Histopathology (H and E 10x) of CSVV patient shows dense perivascular infiltrate with leucocytoclasia (blue arrow), extravasation of RBCs (green arrow)

Possible correlations between dermoscopic and histopathological findings are described in Table 25

Dermoscopic features	**Histopathological features**
Red dots	Extravasation of RBCs
Red globules	Extravasation of RBCs
Red background	Dilatation of vessels
White structureless areas	Sparse perivascular infiltrate
Yellowish areas	Dense perivascular infiltrate

Table 25: Dermoscopic -histopathological correlation

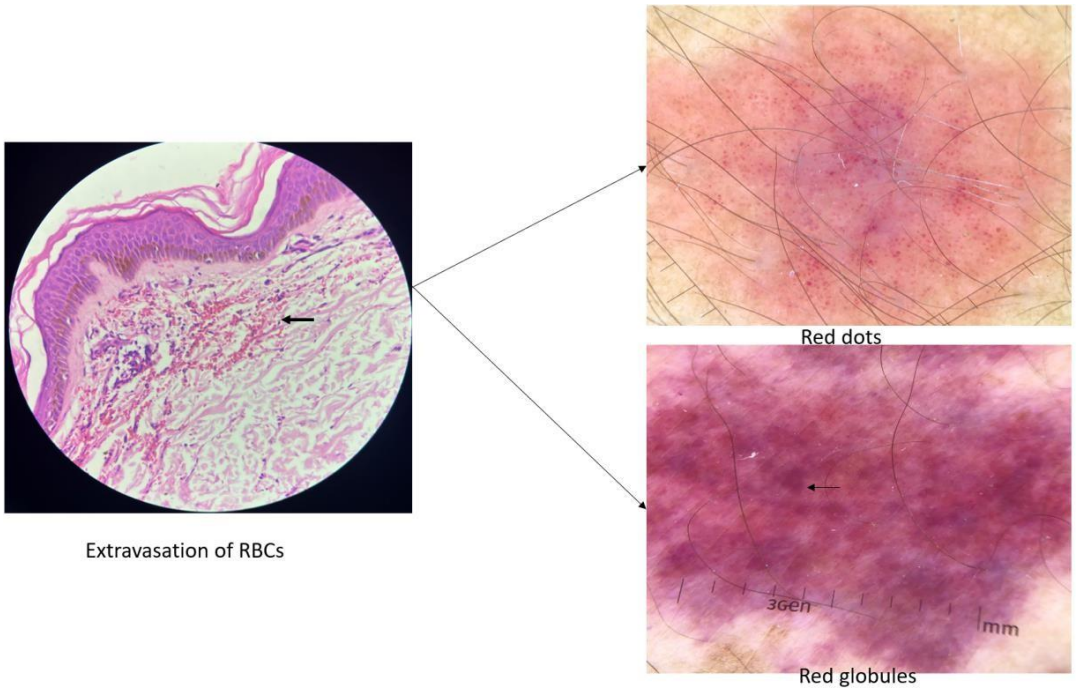


Figure 34: Extravasation of RBCs on HPE correlated with red dots and globules on dermoscopy

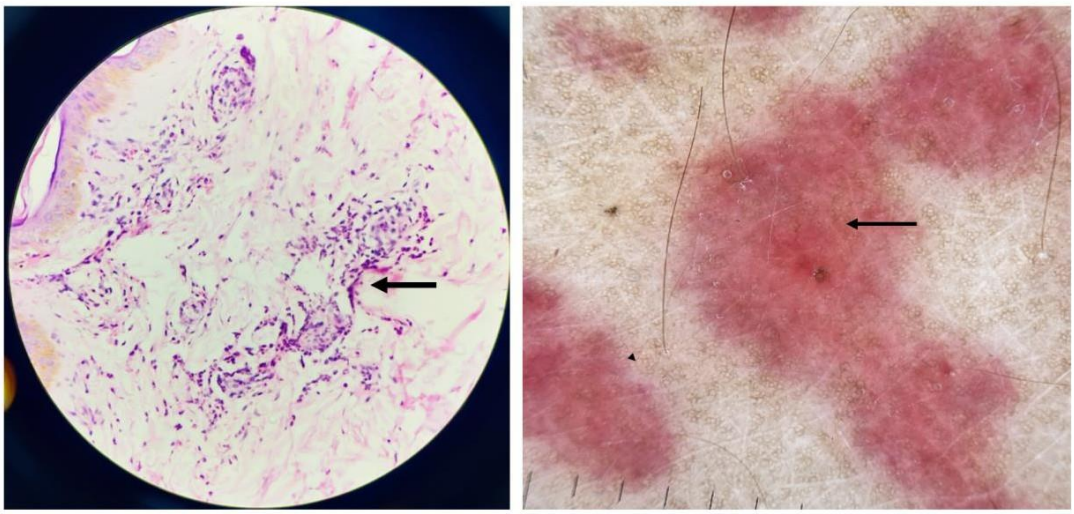
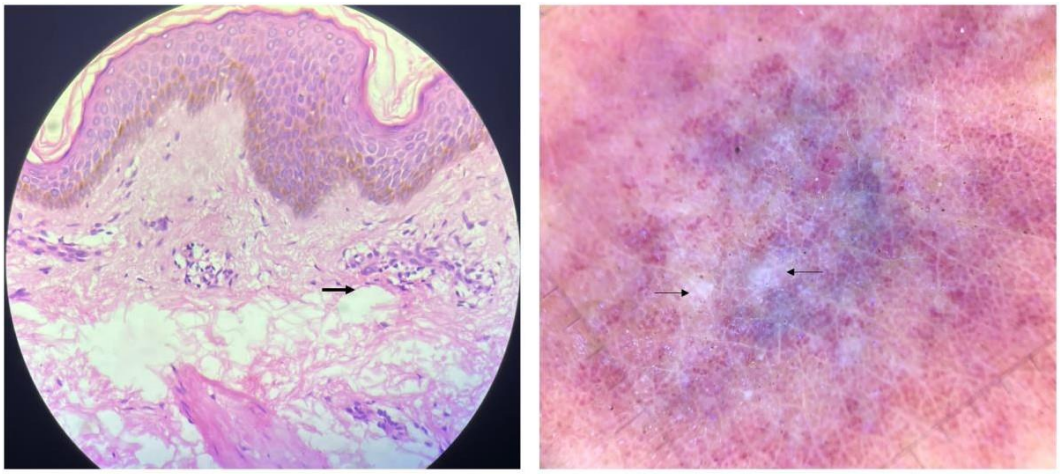
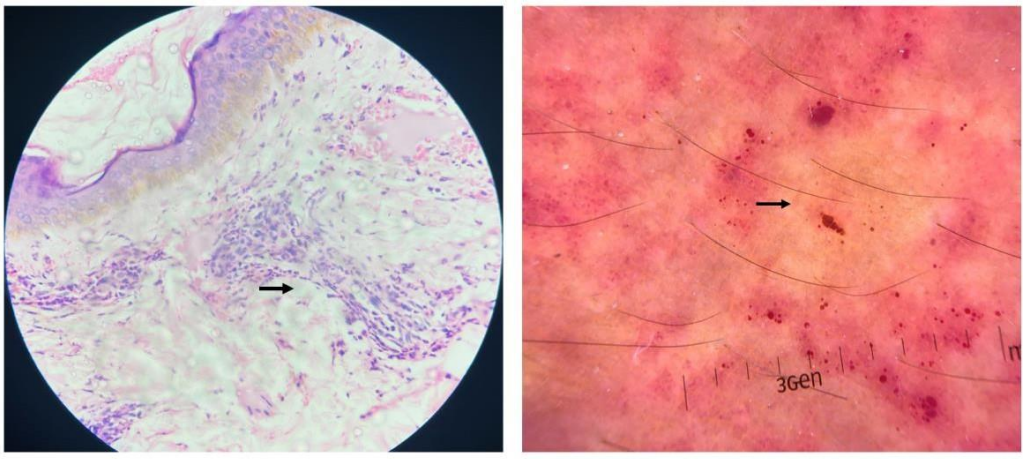


Figure 35: Dilated and congested vessels on HPE correlated with red background dermoscopically



Sparse perivascular infiltrate White structureless areas

Figure 36: Sparse perivascular infiltrate correlated with white structureless areas dermoscopically



Dense perivascular area Yellowish areas

Figure 37: Dense perivascular infiltrate correlated with yellowish areas dermoscopically

Red globules statistically corresponded to extravasation of RBCs whereas but not red dots. Red background did not statistically correspond to dilatation of vessels. White structureless areas and yellowish areas corresponded to sparse perivascular areas and dense perivascular areas respectively depicted in Table 26 to 30. Statistical association between dermoscopic and histopathological features and are represented in Table 31.

Table 26:Association between red dots and extravasation of RBCs

Red dots	Extravasation of RBCs			Chi square test	P value
	Absent	Present	Total		
Absent	9	5	14	3.274	0.07
%	64.3%	31.2%	46.7%		
Present	5	11	16		
%	35.7%	68.8%	53.3%		
Total	14	16	30		
%	100.0%	100.0%	100.0%		
Statistically not significant					

Table 27: Association between red globules and extravasation of RBCs

Red globules	Extravasation of RBCs			Chi square test	P value
	Absent	Present	Total		
Absent	9	3	12	6.451	**0.011**
%	64.3%	18.8%	40.0%		
Present	5	13	18		

%	35.7%	81.2%	60.0%		
Total	14	16	30		
%	100.0%	100.0%	100.0%		
Statistically significant					

Table 28: Association between red background and dilated vessels

Red background	Dilatation of vessels			Fisher's exact P value
	Absent	Present	Total	
Absent	1	1	2	
%	11.11%	4.76%	6.67%%	
Present	8	20	28	0.517
%	88.89%	95.24%	93.33%	
Total	28.57%	22	30	
%	100 %	100.0%	100%	
Statistically not significant				

Table 29: Association between white structureless areas and sparse perivascular infiltrate

White structureless areas	Sparse perivascular infiltrate			Fischer exact P- value
	Absent	Present	Total	
Present	5	14	19	
%	38.5%	82.4%	63.3%	**0.023**
Absent	8	3	11	

%	61.5%	17.6%	36.7%	
Total	13	17	30	
%	100.0%	100.0%	100.0%	
Statistically significant				

Table 30: Association between yellowish areas and dense perivascular infiltrate

Yellowish areas	Dense perivascular infiltrate			Fischer exact P- value
	Absent	Present	Total	
Present	7	12	19	**0.007**
%	41.2%	92.3%	63.3%	
Absent	10	1	11	
%	58.8%	7.7%	36.7%	
Total	17	13	30	
%	100.0%	100.0%	100.0%	
Statistically significant				

Dermoscopic features	**Histopathological features**	**P-value**	**Statistical association**
Red dots	Extravasation of RBCs	0.07	Statistically insignificant
Red globules	Extravasation of RBCs	**0.01**	**Statistically significant**

Red background	Dilated vessels	0.5	Statistically insignificant
Sparse perivascular infiltrate	White structureless areas	**0.02**	**Statistically significant**
Dense perivascular infiltrate	Yellowish areas	**0.007**	**Statistically significant**

Table 31: Statistical association between dermoscopy and histopathological features

Red globules, white structureless areas and yellowish areas demonstrated the diagnostic accuracy with 73.33% each correlated well with extravasation of RBCs, sparse perivascular infiltrate and dense perivascular infiltrate respectively. Red background displayed andiagnostic accuracy of 70% when correlated with dilated vessels histopathologically. whereas the red dots exhibited the accuracy of diagnosis with 66.67%. Table 32depicts the diagnostic accuracy of dermoscopy and histopathological changes in Cutaneous vasculitis

Dermoscopy finding	**Histopathology feature**	**Sensitivity%**	**Specificity%**	**Positive predictive value (%)**	**Negative predictive value (%)**	**Diagnostic accuracy**
Red dots	Extravasation of RBCs	68.75%	64.29%	68.75%	64.29%	66.67%
Red globules	Extravasation of RBCs	81.25%	64.29%	72.22%	75.00%	**73.33%**
Red background	Dilated vessels	95.24%	11.11%	71.43%	50.00%	**70.00%**
White	Sparse	82.35%	61.54%	73.68%	72.73%	**73.33%**

structureless areas	perivascular infiltrate					
Yellowish areas	Dense perivascular areas	92.31%	58.82%	63.16%	90.91%	**73.33%**

Table 32: Diagnostic accuracy of dermoscopic and histopathological features in our study

Dermoscopy finding in 10 patients with NLR > 3.165

Among this subset of 10 patients, red background was the predominant finding seen in 10 (100%), white structureless areas in 9 (90%)patients, red globules in 8 (80%), red dots in 7 (70%) and yellowish areas in 6 (60%) patients. Represented in Fig 38 and Table 33.

Dermoscopy findings	**Frequency of patients**	**Patients in percent**
Red background	10	100%
White structureless areas	9	90%
Red globules	8	80%
Red dots	7	70%
Yellowish areas	6	60%

Table 33: Dermoscopy findings in patients with NLR >3.615

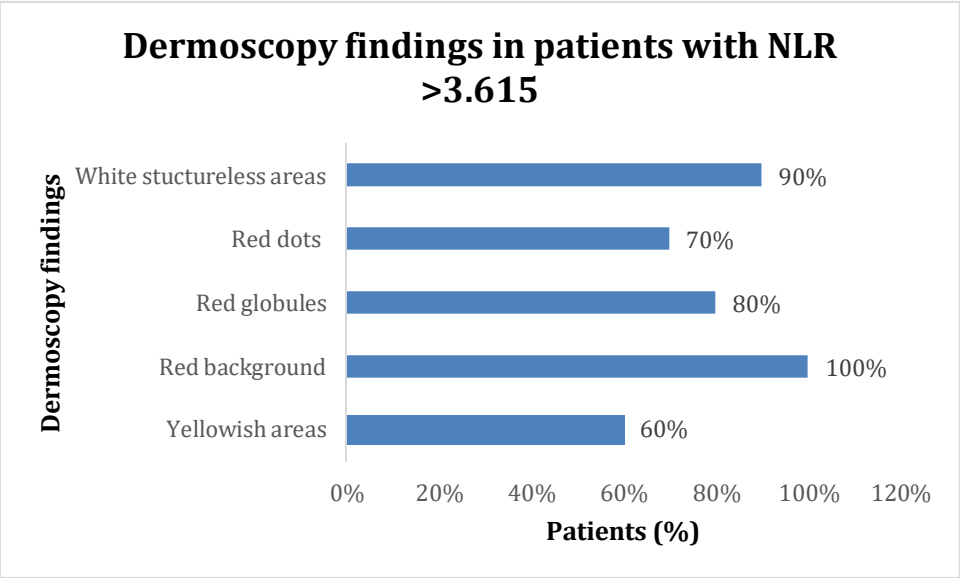


Figure 38: Dermoscopic findings in patients with NLR >3.615

Association between NLR and dermoscopy findings

There was a statistically significant association between NLR and dermoscopy finding of white structureless areas (P value – 0.04) whereas no association was found between NLR and other dermoscopy features red dots, red globules, red background and yellowish areas as portrayed in Table 34 to 38.

Table 34: Association between NLR and red dots

red dots	NLR		Fisher's exact test P-value
	</= 3.615	>3.615	
Absent	11	3	0.260
%	55.0%	30.0%	
Present	9	7	
%	45.0%	70.0%	
Total	20	10	

%	100.0%	100.0%	
Statistically insignificant			

Table 35: Association between NLR and red globules

red globules	NLR		Fisher's exact test P-value
	</= 3.615	>3.615	
Absent	10	2	0.235
%	50.0%	20.0%	
Present	10	8	
%	50.0%	80.0%	
Total	20	10	
%	100.0%	100.0%	
Statistically insignificant			

Table 36: Association between NLR and red background

Red background	NLR		Fisher' exact test P-value
	</= 3.615	>3.615	
Absent	2	0	0.540
%	10.0%	0.0%	
Present	18	10	

%	90.0%	100.0%	
Total	20	10	
%	100.0%	100.0%	
Statistically insignificant			

Table 37: Association between NLR and white structureless areas

White structureless areas	NLR		Fisher's exact test P-value
	</= 3.615	>3.615	
Absent	10	1	**0.049**
%	50.0%	10.0%	
Present	10	9	
%	50.0%	63.3%	
Total	20	10	
%	100.0%	100.0%	
Statistically significant			

Table 38: Association between NLR and yellowish areas

Yellowish areas	NLR		Fisher's exact P-value
	</= 3.615	>3.615	
Absent	7	4	1.000

%	35.0%	40.0%	
Present	13	6	
%	65.0%	60.0%	
Total	20	10	
%	100.0%	100.0%	
Statistically insignificant			

DISCUSSION

Dermoscopy is a non-invasive diagnostic method of magnifying skin lesions that enables one to understand the specifics of changes that take place both at the stratal and substratal surface. Dermoscopy characteristics are reflections of histological alterations.[80] Before confirming the diagnosis with a biopsy, dermoscopic evaluation of individuals with cutaneous small vessel vasculitis enables faster and non-invasive diagnosis. To date, studies pertaining to the correlation of dermoscopy findings with histopathological features of cutaneous vasculitis are lacking except few (3 in number) studies in the literature focussing solely on urticarial vasculitis and not other forms of cutaneous small vessel vasculitis. Also, we have intended to correlate dermoscopy findings with NLR reflecting systemic involvement. Additionally, to correlate NLR and disease duration in this study

This study describes the dermoscopic features of both old and new lesions of Cutaneous vasculitis depicted in Table 22 & 23 and Figure 19 & 28.

Table 39 Summarises the description of dermoscopy findings of urticarial vasculitis cases in the literature and our study

Study	Study population	Predominant Dermoscopy finding	2nd predominant finding	3rd common finding	4th common finding
Patel Madarkar *et al.* [77]	9 Urticarial vasculitis patients	Purpuric dots in 5 (25%)	Purpuric globules in 8 (40%)	-	-
Garcia G B *et al.* [76]	27 Urticarial vasculitis patients	Red linear vessels	Purpuric globules in	-	-

		(74%)	19 (70.4%) patients		
Lopez VF *et al.* [78]	20 Urticarial vasculitis patients	Red lines in 17 (85%)	Purpuric dots and globules in 3 (15%)	-	-
Our study Total 30 patients 16 patients – HSP 14 patients-CSVV	Old established lesions (lesions lasting more than 1 week)	Red background in 28 (93.30%) patients	White structureless and yellowish areas in 19 (63.33%) each	Red globules in 18 (60.0%) patients	Red dots in 16 (60.00%) patients
	New lesions (lesions lasting less than 1 week)	Dull red areas in 30 (100%) patients	Red globules in 8 (26.70%) patients	Red dots in 4(13.30%) patients	

Table 39: Comparision between our study and other studies of urticarial vasculitis in the literature

Red background was the most common finding in established lesions of patients in our study seen in 28 (93.3%) patients. The histopathological correlation of a homogenous red background may be attributed to the presence of increased vascularity (dilatation of vessels). Still, the

histopathological and dermoscopic correlation was not statistically significant (p value 0.05). This could be attributed to additional factors like dermal collagen. The white structureless areas which were seen in 63.33% of the cases in our study, corresponded to sparse but deep perivascular infiltrate with statistically significant histopathological-dermoscopic correlation (p value 0.023).

The yellowish areas were also seen in 63.33% of the cases, attributing to dense but superficial perivascular infiltrate with the dermoscopy-histopathological correlation being statistically significant (P value 0.007).

Red globules were noted in 60% of the cases. This was well correlated with the histopathological feature of extravasation of RBCs with a P-value of 0.011

A study done by Madarkar *et al*.[77]showed that purpuric globules correlate with the extravasated and degraded red blood cells in urticarial vasculitis. This finding is in accordance with our study results.

Red dots were noted in 53.30% of the cases. This also attributes to the extravasation of RBCs histopathologically, but the dermoscopy and histopathological correlation was found to be insignificant (P value – 0.07).

Practically, red dots and globules both signify RBC extravasation; however, statistically, red globules correlate with extravasation but not red dots.

Other less frequent findings in established lesions were perifollicular scaling, follicular keratotic plugs and violaceous patches.

Dermoscopic features in early/ evolving lesions included dull red evolving background, red globules and red dots without findings like white structureless and yellowish areas in contrast to established lesions.

NLR is an inexpensive and feasible diagnostic that can be used to identify inflammatory reactions.[81]

The significance of NLR as a prognostic factor for systemic involvement in IgA vasculitis has already been described in the literature.[8]

"The optimal cut-off value of NLR obtained for determining overall systemic involvement (renal and/or gastrointestinal involvement) in this study was 3.615," with a sensitivity and specificity are 60% and 93.33% respectively. This demonstrates the value of NLR as a "better measure of concurrent systemic involvement in cutaneous vasculitis."

Our results were in accordance with those obtained from other previous studies which includes a study done by George RM *et al*.[8] derived an optimal NLR cut-off of 3.25 with a sensitivity of 59% and specificity of 100%. A retrospective assessment of 40 IgA vasculitis patients by Nagy *et al*.[7] found that the "optimal cut-off value of NLR to anticipate systemic involvement being 3.34, the sensitivity and specificity being 85% and 95% respectively." An ideal NLR cut-off value of 3.18 for predicting a quick recovery without relapse with a sensitivity of 74.1% and specificity of 75% and 3.90 for predicting GI bleeding can be employed in adult patients with HSP, according to a similar study by Park *et al*[56].

Table40: Sensitivity and specificity association with NLR

Study	Sensitivity	Specificity	Optimal NLR
Nagy *et al*	85%	95%	3.34
George *et al.*	59%	100%	3.25
Park *et al.*	74.1%	75%	3.18
This study	60%	93.33%	3.615

There was a statistically significant association between NLR and systemic involvement (p value 0.001) (Table 21). Additionally a positive moderate correlation between the duration of lesions and NLR was found between NLR and duration of the lesions (Figure 14) value implying that NLR is directly proportional to the duration of the lesions implying longer the duration of cutaneous lesions, greater the NLR value.

There were a total of 10 (33.33%) patients who had NLR values greater than the ideal cut-off of 3.615 obtained in this study. Among these 10 patients, red background was the predominant finding seen followed by white structureless areas, red globules, red dots and yellowish areas in a descending fashion. There was a significant association derived statistically between NLR and dermoscopy finding of white structureless areas whereas no such association was found between NLR and other dermoscopic findings probably implicating white structureless areas may probably be seen predominantly in patients with increased NLR associated with systemic involvement.

Limitations of this study include small sample size due to the COVID pandemic and ongoing therapy was not regarded as an exclusion factor which might have affected the dermoscopic characteristics.

CONCLUSION

Vasculitis is a specific type of blood vessel wall inflammation that can affect any organ of the body. Cutaneous vasculitis can be

1. Skin-specific disease
2. A primary cutaneous vasculitis with secondary systemic involvement
3. A cutaneous manifestation of systemic vasculitis [42]

In this study, we intend to analyse the dermoscopic findings in both old and new lesions of cutaneous vasculitis and correlate them with histopathological findings with respect to established lesion. We also evaluated the significance of dermoscopy findings in predicting systemic involvement using NLR. We also correlated NLR with the duration of the disease. The following conclusions were drawn from the study:

1. Cutaneous small vessel vasculitis and HSP were observed in 14 (46.70%) and 16 (53.30%) of the 30 patients with a diagnosis of cutaneous vasculitis, respectively.
2. Patients in the study ranged in age from 10 to 80 years old, with young adults in the 20 to 30 age range being the most often affected group.
3. Males outnumbered females by a ratio of 1.3:1.
4. The majority of patients arrived with lesions that had lasted less than one week as opposed to more than one week in duration.
5. Cutaneous manifestation preceded by drug intake was noted in 30 % of the cases
6. Recurrence was noted in 23.3% of the cases

7. Optimum cut-off of NLR predicting systemic involvement was found to be 3.615 with sensitivity and specificity of 60% and 93.33% respectively. There was a statistically significant association between NLR and systemic involvement.
8. A moderately positive correlation between NLR and the duration of the cutaneous lesions was found.
9. Red background was the most frequent dermoscopic finding in established lesions of cutaneous vasculitis lesions, followed in descending order by white structureless areas, yellowish areas, red globules, and red dots. Perifollicular scaling, follicular keratotic plugs, and violaceous patches were other less frequent observations.
10. Dermoscopy in early/evolving lesions (lesions that had been present for less than 48hours) revealed dull red background as the most common finding followed by red globules and red dots.
11. In terms of dermoscopy-histopathological connection statistically, red globules but not red dots were indicative of RBC extravasation. The sparse and dense perivascular infiltrates were represented by white structureless areas and yellowish areas, respectively. On histopathology, a red background did not statistically correlate with dilated vessels.
12. Red background was the most prevalent dermoscopic finding in 10 individuals with NLR >3.165, followed in descending order by white structureless patches, red globules, red dots, and yellowish areas.
13. Additionally, there was a statistically significant correlation between NLR and the dermoscopy finding of white structureless areas but not with others.

To conclude, dermoscopy is a viable supplementary approach for the diagnosis of cutaneous small vessel vasculitis in terms of confirming a clinical diagnosis, even though it cannot replace

histopathology. Additionally, it can be used to correlate systemic involvement through its marker NLR. It can be used as an indirect noninvasive tool for foretelling systemic involvement in patients with cutaneous vasculitis.

SUMMARY

A hospital-based, cross-sectional study was conducted during the period of January 2021 to June 2022 to analyse dermoscopic findings in both established and new lesions of patients with Cutaneous vasculitis and correlate its features with histopathological changes. Additionally, to evaluate how it relates to systemic involvement and NLR values.

The salient features found in this study are listed below:

1. Cutaneous vasculitis was most prevalent in young adults, with a slight male predominance.
2. Systemic involvement (renal and gastrointestinal involvement) was noted in half of the total patients
3. Optimal cut-off of NLR for predicting combined systemic involvement was 3.615 with sensitivity and specificity of 60% and 93.33% respectively and a significant statistical association between NLR and systemic involvement
4. Positive moderate correlation between NLR and duration.
5. Red background was the most prevalent dermoscopic feature in established cutaneous vasculitis lesions, followed by white structureless areas, yellowish areas, red globules, and dots.
6. Dull red areas, red globules, and red dots were the most frequent dermoscopic findings in early lesions of cutaneous vasculitis.
7. We also found agreement between dermoscopic and histopathological findings namely red globules with extravasation of RBCS, yellowish areas with dense perivascular infiltrate, white structureless areas with sparse perivascular infiltrate

8. There is a statistically significant correlation between the NLR and dermoscopic finding of white structureless areas, suggesting that this feature may be present predominantly in patients who have systemic involvement as shown by an increase in the NLR value.

Although dermoscopy cannot completely replace histopathology, it is a useful adjunct method for diagnosing cutaneous small vessel vasculitis and confirming a clinical diagnosis. A particular dermoscopy finding like white structureless areas in our study may indicate systemic involvement and be linked to a higher NLR value.

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ETHICAL CLEARANCE CERTIFICATE

IEC/NO-09/2021
Date-22/01/2021

B.L.D.E. (DEEMED TO BE UNIVERSITY)
(Declared vide notification No. F.9-37/2007-U.3 (A) Dated. 29-2-2008 of the MHRD, Government of India under Section 3 of the UGC Act, 1956)
The Constituent College
SHRI. B. M. PATIL MEDICAL COLLEGE, HOSPITAL AND RESEARCH CENTRE

INSTITUTIONAL ETHICAL CLEARANCE CERTIFICATE

The Institutional ethical committee of this college met on 11-01-2021 at 11-00 am to scrutinize the synopsis of Postgraduate students of this college from Ethical Clearance point of view. After scrutiny the following original/corrected and revised version synopsis of the Thesis has been accorded Ethical Clearance

Title: A hospital based cross-sectional study to estimate serum levels of interleukin-6 and high sensitivity c-reactive protein and their correlation with the vitiligo disease activity and exten.

Name of PG student: Dr Bhargavi Uttmani, Department of Dermatology

Name of Guide/Co-investigator: Dr Keshavmurthy Adya, Associate Professor of Dermatology

DR .S.V.PATIL
CHAIRMAN, IEC
Institutional Ethical Committee
B L D E (Deemed to be University)
Shri B.M. Patil Medical College,
VIJAYAPUR-586103 (Karnataka)

Following documents were placed before Ethical Committee for Scrutinization:

1. Copy of Synopsis / Research project
2. Copy of informed consent form
3. Any other relevant documents.

5

CONSENT FORM

B.L.D.E (Deemed to be university) SHRI B.M PATIL MEDICAL COLLEGE

HOSPITAL AND RESEARCH CENTRE, VIJAYAPURA-586 103

INFORMED CONSENT FOR PARTICIPATION IN DISSERTATION/RESEARCH

TITLE OF THE PROJECT : DERMOSCOPIC ASSESSMENT OF CUTANEOUS SMALL VESSEL VASCULITIS AND CORRELATION WITH CLINICAL AND HISTOPATHOLOGICAL FINDINGS- A CROSS SECTIONAL STUDY.

PG GUIDE: DR. KESHAVMURTHY ADYA

PG STUDENT: DR. KAVYADEEPU R.M

PURPOSE OF RESEARCH:

I have been informed that this project dermoscopic assessment of cutaneous small vessel vasculitis and correlation with clinical and histopathological findings at Shri BM Patil Medical College and Research Centre, VIJAYAPURA.

BENEFITS:-

I understand that my participation in this study will help the investigator to dermoscopically assess cutaneous small vessel vasculitis and correlate with clinical and histopathological findings

PROCEDURE:-

I understand that relevant history will be taken and the personal data will be protected.

CONFIDENTIALITY:-

I understand that medical information produced by this study will become a part of my hospital records and will be subjected to the confidentiality and privacy regulation of the said hospital. Information of a sensitive personal nature will not be a part of the medical records, but will be stored in the investigator's research file.

If the data are used for publication in the medical literature or for teaching purposes no names will be used and other identifiers such as photographs and audio or videotapes will be used only with my special written permission. I understand I may see the photographs, videotapes and hear the audiotapes before giving this permission.

REQUEST FOR MORE INFORMATION:-

I understand that I may ask more questions about the study at any time concerned. Dr. KavyaDeepu R.M is available to answer my questions or concerns. I understand that I will be informed of any significant new findings discovered during the course of this study, which may influence my continued participation.

REFUSAL OR WITHDRAWAL OF PARTICIPATION:-

I understand that my participation is voluntary and I may refuse to participate or may withdraw consent and discontinue participation in this study at any time without prejudice. I also understand that Dr.KavyaDeepu R.M may terminate my participation in this study at any time after she has explained the reasons for doing so and has helped arrange for my continued care by my own physician, if this is appropriate.

INJURY STATEMENT:-

I understand that in the unlikely event of injury to me resulting directly from my participation in this study and if such injury were reported promptly, then medical treatment will be available to me, but no further compensation will be provided. I understand that by my agreement for my participation in this study, I am not waiving any of my legal rights.

I have explained to (patient's / relevant guardian's name) the purpose of the research, the procedures required, and the possible risks and benefits to the best of my ability in patient's own language.

_____ _____

Investigator / P. G. Guide Date

I confirm that Dr. KavyaDeepu R M(Name of the PG guide / chief researcher) has explained to me the research, the study procedures that I undergo and the possible risks and discomforts as well as benefits that I may experience. I have read and I understand this consent form. Therefore, I agree to give my consent for my participation as a subject in this research project.

Participant / guardian	Date
Witness to signature	Date

PROFORMA

Department of Dermatology, Venerology and Leprosy

S.No: **Date:**

Name: **Hospital Number:**

Age / Sex:

Address and Contact Details:

Presenting Features:

History suggestive of preceding infection:

H/O any drug intake before the onset of the lesions:

- **Drug details:**

H/O recurrent episodes:

H/O any chronic renal/ gastrointestinal/ hematological disorders:

H/O haematemesis/ haematochezia 2 days prior to presentation:

Cutaneous lesions:

Mucosal lesions:

Other systemic involvement:

Constitutional: Fever, weight loss, fatigue

Musculocutaneous: arthralgias, myalgias.

Renal: hematuria

Gastro-enterologic: Abdominal pain, bloody stools

Neurologic: numbness, paraesthesias, weakness

Cardiopulmonary: shortness of breath, chest pain, cough, hemoptysis

Ear/ Nose/ Throat: sinusitis

Joint pain:

Scrotal pain:

Hypertension/ headache:

Provisional diagnosis:

Dermoscopy Findings:

Investigations:

Histopathological findings:

Immunofluorescence findings:

Final Diagnosis:

KEY TO MASTER CHART

F- Female, M- Male

P-Present, A-Absent

NLR- Neutrophilic lymphocyte ratio

cNLR -Categorization of NLR based on cut-off of NLR

DIF- Direct immunofluorescence

IgA-Immunoglobulin A, IgM- Immunoglobulin M

CSVV- Cutaneous small vessel vasculitis

HSP- Henoch Schonlein purpura

MASTERCHART

S. No.	Age	Sex	Duration (in days)	Prior infection	Drug intake	Recurrence	cNLR	NLR	Albuminuria	Hematuria	stool occult blood	Systemic involvement	Dermoscopy of old lesions								Dermoscopy of new lesions			HPE						DIF	Final diagnosis
													Red dots	Red globules	Yellowish areas	Red background	Whitestructureless areas	Perifollicular scaling	Follicular keratotic plugs	Violaceous patches	Red dots	Red globules	Dull red areas	Sparse infiltrate	Dense infiltrate	Leucocytoclasis	Extravasation of RBCs	Dilated vessels	Fibrin deposition		
1	26	F	7	P	A	P	>3.615	5.5	P	P	P	P	P	P	A	P	P	P	P	A	P	P	P	P	A	P	P	P	P	IgA & fibrinogen	HSP
2	16	M	3	A	A	P	≤3.615	1.7	A	A	A	A	P	P	A	P	A	A	A	A	A	P	P	P	A	P	P	A	A	not done	CSVV
3	29	F	14	P	A	P	>3.615	21.11	P	P	P	P	P	P	P	P	P	A	A	A	A	A	P	P	A	P	P	P	P	IgA ,C3	HSP
4	58	F	5	A	A	A	≤3.615	0.85	A	A	A	A	P	P	P	P	P	A	A	A	A	A	P	P	A	P	P	A	A	IgM,C3 & fibrinogen	CSVV
5	41	M	10	A	A	P	≤3.615	2.3	A	A	A	A	P	A	A	A	A	A	A	P	A	P	P	P	A	P	A	P	A	IgA, fibrinogen	CSVV
6	23	M	21	P	A	A	≤3.615	2.9	A	A	A	A	A	A	P	A	A	A	A	A	A	A	P	A	P	A	A	A	A	IgM,IgA& fibrinogen	CSVV
7	40	M	10	A	A	P	≤3.615	3.17	A	A	A	A	A	A	A	P	P	A	P	A	A	P	P	P	A	P	P	P	P	IgA, fibrinogen	HSP
8	14	F	10	A	A	A	≤3.615	3.14	P	P	P	P	P	P	P	P	A	A	A	P	P	P	P	A	P	P	P	A	A	IgM,IgA& fibrinogen	CSVV
9	18	M	7	A	A	P	≤3.615	0.94	P	A	A	P	P	A	P	P	A	P	A	A	A	A	P	A	P	P	A	P	A	IgA ,c3& fibrinogen	HSP
10	10	M	10	A	A	P	≤3.615	2.7	P	A	A	P	P	P	P	P	A	A	P	A	A	A	P	A	P	P	P	P	P	IgA ,c3& fibrinogen	HSP
11	45	M	2	A	A	A	≤3.615	1.3	A	A	A	A	A	A	A	P	P	A	P	A	A	A	P	P	A	A	A	A	P	not done	CSVV
12	58	F	7	A	P	A	≤3.615	2.5	A	A	A	P	A	P	P	P	A	P	P	A	A	A	P	A	P	A	A	P	P	C3 and fibrinogen	CSVV
13	50	F	14	A	P	A	>3.615	6.3	A	A	A	P	P	P	P	P	P	P	P	A	A	A	P	P	A	P	P	P	P	IgM,C3 &	

																													fibrinogen	CSVV
14	24	F	14	A	A	A	≤3.615	3.5	A	A	A	A	A	P	A	P	P	A	A	A	P	A	P	P	A	P	P	P	A	not done	CSVV
15	36	M	10	A	A	P	≤3.615	1.7	A	P	A	P	P	A	P	P	A	A	P	A	A	A	P	A	P	P	A	A	P	IgA , fibrinogen	HSP
16	40	M	3	A	A	A	≤3.615	2.71	A	A	A	A	P	P	P	P	P	P	P	A	A	A	P	A	P	P	P	P	P	C3, fibrinogen	CSVV
17	47	M	20	A	A	A	>3.615	7.2	P	P	A	P	P	A	P	P	P	P	P	A	A	A	P	A	P	P	A	P	P	C3 & fibrinogen	CSVV
18	15	F	20	A	A	A	≤3.615	2	A	A	A	A	A	A	A	P	A	A	P	A	A	A	P	A	P	P	P	P	P	IgM, fibrinogen	CSVV
19	31	M	2	A	A	A	≤3.615	2.14	P	P	A	P	A	A	P	P	A	A	P	A	A	P	P	A	P	P	P	P	A	IgA	HSP
20	22	F	15	A	A	A	≤3.615	3.38	A	A	A	A	P	P	P	P	P	A	A	A	A	A	P	A	P	P	A	A	P	IgA, C3, fibrinogen	HSP
21	34	M	5	P	A	A	>3.615	3.63	P	A	A	P	A	P	P	P	P	A	A	A	A	A	P	P	A	P	A	P	A	IgA, C3 , fibrinogen	HSP
22	22	F	7	P	A	A	≤3.615	1.68	A	A	A	A	A	P	P	P	P	A	A	A	A	A	P	P	A	P	A	P	A	fibrinogen	CSVV
23	55	M	15	A	A	A	>3.615	7.6	P	A	A	P	P	P	P	P	P	P	A	A	A	A	P	P	A	P	P	P	P	IgA, C3 , fibrinogen	HSP
24	42	M	30	P	A	A	>3.615	3.8	A	A	P	P	A	P	P	P	A	P	A	A	A	A	P	P	A	P	P	P	A	IgA, C3, fibrinogen	HSP
25	39	M	7	P	A	A	>3.615	4.5	A	P	A	P	A	A	A	P	P	P	A	A	A	P	P	P	A	P	A	P	A	IgA, IgM ,C3, fibrinogen	HSP
26	30	M	1	P	A	A	≤3.615	0.9	A	A	A	A	A	P	P	P	P	P	A	A	P	A	P	A	P	P	A	A	P	IgA, C3 & fibrinogen	HSP
27	23	F	1	A	A	A	≤3.615	1	A	A	A	A	A	A	P	P	P	A	A	A	A	A	P	A	P	P	A	P	A	IgA, C3	HSP
28	71	M	15	A	A	A	>3.615	11	P	A	A	P	P	P	A	P	P	A	A	A	A	A	P	P	A	P	P	A	P	IgA, C3, fibrinogen	HSP
29	24	F	20	A	A	A	≤3.615	3.6	A	A	A	A	A	A	A	P	P	P	A	A	P	A	P	P	A	P	A	P	A	IgA	HSP
30	55	F	10	P	A	A	>3.615	3.9	A	P	A	P	P	P	A	P	P	P	A	A	A	P	P	P	A	P	P	P	A	IgM, fibrinogen	CSVV