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Original Research Article

A study on clinico- epidemiological profile & histopathological profile of cutaneous vasculitis

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ABSTRACT

Objective: The study aimed to analyse the potential etiological factors, clinical presentation, past medical history & laboratory findings in patients with biopsy-proven cutaneous vasculitis to better understand the disease and identify the disease classifications. The objective of this study was to establish a database of the clinic-epidemiological profile and histopathological features of cutaneous vasculitis in a tertiary hospital in Eastern Nepal.

Materials and Methods: A Descriptive cross-sectional study was planned to analyse and study the clinic-epidemiological profile and histopathological features of cutaneous vasculitis in Nepal. This study has reviewed the facts which were published earlier to determine the current scenario by vast study of statistics and derivation of facts. Proper examination of data was made to evaluate with final conclusion. The study included sample size of 30 consecutive patients with biopsy-proven cutaneous vasculitis attending the Dermatology outpatient department and admitted to the dermatology ward at B.P. Koirala Institute of Health Science, Dharan.

Result: The study population of 30 patients with biopsy-proven cutaneous vasculitis, with an average age of 32.96 years, and a female-to-male ratio of 1.3:1. The majority of patients (66.67%) had lesions lasting less than 6 weeks, and acute disease was observed in 86.66% of the cases. The most common symptoms were itching (73.66%) and arthralgia (66.67%). Palpable purpura was the predominant cutaneous manifestation (70%), mainly distributed on the legs and ankles (93.33%). Elevated ESR was the most common laboratory abnormality (73.33%). Histopathological examination revealed leukocytoclastic vasculitis in 97% of cases, with predominantly neutrophilic infiltrates. Henoch-Schoenlein purpura (HSP) was the most common classification (43.33%), followed by urticarial vasculitis (26.67%).

Conclusion: This study provides valuable insights into the clinic-epidemiological profile and histopathological features of cutaneous vasculitis in the Nepalese population. It highlights the diverse clinical presentation and laboratory abnormalities associated with the condition, as well as potential etiological factors and disease classifications. The findings contribute to improved understanding, diagnosis, and management of cutaneous vasculitis. Further studies with larger cohorts are needed to validate and expand upon these findings.

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1. Introduction

Vasculitis is a complex histological diagnosis characterized by inflammation affecting blood vessel walls, leading to haemorrhagic and/or ischaemic events. The spectrum of

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vasculitis includes primary vasculitis, which is idiopathic, such as cutaneous leukocytoclastic angiitis (CLA), Wegener's granulomatosis (WG), Churg-Strauss syndrome (CSS), and microscopic polyangiitis (MPA). Secondary vasculitis can manifest as a result of connective tissue diseases (CTD), infections, adverse drug eruptions, or paraneoplastic phenomena. There is also an incidental form of vasculitis, a histological finding that arises as a consequence of other pathological processes.[1]

Clinically, cutaneous vasculitis can present with diverse morphologies, including urticaria, purpura, haemorrhagic vesicles, ulcers, nodules, livedo, infarcts, and digital gangrene. Accurate recognition and classification of patients presenting with cutaneous vasculitis are challenging due to the broad range of presentations and the numerous disorders that can mimic vasculitis.[2] To facilitate diagnosis and differential diagnosis, this study focuses on the histological spectrum of cutaneous vasculitis, elucidating how specific cutaneous histological patterns can aid in generating relevant clinical differential diagnoses. When combined with clinical and laboratory data, these histological patterns allow for a more precise and accurate diagnosis of vasculitis syndromes.[3]

Various classification systems for vasculitis have been proposed, with the Chapel Hill Consensus Conference (CHCC) and the American College of Rheumatology (ACR) criteria being the most widely adopted. However, these systems have limitations when applied to individual patients, as they may lack recognition of specific disorders and exhibit overlaps among primary vasculitis. Cutaneous polyarteritis nodosa (CPAN) is a subset of vasculitis that predominantly affects the skin and may present with extracutaneous manifestations such as fever, malaise, myalgias, arthralgias, and neuropathy. Distinguishing between systemic PAN and CPAN is crucial due to their distinct clinical courses and management.[4]

Despite the pervasiveness of multi-organ involvement in systemic PAN, cutaneous findings often serve as the initial evidence of the disease. The aetiology of CPAN remains uncertain, but it is believed to be mediated by immune complexes, with evidence of IgM and C3 deposits in affected arterial walls. Infections and autoimmune diseases have been associated with CPAN, as well as certain drugs and vaccinations.[5]

While some anecdotal case reports of CPAN exist, there is a lack of comprehensive epidemiological data on CPAN in Nepal. Therefore, the objective of this study is to establish a database of epidemiological, clinical, and laboratory information of CPAN patients admitted to vasculitis clinics in a tertiary hospital in Nepal. By collecting and analyzing this data, a better understanding of the epidemiological profile and histopathological features of cutaneous vasculitis can be achieved, ultimately contributing to improved patient care and management.[6]

2. Materials and Methods

A Descriptive cross-sectional study was planned to analyse and study the clinic-epidemiological profile and histopathological features of cutaneous vasculitis in Nepal. This study has reviewed the facts which were published earlier to determine the current scenario by vast study of statistics and derivation of facts. Proper examination of data was made to evaluate with final conclusion.

2.1. Materials

All consecutive patients with biopsy-proven cutaneous vasculitis attending the outpatient department (OPD) and admitted in the dermatology ward at B.P. Koirala Institute of Health Science, Dharan were included in the study.

2.2. Study design

This study followed a descriptive cross-sectional design.

2.3. Inclusion criteria

1. All patients attending the OPD and admitted ward with cutaneous vasculitis.
2. Patients of any age and sex irrespective of the duration of the disease.
3. Those willing to participate in the study.

2.4. Exclusion criteria

1. Patients not willing to participate in the study.
2. Patients with thrombocytopenia.
3. Patients with disorders of coagulation.
4. Patients on warfarin/heparin.

2.5. Study period

The study was conducted for a period of 1 year, from 16th April 2014 to 15th April 2015.

Sample Size: The sample size was determined on the basis of available literature. With the application of electronic databases- PubMed, Google Scholar, Web of Science, Medline Plus, Health line & Cleveland Clinic and NIH web search was done. According to previous studies, the frequency of infection as an etiology in cutaneous vasculitis cases ranged from 10% to 15%. Considering an average frequency of 15% of cases attributed to infection, the sample size was calculated as follows:

Sample size = Z^2 * P * Q / L^2

Where

Z = Z-score for a 95% confidence level (1.96)

P = Estimated proportion (0.15)

Q = 1 - P

L = Precision (0.032)

Sample size for an infinite population = 554

As the total number of biopsy-proven cutaneous vasculitis cases in BPKIHS, Dharan in a 1-year period was 32, the sample size for a finite population was calculated as follows:

Sample size (n) = n0 / (1 + n0 / N)

Where

n0 = Sample size for an infinite population (554)

N = Total population (32)

Sample size for the finite population = 30

2.6. Methodology

2.6.1. Enrolment of the patients

All consecutive patients with biopsy-proven cutaneous vasculitis attending the Dermatology outpatient department at B.P. Koirala Institute of Health Science, Dharan were enrolled in the study. Informed and written consent were obtained from all willing adult patients and from the parents of paediatric patients. Demographic data were recorded using a predefined proforma, and a detailed medical history was obtained from each patient.

2.6.2. Clinical examination

A thorough clinical examination, including general examination, cutaneous examination, and systemic examination, was performed in all patients. The type of lesion, site of involvement, presence of secondary changes, and history of systemic involvement were noted.

2.6.3. Investigations

Various investigations were carried out, including complete blood count (CBC), erythrocyte sedimentation rate (ESR), bleeding time (BT), clotting time (CT), serum-urea and serum creatinine levels, liver function tests (LFT), chest X-ray, urine examination, stool for occult blood, anti-streptolysin O (ASO) titre, C-reactive protein (CRP), and skin biopsy.

2.6.4. Histopathological examination

A deep punch biopsy extending to the subcutis was taken from the most tender, reddish, or purpuric skin lesion under local anaesthesia. Biopsy samples were transported in formalin-fixed containers with patient information and site of biopsy. The samples were subjected to haematoxylin and eosin staining for light microscopic examination.

2.6.5. Classification of patients

Patients were classified according to the standard criteria the American College of Rheumatology (ACR) laid with some modifications. The criteria for giant-cell arteritis (GCA), Takayasu's arteritis (TA), polyarteritis nodosa (PAN), Wegener's granulomatosis (WG), Churg-Strauss syndrome (CSS), hypersensitivity vasculitis (HSV), Henoch-Schonlein purpura (HSP), and unclassified vasculitis were used.

2.6.6. Statistical analysis

Data were entered into MS Excel 2010 and then converted into Statistical Package for Social Science (SPSS) version 11.5 for statistical analysis. Descriptive data analysis, including mean, median, standard deviation, proportion, and percentage, were calculated. The epidemiological results were presented using graphical and tabular representations.

3. Results

resents the distribution of the duration of cutaneous vasculitis lesions in the study population. Among the 30 patients, 20 (66.67%) had lesions with a duration of 0 to 6 weeks, 9 (30%) had lesions lasting from 6 weeks to 6 months, and only 1 (3.33%) patient had lesions lasting more than 6 months.

Regarding the etiological factors, 17 individuals (56.67%) had cutaneous vasculitis of unknown aetiology. Infections were the cause in 6 patients (20%), while medications accounted for 4 cases (13.33%). Connective tissue disorders were identified as the cause in 3 patients (10%).

rovides information about the diseases associated with cutaneous vasculitis in the study population. Among the associated conditions, recurrent sore throat was observed in 4 patients (13.33%), followed by hypertension and diabetes mellitus in 2 patients each (6.67%). Recurrent urinary tract infection (UTI), systemic lupus erythematosus (SLE), and atopy were each present in 3 patients (10%). Disseminated pulmonary tuberculosis (PTB) was associated with cutaneous vasculitis in 1 patient (3.33%).

isplays the laboratory findings in the study participants. Elevated erythrocyte sedimentation rate (ESR) was the most common abnormality, present in 22 patients (73.33%). Anemia and neutrophilia were each found in 8 patients (26.67%), while eosinophilia was observed in 6 patients (20%). Stool for occult blood and pyuria were detected in 2 patients (6.67%) each. Elevated serum creatinine and abnormal liver function tests (LFT) were seen in 3 patients (10%) each. Nine patients (30%) had albuminuria, and 4 patients (13.33%) had hematuria. High anti-streptolysin O (ASO) titers were found in 4 patients (13.33%), while anti-neutrophilic cytoplasmic antibody (P-ANCA) was present in 1 patient (3.33%). Six patients (20%) had positive antinuclear antibodies (ANA), and 2 patients (6.67%) had positive anti-double-stranded DNA (Anti-Ds DNA). Raised C-reactive protein (CRP) levels were observed in 10 patients (33.33%). Abnormal chest X-ray, Mantoux test, and 24-hour urinary protein were each detected in 1 patient (3.33%).

These results provide an overview of the demographic, clinical, and laboratory characteristics of the study population with cutaneous vasculitis, shedding light on the distribution of the disease duration, etiological factors,

associated conditions, and laboratory abnormalities in the patients.

Table 1: Distribution of duration of cutaneous vasculitis

Duration of lesion	Number (%)
0-6wks	20(66.67)
6wks- 6months	9(30)
>6 months	1(3.33)

Etiological Factor:

Unknown etiological factors were the cause of cutaneous vasculitis in 17 individuals (56.67%), whereas infections, medications, and connective tissue disorders accounted for 6 (20%), 4 (13.33%), and 3 (10%) of the cases, respectively.

Factor	Number (%)
None	17(56.67)
Infection	6(20)
Drugs	4(13.33)
connective tissue disorder	3(10)

Table 2: Disease associated with cutaneous vasculitis

Associated diseases	No. of patients (%)
Recurrent sore throat	4(13.33)
Hypertension	2(6.67)
Diabetes mellitus	3(10)
Recurrent UTI	3(10)
SLE	3(10)
Disseminated PTB	1(3.33)
Atopy	3(10)

Table 3: Laboratory finding

Laboratory parameters	Number of patients	Percentage
Anemia	8	26.67
Leukocytosis	2	6.67
Neutrophilia	8	26.67
Eosinophilia	6	20
Raised ESR	22	73.33
Stool for occult blood	2	6.67
Elevated serum creatinine	3	10
Abnormal LFT	3	10
Albuminuria	9	30
Pyuria	3	10
Hematuria	4	13.33
High ASO titre	4	13.33
P-ANCA	1	3.33
ANA	6	20
Anti-Ds DNA	2	6.67
Raised CRP	10	33.33
Abnormal Chest X-ray	1	3.33
Abnormal mantoux	1	3.33
Abnormal 24 hr urinary protein	1	3.33

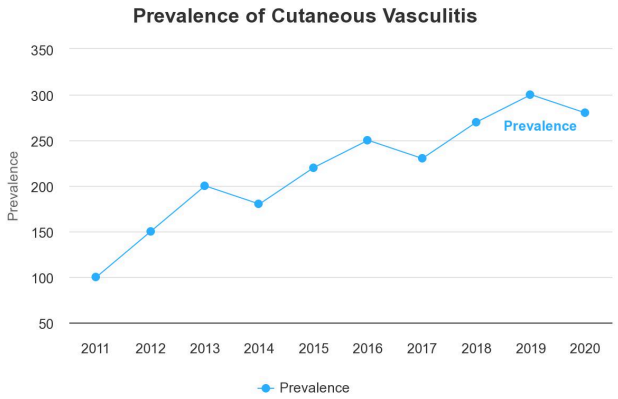

Figure 1: Prevalence of cutaneous vasculitis for last decade

4. Discussion

Cutaneous vasculitis is a complex and poorly understood condition characterized by a diverse clinical presentation and overlapping features with various infections, connective tissue disorders, and malignancies (Gupta et al., 2009). In this study, we aimed to analyze the clinic-epidemiological profile and histopathological profile of cutaneous vasculitis by examining the clinical features, past medical history, and laboratory findings in patients with biopsy-proven cutaneous vasculitis.[7]

The study population comprised 30 patients with biopsy-proven cutaneous vasculitis. The age of the patients ranged from 10 to 75 years, with an average age of 32.96 years. This average age was lower compared to other studies, such as Sias et al. (1998), where the average age was 51 years, indicating a relatively younger age group affected in our study. The majority of patients fell within the age range of 21 to 40 years (50%), followed by <20 years (23.33%), 41 to 60 years (20%), and >60 years (6.67%). These findings align with previous studies reporting a higher incidence in young adults (Khetan et al., 2012; Alexander et al., 2003). The study also demonstrated a higher incidence of cutaneous vasculitis in females (56.67%) compared to males (43.33%), with a female-to-male ratio of 1.3:1, consistent with earlier studies (Sias et al., 1998).[8]

Regarding the duration of the disease, the study showed that most patients (66.67%) presented with a duration of less than 6 weeks. Acute disease was observed in 86.66% of the patients, with a duration of less than 3 months, and only 13.33% had a chronic disease duration of more than 3 months. These findings are in line with other studies reporting variable disease durations, with some cases presenting acutely and others chronically (Chen et al., 2008).[9]

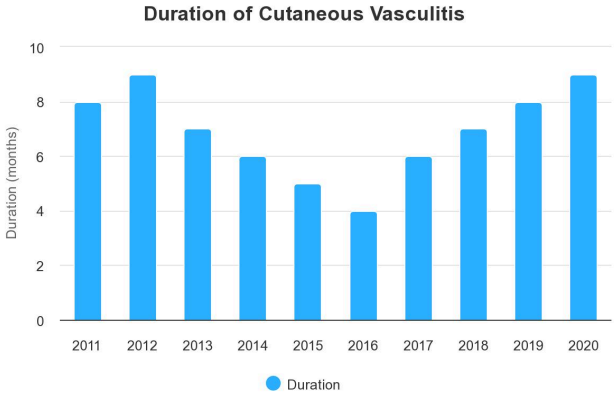

Figure 2: Duration of cutaneous vasculitis for last decades

The most common symptom reported by patients was itching at the lesion site (73.66%), followed by burning (40%) and pain (33.3%). Constitutional features were present in 66.67% of the patients, with arthralgia being the most common (66.67%), followed by fever (36.67%) and myalgia (26.6%). Abdominal pain was the most frequent systemic symptom, reported in 37.67% of the patients. These findings are in agreement with previous studies reporting itching and pain as common symptoms and arthralgia as a prominent constitutional feature (Sias et al., 1998; Gupta et al., 2009).[10]

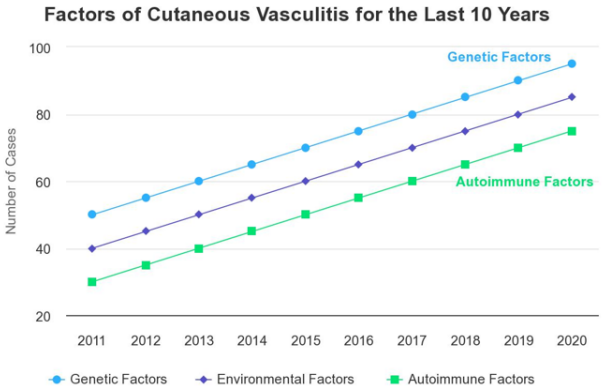

Figure 3: Factors ofcutaneous vasculitis for last decade

Cutaneous examination findings revealed palpable purpura as the most common cutaneous manifestation (70%), consistent with earlier studies (Gupta et al., 2009; Khetan et al., 2012; Sias et al., 1998). Lesions were predominantly distributed on the legs and ankles (93.33%) and thighs (63.33%). This distribution pattern corroborates previous findings (Gupta et al., 2009; Khetan et al., 2012; Sias et al., 1998).[11]

Laboratory investigations indicated elevated ESR in 73.33% of the patients, anemia in 26.7%, and eosinophilia in 20%. Albuminuria, hematuria, and pyuria were observed in

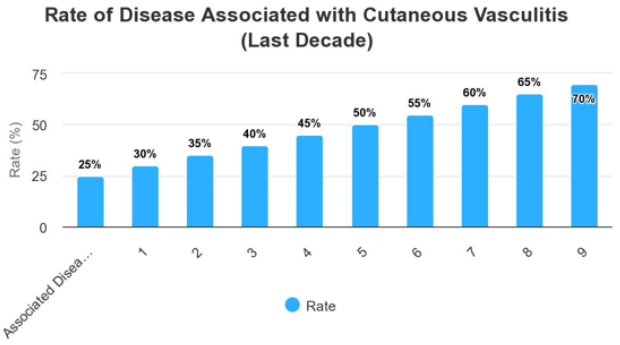

Figure 4: Rate ofdisease associated with cutaneous vasculitis for last decade

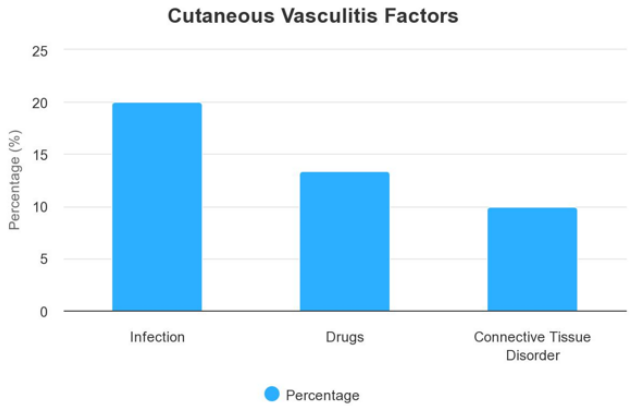

Figure 5: Important factors associated with cutaneous vasculitis(%)

30%, 13.33%, and 10% of the patients, respectively. These findings are in concordance with earlier studies showing elevated ESR and various hematological abnormalities in cutaneous vasculitis patients (Gupta et al., 2009; Sias et al., 1998).[12]

Histopathological examination of skin biopsy specimens revealed leukocytoclastic vasculitis in 97% of the cases, consistent with previous studies (Alexander et al., 2003). Small vessel vasculitis (SVV) was seen in all patients, with neutrophils being the predominant infiltrate in 76.7% of biopsy specimens. The presence of eosinophils in the infiltrate was noted in 20% of the patients. These findings align with earlier studies showing leukocytoclastic vasculitis and predominantly neutrophilic infiltrates in cutaneous vasculitis (Sias et al., 1998; Bagai et al., 2001).[8,9]

Based on the clinical presentation, the patients were classified according to the criteria laid down by the American College of Rheumatology (ACR) with some modifications (Khetan et al., 2012)[7,9]. In this study, 43.33% of patients were diagnosed with Henoch-Schönlein purpura (HSP), and 26.67% were diagnosed with urticarial vasculitis.[10] The remaining patients (30%) were categorized

as idiopathic cutaneous small vessel vasculitis. These findings differ from some previous studies but align with others (Gupta et al., 2009; Khetan et al., 2012).[11,12]

Regarding etiology, the majority of patients (56.67%) had cutaneous vasculitis without any identified precipitating factor. Infections (20%), drugs (13.33%), and connective tissue disorders (10%) were the identified etiological factors in other cases.[13] Infections, especially upper respiratory tract infections, were the most common precipitating factor. Non-steroidal anti-inflammatory drugs (NSAIDs) and methotrexate were the most frequently implicated drugs. These findings corroborate the role of infections and medications as common triggers for cutaneous vasculitis (Gupta et al., 2009).[14,15]

5. Conclusion

This study provides valuable insights into the clinic-epidemiological profile and histopathological features of cutaneous vasculitis in our population. Most of the patients with cutaneous vasculitis presented with polymorphic lesions though the majority of the patients presented with palpable purpura. Leukocytoclastic vasculitis was the commonest type of vasculitis on histopathological examination. A skin biopsy showing leukocytoclastic vasculitis did not prove systemic involvement and it cannot prove the involvement of larger vessels as well. The findings highlight the diverse clinical presentation and laboratory abnormalities associated with the condition. Additionally, the identification of potential etiological factors and disease classification can aid in better management and understanding of cutaneous vasculitis. Further studies with larger cohorts are needed to validate these findings and improve our understanding of this complex condition.

6. Source of Funding

None.

7. Conflict of Interest

None.

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