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CLINICO-SOCIO-DEMOGRAPHIC PROFILE OF ERYTHEMA NODOSUM IN A TERTIARY CARE CENTRE IN NORTH-EAST INDIA

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ABSTRACT

Background: Erythema nodosum (EN) is a common form of acute panniculitis characterized by painful, erythematous subcutaneous nodules, predominantly involving the pretibial region. It may be associated with various infectious and non- infectious conditions. This study aimed to determine the clinico-sociodemographic profile of patients with erythema nodosum presenting at a tertiary care center.

Materials and Methods: A retrospective observational study was conducted among patients with biopsy- proven erythema nodosum attending the Department of Dermatology, Venereology and Leprosy, JNIMS, Porompat, over a two-year period from 1 July 2022 to 31 June 2024. A total of 55 patients were included using universal sampling. Pregnant and lactating women and patients with panniculitis other than EN were excluded. Sociodemographic and clinical details were collected through structured proforma, followed by general, systemic and detailed cutaneous examination. Data were analyzed using Microsoft Excel and IBM SPSSv20.

Results: The mean (SD) age of patients was 39.96 (13.58) years, with the largest proportion aged 41-50 years (29.1%). Females predominated (81.8%), while 50.9% were housewives, 79.4% were married and 74.5% belonged to the lower socioeconomic group. All patients had acute, raised, multiple, solid and painful/tender lesions. Lesions were predominantly reddish (96.4%) and involved the anterior shin (94.4%). The mean (SD) duration was 6.98(2.39) weeks, and mean (SD) lesion size was 5.7(3.26) cm2. No seasonal or diurnal variation was observed. The mean (SD) BMI was 21.14(3.15) kg/m2, with 49.1% having normal BMI. Cutaneous examination showed no significant abnormalities of the hair, nails, mucosae or conjunctiva.

Conclusion: Erythema nodosum predominantly affected adult females, particularly those in the fourth and fifth decades. The characteristic clinical presentation consisted of acute, multiple, symmetrical, painful erythematous nodules predominantly over the anterior shins. Recognition of these typical clinic-sociodemographic features can facilitate early clinical identification and appropriate evaluation of patients with erythema nodosum.

Keywords: Clinico-socio-demographic profile, Erythema nodosum, Panniculitis, Subcutaneous nodules.

INTRODUCTION

Erythema nodosum (EN) is one of the most common forms of acute panniculitis, characterized by sudden onset of firm, erythematous, solid and deep nodules or plaques painful on palpation and are mainly localized on extensor surface of legs.[1] The condition usually has acute onset and is often self-limiting.[2]

It occurs more often in women between 25 and 40 years but can be observed in any age. Compared to men, women are affected three to six times more,[1] and there is a high incidence of EN during pregnancy.[3] Some pregnant patients may develop erythema nodosum during the second trimester. In addition, recurrence of the disorder may also occur in future pregnancies.[1] The epidemiology of Erythema Nodosum is diverse in different geographic regions. This diversity is expressed in prevalence and etiological cause. A higher incidence (12-14 cases/100,000 person-years) of EN was reported in Scandinavia.[3] It is rare without sex predominance in the pediatric population.[1] Estrogen may have a role in the etiology.[4] Multiple members with the same HLA have been reported to have EN.[5-10] The exact incidence of erythema nodosum is not known in India. Idiopathic (55%) is the most prevalent cause of EN globally. This condition is commonly linked to streptococcal infections, especially in children.[5]

Erythema nodosum is a delayed-type hypersensitivity response to various antigens from a wide range of precipitating factors such as infection, inflammation, neoplasm, and drugs.[6] EN can be classified according to the etiologies as primary or idiopathic EN and secondary EN when there is an identifiable cause.[7] No obvious etiology has been found in about 30% to 50% published cases. Infectious etiologies include bacterial causes (streptococcal infections- most common etiology commonly streptococcal pharyngitis 28 to 48%), tuberculosis, leprosy, leptospirosis, mycoplasma pneumonia, Yersinia, Brucellosis, Tularemia, Salmonella, Bartonella etc.), viral causes (Hepatitis B & C, Infectious mononucleosis, Human immunodeficiency virus HIV, Epstein Barr virus EBV, Herpes Simplex virus HSV, para vaccinia etc.), fungal causes (Histoplasmosis, coccidioidomycosis, Blastomycosis), parasitic (Giardiasis, amoebiasis). Non-infectious causes include drugs such as antibiotics (penicillin, sulfonamides), oral contraceptives, bromides, iodides, etc.; malignancies (leukemia, lymphoma, occult malignancies); Inflammatory Bowel disease (Crohn's disease, ulcerative colitis), miscellaneous causes (Sarcoidosis-Lofgren syndrome, pregnancy, Whipple disease, Behcet disease) etc. Regardless of the etiology, the nodules of erythema nodosum are characterized by a typical histological appearance marked by acute inflammation of the dermo-hypodermic junction and interlobular septa of the hypodermic fat evolving without necrosis or sequelae.[1]

It has proposed that EN may be the result of the formation of immune complexes and their deposition in the venules of the septae of the subcutaneous fat. Evidence of circulating immune complexes in early lesions supports the suggestion that the antigen, antibody, and complement play a significant role in the pathogenesis and circulating immune complexes may contribute to tissue injury. However, some authors have reported a lack of circulating immune complexes in uncomplicated EN, and a type IV delayed hypersensitivity reaction has been proposed. Several adhesion molecules and inflammatory mediators are involved in the development of the lesions. Expression of adhesion molecules, such as E-selectin, P-selectin, platelet endothelial cell adhesion molecule, vascular cell adhesion molecule-1, and intercellular adhesion molecule-1, on endothelial cells in patients with EN has been observed. Early lesions are characterized by a neutrophilic inflammatory infiltrate in which activated neutrophils might cause oxidative tissue damage and inflammation owing to the production of reactive oxygen intermediates. High levels of cytokines and growth factors, mainly involved in neutrophil recruitment and activation, have been reported both in the skin (mainly interleukin [IL]-6, IL-8, IL-12, interferon-gamma, granulocyte colony-stimulating factor and monocyte chemoattractant protein-1) of patients with EN. Increased acute-phase reactants have been detected in patients in EN.[8]

Erythema nodosum nodules vary from 0.4 to 4 inches (1 to 10cm) in diameter and are poorly demarcated, reflecting their subcutaneous anatomic location. Pretibial involvement is most common, although the extensor surfaces of the forearm, the thighs, and the trunk also may be affected. Initially, erythema nodosum nodules can be firm, but they usually become more fluctuant during the clinical evolution. Individual nodules may last for two weeks; new outcroppings may continue to arise for up to six weeks. These nodules often take approximately one to two months to heal completely and may assume a bruise- like appearance as they fade. They do not tend to ulcerate and usually resolve without atrophy or scarring.[9] Bruise-like evolution lesions are known as "erythema contusiformis". Co-existence of lesions in different stages of the evolution can be seen in the same patient. The skin lesions are frequently accompanied by systemic symptoms, such as fever, malaise, headache, gastrointestinal complaints, cough, lymphadenopathy, weight loss, and arthralgia, mainly ankles and knees. Some of these findings might be suggestive of EN secondary to systemic disease, and these findings can provide important diagnostic clues.[8]

MATERIALS AND METHODS

The aim of the study was to determine the clinic-socio-demographic profile of Erythema Nodosum in a Tertiary Care Centre. The study was conducted as a retrospective observational study at Out Patient Department of Dermatology, Venereology and Leprosy, JNIMS, Porompat, during the period of 2 years i.e. from 1st July, 2022 to 31st June, 2024. All patients with biopsy proven erythema nodosum attending OPD of Department of Dermatology, Venereology and Leprosy were included using universal sampling. Pregnancy, lactation and panniculitis with causes other than erythema

nodosum were excluded from the study. The final sample size was 55 patients.

After obtaining ethical clearance from institute's ethical committee, all the patients fulfilling the inclusion criteria were enrolled and written consent was obtained from all of them. All the patients were then subjected to through history taking using proforma, which included history regarding sociodemographic variables such as name, age, sex, occupation, marital status, contact details, etc. Clinical history was obtained regarding clinical complaints, with their characteristics and duration. Seasonal or diurnal variations if any and associated aggravating or reliving factors were enquired and documented. Further, past history, family history, personal history and treatment history was obtained and documented.

All the patients were then subjected to clinical examination which included general physical examination, and systemic examination as specified in proforma. Special emphasis was given to cutaneous examination. Patients were examined in natural light and entire cutaneous surface including skin, hair, nail, mucosa (oral, genital, conjunctival & nasal) were examined. Skin lesions were described in detail as per proforma.

Data was compiled using MS Excel and analysed using IBM SPSS softwarev20. Categorical variables were expressed as frequency and percentage whereas continuous variables were expressed as mean and standard deviation. Descriptive statistical analysis was performed to summarize the sociodemographic and clinical characteristics of the study participants. Level of significance was considered as $p<0.05$.

RESULTS

Completed data sets could be collected from 5 study participants. There was no refusal.

Table 1: Distribution of cases according to socio-demographic variables (n=55)

Socio-demographic variables	Frequency	Percentage
Age (in years)		
≤20	05	9.1
21-30	09	16.4
31-40	14	25.5
40-50	16	29.1
>50	11	20.0
Sex		
Male	10	18.2
Female	45	81.8
Occupation		
Business	01	1.8
Engineer	01	1.8
Govt. employee	09	16.4
Home-maker	28	50.9
Policeman	01	1.8
Student	02	3.6
Teacher	02	3.6
Unemployed	05	9.1
Marital status		
Married	42	76.4
Unmarried	13	23.6
Socio-economic class		
Low	41	74.5
Middle	14	25.5
BMI		
<18.5	10	18.2
18.5-22.9	27	49.1
23-24.9	10	18.2
≥25	08	14.5

The mean (SD) age of patients with biopsy proven erythema nodosum enrolled in our study was 39.96 (13.58) years and majority of patients belonged to age group of 41 to 50 years (29.1%), followed by 25.5% cases belonging to 31 to 40 years of age. Majority of patients with biopsy proven erythema nodosum were females (81.8%), and more than half of them were housewives (50.9%), followed by government employee (16.4%) and students (14.5%). About 9.1% cases enrolled in our study were unemployed.

Out of 55 cases with biopsy proven erythema nodosum, approximately three fourth (76.4%) of the cases were married and 74,5% cases belonged to lower socioeconomic status.

Mean (SD) BMI in patients with erythema nodosum was 21.14 (3.15) kg/m2. Majority of cases had normal BMI i.e. 49.1% cases had BMI in the range of 18.5-22.9 kg/m2 whereas 18.2% cases were under-weight and overweight each. However, 14.5% cases were obese. [Table 1]

The lesions in all the patients were of acute onset with a mean (SD) duration of 6.98 (2.39) weeks. All lesions were raised in type, solid in consistency, without any flaking, with pain and tenderness present on them. The mean (SD) size of the lesions was 5.7 (3.26) cm. All patients had multiple lesions. Further, all the lesions were erythematous nodules in morphology, grouped in configuration, symmetrical

in distribution, without any xerosis, with indistinct margins and smooth. Most of the lesions (23; 41.8%) had a duration of 6-8 weeks. The color of the lesions was reddish in almost all cases (53; 96.4%) and the anterior shin was the most common site involved. [Table 2]

Table 2: Distribution of cases according to features and characteristics of skin lesions (n=55)

Features of skin lesions	Frequency	Percentage
Duration (in weeks)		
2-5	15	27.3
6-8	23	41.8
8-11	17	30.9
Color		
Reddish	53	96.4
Yellow	02	3.6
Site		
Anterior shin	53	96.4
Anterior shin & ankle	02	3.6

Table 3: Distribution of cases according to associated factors with skin lesions (n=55)

Associated factors with lesions	Frequency	Percentage
Seasonal/diurnal variation		
• No	55	100
Aggravating factors		
• None	54	98.2
• Standing	01	1.8
Relieving factors		
• Leg elevation	01	1.8
• Paracetamol	54	98.2

Seasonal or diurnal variation was noted in none of the cases. Pain was aggravated by standing in 01 (1.8%) case whereas, the relieving factors were paracetamol in 98.2% cases. There was no history of similar illness in past or in family. [Table 3]

Table 4: Distribution of patients according to vitals (n=55)

Vitals	Mean	SD
Pulse rate per min	79.44	4.345
Systolic blood pressure (mm Hg)	126.56	2.767
Diastolic blood pressure (mm Hg)	83.29	4.135
Respiratory rate per min	18.13	1.599
SpO2	97.29	1.181

The distribution of patients according to vitals, which were found to be within normal range. Mean (SD) pulse rate in patients with erythema nodosum was 79.44 (4.345) per minute whereas the mean systolic and diastolic blood pressure was 126.56 (2.767) and 83.29 (4.135) mmHg respectively. Mean (SD) respiratory rate in patients with erythema nodosum was 18.13 (1.599) per minute and mean (SD) oxygen saturation was 97.29 (1.18%). (Table 4)

On cutaneous examination, the hair, nail, oral mucosa, nasal mucosa and conjunctiva were all found to be normal.

DISCUSSION

The mean (SD) age of patients diagnosed with biopsy-proven erythema nodosum in our study was 39.96 (13.58) years, with a predominant representation in the age group of 41 to 50 years (29.1%), followed by 31 to 40 years (25.5%). This distribution aligns with previous studies done by Limtong P et al, Garcia-Porrua C et al and Requena L et al which have also reported a peak incidence of erythema nodosum in the third to fifth decades of life.[4,7,10] Baima de MC et al also reported that majority of the cases were seen between the ages of 31 and 49 years old.[11]

Our study revealed a striking predominance of females among patients with erythema nodosum, accounting for 81.8% of the cases. This observation is consistent with existing literature Garcia-Porrua C et al,[10] which consistently reported a higher prevalence of EN in females. The exact reasons for this gender disparity remain unclear and warrant further investigation. Bjorn-Mortensen K et al,[5] in their study reported that majority of EN cases were among women (58%). Limtong P et al,[7] reported that majority of EN cases i.e., 85.2% were females.

In terms of occupation, more than half of the EN patients in our study were housewives (50.9%), followed by government employees (16.4%) and students (14.5%). The association between occupation and EN prevalence has not been extensively studied; however, factors such as lifestyle, stress levels, and exposure to environmental triggers may contribute to variations in disease incidence among different occupational groups. A significant proportion of EN patients in our study were married, comprising approximately three-fourths (76.4%) of the cases. Additionally, the

majority of patients belonged to lower socioeconomic status (74.5%). These finding were consistent with the findings of Baima de MC et al,[11] who reported that EN was more commonly seen in patients with low education level. These findings underscore the potential influence of marital status and socioeconomic factors on disease prevalence and severity.

Across the study, all lesions were noted to be raised, demonstrating an acute onset with solid consistency. This aligns with the classical presentation of EN in study of Requena et al.[4,9] The lesions in our study were multiple and associated with pain and tenderness. This observation corroborates study of Hafsi W et al,[1] and highlights the inflammatory nature of EN and highlights the need for symptomatic management to alleviate patient discomfort.

The mean (SD) duration of erythema nodosum lesions in our study was 6.98 (2.39) weeks, with a substantial proportion of cases presenting with symptoms lasting 6 to 8 weeks (41.8%). The reddish coloration of lesions was predominant (96.4%), while the anterior shin emerged as the predominant site of lesion occurrence (96.4%). These findings are consistent with previous reports such as Hafsi et al and De Souza PK et al.[1,12]

The mean (SD) size of lesions in our study was 5.7 (3.26) cm2, indicating variable dimensions among EN patients. While the precise determinants of lesion size in EN remain unclear as suggested by Requena L et al, factors such as disease severity, inflammatory response, and individual patient characteristics may contribute to lesion variability.[4] Bhadriraju S et al in their case study in a female and she had a lesion at her upper thighs which were mainly 3 cm in size.[13] Rizvi Z et al also in their case documented tibial nodules were erythematous, with a diameter of 1-3 cm and a weak demarcation.[14]

Our study found that none of the erythema nodosum cases exhibited seasonal or diurnal variation in symptom presentation. This contrasts with some reports like Requena L et al[7] suggesting a possible association between EN flare-ups and certain seasons or times of day. However, the absence of such variation in our study may indicate that EN lesions maintain a relatively stable clinical course regardless of seasonal or diurnal influences.

In the majority of EN cases, pain associated with the skin lesions was exacerbated by standing (1.8%), while the administration of paracetamol provided relief in 98.2% of cases. Additionally, leg elevation was identified as a relieving factor in 1.8% of cases. These findings are consistent with previous reports such as Perez GDM et al & Blake T et al,[8,15] highlighting that compression bandages and limb elevation may be used for edema and pain relief. These findings underscore the importance of identifying aggravating and relieving factors in managing EN-associated pain.

Our study found that the mean (SD) BMI in patients with erythema nodosum (EN) was 21.14 (3.15) kg/m². The distribution of BMI among the patients indicated that the majority had a normal BMI (49.1%). Additionally, 18.2% of the patients were underweight, another 18.2% were overweight, and 14.5% were classified as obese. The predominance of patients with a normal BMI aligns with other studies that have reported a similar distribution among EN patients. For instance, research conducted by Mert A et al,[16] and Harpsoe M et al also observed a substantial proportion of EN patients falling within the normal BMI range i.e. 18.5-22.9 kg/m².[16,17] This suggests that while BMI might not be a significant stand-alone risk factor for the development of EN, it reflects the general population distribution.

The presence of underweight patients (18.2%) in our study is noteworthy. Underweight individuals may have underlying nutritional deficiencies or chronic illnesses that could predispose them to inflammatory conditions like EN. This aligns with findings by Requena L et al, who noted that EN can occur in patients with a variety of underlying conditions, including those affecting nutritional status.[9] Interestingly, 18.2% of our patients were overweight, and 14.5% were obese. Obesity and overweight are known to be associated with systemic inflammation, which might contribute to the pathogenesis of EN. Similarly, a study by Katugampola RP et al have highlighted the role of systemic inflammation in the development of EN.[18] Moreover, a study by Monteiro R et al suggested that metabolic factors associated with higher BMI could exacerbate inflammatory conditions.[19]

Our study provides a detailed analysis of the vital signs in patients with erythema nodosum (EN), offering a comprehensive understanding of the physiological status of these individuals. The mean pulse rate, SBP, DPP and RR observed in our patients were within normal limits for an adult. This finding is consistent with other studies Requena L et al and Mert A et al,[9,16] indicating that EN typically does not significantly cause abnormalities in pulse rate.

Our study's comprehensive cutaneous examination of patients with erythema nodosum (EN) revealed no significant abnormalities in the hair, nails, oral mucosa, genital mucosa, nasal mucosa, or conjunctiva. This lack of significant cutaneous or mucosal abnormalities aligns with the typical presentation of EN, which is primarily characterized by inflammatory nodules on the anterior shins rather than widespread cutaneous or mucosal involvement. Previous studies like Requena L et al and Mert A et al have also noted that EN primarily manifests as localized subcutaneous inflammatory nodules without affecting other cutaneous structures such as hair or nails.[4,16] The absence of abnormalities in the mucosal surfaces, including the oral, genital, nasal, and conjunctival mucosa, is consistent with findings from Dogan S et al,[20] who reported that EN generally does not involve mucosal tissues.

In our study, pain was a universal symptom among these patients, whereas xerosis (dryness of the skin) was notably absent. The presentation of erythematous nodules is a hallmark of EN and is consistent with

numerous studies as Requena L et al and Mert A et al,[4,16] that describe EN lesions as tender, red nodules primarily located on the anterior shins. The symmetrical distribution of these lesions further supports the typical presentation pattern of EN, which often affects both legs simultaneously, providing a key diagnostic clue.

The grouping of lesions with smooth surfaces and indistinct margins was observed in all cases, aligning with descriptions found in other studies. Habibullah T et al noted that EN lesions often appear in clusters and have a smooth surface due to the subcutaneous inflammation.[21] The indistinct margins are a result of the inflammatory process extending into the surrounding tissues, making the edges of the lesions less defined.

Pain is a significant symptom associated with EN and was present in all our cases, which is consistent with the findings of other researchers like Schwartz RA et al who reported pain and tenderness as primary symptoms of EN.[7] This pain is typically exacerbated by pressure and movement, contributing to patient discomfort and difficulty in daily activities.

CONCLUSION

This study highlights the clinico-socio-demographic profile of biopsy proven erythema nodosum in a tertiary care centre. It was predominantly observed among adult females, with highest proportion belonging to 41–50-year age group. A substantial proportion were housewives and belonged to lower socioeconomic group. Clinically, all patients presented with acute onset, multiple, raised solid, painful and tender erythematous nodules with a characteristic symmetrical distribution over anterior shin. Most patients had normal BMI, and no significant abnormalities on examination of hair, nails, mucosae, or conjunctiva. Overall, the findings reinforce the characteristic clinical presentation of erythema nodosum. Larger and multicentric studies are warranted to better establish the epidemiological patterns and etiological factors of erythema nodosum in the Indian population.

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