

MANTOUX TEST POSITIVITY IN ERYTHEMA NODOSUM PATIENTS - A PROSPECTIVE OBSERVATIONAL STUDY

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Received : 31/07/2026
Received in revised form : 26/08/2026
Accepted : 09/09/2026

Keywords:

Antitubercular therapy, Erythema nodosum; Mantoux test, recurrence, Panniculitis.

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DOI: 10.47009/jamp.2026.8.5.51

Source of Support: Nil,
Conflict of Interest: None declared

Int J Acad Med Pharm
2026; 8 (5); 325-328



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ABSTRACT

Background: Erythema nodosum (EN) is the most common form of acute panniculitis and may be associated with a variety of infectious and non-infectious conditions. Tuberculosis is an important underlying cause in endemic regions such as India. The present study was undertaken to assess the prevalence of Mantoux test positivity among patients with biopsy-proven EN and to evaluate their response to antitubercular therapy. **Materials and Methods:** A prospective observational study was conducted over a period of two years in the Department of Dermatology, Venereology and Leprosy, JNIMS, Imphal. Fifty-five patients with biopsy-proven EN fulfilling the inclusion criteria were enrolled by universal sampling. Detailed history and clinical examination were performed, along with baseline investigations including Mantoux testing. A standard dose of 5 TU PPD RT23 was administered intradermally and read at 48–72 hours. Patients with a positive Mantoux test were treated with antitubercular therapy consisting of 2 months of HRZE followed by 4 months of HR. Patients were followed up for three months after completion of treatment. Statistical analysis was performed using SPSS v 20. **Result:** Of the 55 patients, 45 (81.8%) were females and 10 (18.2%) were males. The mean (SD) age was 39.96 ± 13.58 years, with the 41–50-year age group being the most commonly affected. The mean (SD) duration of disease was 6.98 ± 2.39 months. Mantoux positivity was observed in 49 (89.1%) patients. Fifty-four patients completed treatment, while one was lost to follow-up. Overall, 53 patients (96.4%) had no recurrence following treatment. The treatment response differed significantly between the Mantoux-positive and Mantoux-negative groups. **Conclusion:** Mantoux test positivity was high among patients with biopsy-proven EN in this study, highlighting the importance of screening for tuberculosis, particularly in endemic regions. Patients with Mantoux positivity showed a favorable response to antitubercular therapy, suggesting that identification and appropriate treatment of tuberculosis-associated EN may help prevent recurrence.

INTRODUCTION

Erythema nodosum is one of the most common form of acute panniculitis, characterized by sudden onset of firm, erythematous, solid and deep violaceous symmetrical plaques or nodules, which are painful on palpation and are mainly localized on extensor aspect of lower limbs or pretibial area.^[1-3] It is often self-limiting.^[4] Erythema nodosum can be associated with various underlying conditions such as infectious

causes, non-infectious causes and idiopathic. Regardless of the underlying aetiology, the nodules associated with erythema nodosum are typically 1 characterized by common histological appearance with acute inflammation of interlobular septa of the hypodermic fat as well as dermo-hypodermic junction, with no evident necrosis or sequelae.^[1-3]

Erythema nodosum can occur at any age and in both the sexes. However, it is reported to be more common in women, belonging to 25 to 40 years of age.^[5]

Though the exact pathogenesis of erythema nodosum remains unclear, it is mainly immunologically mediated and is thought to be due to delayed hypersensitivity (type IV) response to variety of antigens associated with aetiological factors.^[6]

The diagnosis of erythema nodosum is mainly clinical, however, thorough investigations are needed to determine associated aetiologies underlying erythema nodosum. Mantoux test is recommended when the possibility of tuberculosis is likely or there is suspicion of Löfgren syndrome.^[5] The Mantoux test is an important test for diagnosis of tuberculosis. Assessment of testing Mantoux positivity is an essential step in management of patients with Erythema Nodosum as this may help in differentiating the aetiologies of erythema nodosum. Previous studies have assessed the effect of antitubercular therapy in Erythema Nodosum.^[7] However, studies assessing the Mantoux positivity in erythema nodosum patients are scarce. This study was therefore conducted at tertiary care centre to establish Mantoux test positivity in Erythema Nodosum patients and to treat the patients with Erythema Nodosum.

Aims

The aims of the study were to establish Mantoux test positivity in Erythema Nodosum patients and to assess the treatment outcome.

MATERIALS AND METHODS

A prospective observational was conducted in the outpatient department of the Department of Dermatology, Venereology and Leprosy, JNIMS, Porompat, Imphal, India over a period of 2 years (2023-25). All patients with biopsy proven erythema nodosum attending OPD of Department of Dermatology, Venereology and Leprosy were included in the study using universal sampling. Exclusion Criteria included pregnancy, lactation, patient not willing to undergo treatment, already on antitubercular therapy, panniculitis other than the Erythema nodosum.

Procedure of Mantoux test: After obtaining ethical clearance from institute's ethical committee, all the patients fulfilling the inclusion criteria were enrolled and written consent was obtained. All the patients were then subjected to thorough history taking, clinical examination and baseline investigations consisting of CBC, ESR, RBS, KFT, LFT, Chest X-ray, skin biopsy and Mantoux test were done

A standard dose of five tuberculin units (TU) (0.1ml) was injected intradermally (into the skin) and read 48 to 72 h later. For the sake of standardization of reading and interpretation of results, 5TU of tuberculin PPD RT23 was used universally. It was injected intradermally in left forearm, using 28 or 26-gauge needle and tuberculin syringe from which 0.1 ml can be delivered accurately. A discrete, pale elevation of the skin (a wheal) 6 to 10 mm in diameter

should be produced when the injection is given correctly. If it was recognized that, the first test was improperly administered, another test dose was given at once, selecting a site several centimetres away from the original injection. The patient was instructed to keep the test site clean, uncovered, and to not scratch or rub the area. The patients were instructed for follow-up after 48 and 72 h after administration for interpretation of test. The positivity of Mantoux test was read as 5 mm or more in HIV-positive person, recent contacts of active tuberculosis cases, persons with nodular or fibrotic changes on chest X-ray consistent with old healed TB, organ transplant recipients and other immunosuppressed patients who were on cytotoxic immune-suppressive agents such as cyclophosphamide or methotrexate, patients on long term systemic corticosteroid therapy (> than six weeks) and those on a dose of prednisolone >15 mg/day or equivalent and end stage renal disease 34. 10mm or more was considered positive in recent arrivals (less than five years) from high prevalence countries, injecting drug users, residents and employees of high-risk congregate settings (e.g., prisons, nursing homes, hospitals, homeless shelters, etc) , mycobacteriology lab personnel, persons with clinical conditions that place them at high risk (e.g., diabetes, prolonged corticosteroid therapy, leukemia, end-stage renal disease, chronic malabsorption syndromes, low body weight, etc. children less than four years of age, or children and adolescents exposed to adults in high-risk categories, infants, children and adolescents exposed to adults in high-risk categories. 15 mm or more was positive in persons with no known risk factors for TB, reactions larger than 15 mm are unlikely to be due to previous BCG vaccination or exposure to environmental mycobacteria. All established case of Erythema nodosum or strongly positive Mantoux test underwent treatment with antitubercular treatment Isoniazid, Rifampicin, Pyrazinamide and Ethionamide for 2 months; Isoniazid and Rifampicin for 4 months. Patients were followed up 3 months after Antitubercular treatment was stopped.

Data was compiled using Ms Excel and analysed using IBM SPSS software version 20. Categorical variables were expressed as frequency and percentage whereas continuous variables were expressed as mean and standard deviation. Association between Categorical variables was assessed using the chi square and fisher exact test whereas for continuous variables student's t-test was used. Level of significance was considered as $p < 0.05$.

RESULTS

Of the 55 cases, there were 45 females (81.8%) and 10 males (18.2%). The mean (SD) age of the patients was 39.96 (13.58) years. The majority of patients belonged to the age group of 41 to 50 years (29.1%). [Table 1]

Table 1: Distribution of cases according to age

Age (in years)	Frequency (n=55)	Percentage
<20	5	9.1
21-30	9	16.4
31-40	14	25.5
41-50	16	29.1
>50	11	20.0

The mean duration of the disease was 6.98±2.39 years. Mantoux test was positive in 89.1% cases [Table 2]

Table 2: Distribution of cases according to Mantoux test

Mantoux test	Frequency (n=55)	Percentage
Negative	6	10.9
Positive	49	89.1

All the patients were given 2 months of HRZE, followed by 4 months of HR in both the Montoux test positive as well as negative patients and were followed up after 3 months to assess the response rate. Of the 55 cases, 54 completed the treatment and

1 out of this 54 was lost to follow-up after completion of the treatment. Table No. 3 depicts the treatment response in both the Montoux positive and the negative groups and the difference was found to be statistically significant (p=0.015).

Table 3: Association between Montoux test result and treatment response

Response to treatment	Montoux test result	
	Negative (%)	Positive (%)
No recurrence	5 (83.3)	48 (98.0)
Loss to follow-up	1 (16.7)	-
X2	8.41	
P value	0.015	

DISCUSSION

The mean 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 Garcia-Porrúa C et al (2000), which have also reported a peak incidence of erythema nodosum in the third to fifth decades of life.^[8] Requena L et al (2008) also reported that majority of patients were in the age group of 20 to 30 years.^[9] Sarvesvare KN et al (2001) in their study reported that the mean age was 31 years, and range was from 9 years to 53 years.^[10] Limtong P et al (2021) reported mean age 40.6±17.3 years.^[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-Porrúa C et al (2000), which consistently reported a higher prevalence of EN in females.^[12] The exact reasons for this gender disparity remain unclear and warrant further investigation. Bjorn-Mortensen K et al (2016) in their study reported that majority of EN cases were among women (58%).^[13] Limtong P et al (2021) reported that majority of EN cases i.e., 85.2% were females.^[14]

The high rate of Mantoux test positivity in our study aligns with other reports of Requena L et al (2008), particularly from regions with higher tuberculosis prevalence, where EN is often found to be associated with tuberculosis.^[9] This is particularly relevant in

the Indian context, where tuberculosis remains endemic, and latent tuberculosis is common. Studies conducted in similar settings by Kumar B et al (2004) have reported comparable rates of Mantoux test positivity in EN patient.^[7] and Kritsotakis E et al (2017) has documented TST reaction of 24 mm with blistering, reinforcing the need for thorough screening for tuberculosis in these patients.^[15]

The management of erythema nodosum often involves addressing underlying triggers, symptomatic relief, and preventing recurrence. In our study, we assessed the response to treatment among EN patients who received a standard regimen of 2 months of HRZE (isoniazid, rifampicin, pyrazinamide, ethambutol), followed by 4 months of HR (isoniazid, rifampicin).

The results of our study demonstrate a high response rate to treatment, with no recurrence observed in 96.4% of cases. This finding suggests that the standard anti-tubercular therapy regimen, which is commonly used to treat tuberculosis, is effective in managing EN associated with tuberculosis infection or latent tuberculosis. Kumar B et al, (2004) reported in their study that after treatment with antitubercular drugs, new lesions stopped appearing in 45 patients within 6-8 weeks.^[7] Our findings are consistent with previous studies that have reported favourable response rates to anti-tubercular therapy in EN patients. Rizvi Z et al (2019) reported a similar response rate to anti-tubercular therapy in their study cohort, highlighting the efficacy of this treatment approach.^[16]

Limitations: The present study was not free of limitations. The sample size of the study was small.

Only 55 patients with erythema nodosum could be enrolled during the study period that were followed up till 6 months of treatment, however 1 patient who lost to follow up was considered as a case of treatment not completed. Since the follow-up was only till for 3 months, long term outcome of patients and long-term recurrence rate could not be assessed. Biopsy proven cases were taken as inclusion criteria and clinically suspected cases were excluded and thus our study may have selection bias and rate of Mantoux positivity may have been higher. Only Mantoux test was assessed, however, tests to confirm underlying tubercular infection e.g. CBNAAT could not be assessed. Also, in our setting BCG vaccination, HIV, other factors associated with false positive Mantoux test were not taken into consideration.

All the patients were given 2 months of HRZE, followed by 4 months of HR in both the Mantoux test positive as well as negative patients and were followed up after 3 months to assess the response rate. Of the 55 cases, 54 completed the treatment and 1 out of this 54 was lost to follow up after completion of the treatment. Table no 4 depicts the treatment response in both the Mantoux positive and the negative groups and the difference was found to be statistically significant.

CONCLUSION

The study demonstrated a high prevalence of Mantoux test positivity (89.1%) among patients with erythema nodosum, emphasizing the importance of evaluation for tuberculosis, particularly in tuberculosis-endemic regions. The marked female predominance and the favourable response to antitubercular therapy observed in our study further support the role of tuberculosis as an important underlying association in erythema nodosum. A high proportion of patients remained recurrence-free following treatment. Therefore, routine assessment for tuberculosis, including Mantoux testing wherever clinically appropriate, should be considered in patients presenting with erythema nodosum in endemic settings. Larger, multicentric studies with longer follow-up are required to further establish the

relationship between Mantoux positivity, tuberculosis and recurrent erythema nodosum.

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