



## Histopathological Analysis of Granulomatous Lesions of Skin and Its Correlation with Clinical Diagnosis at a Tertiary Care Hospital, Bhavnagar

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### Abstract

**Background:** Granulomatous diseases comprise some of the most widespread diseases in the world, such as leprosy and tuberculosis. The incidence of various granulomatous skin lesions varies with geographic location, and the pattern differs between countries and regions within a single nation. With changes in the region, the prevalence of various types of granulomas can differ. Thus, this study helps to identify the most common cause of lesions in the study population.

**Materials and Methods:** The study included all the biopsies from patients who were either clinically suspected of granulomatous lesions of the skin or were diagnosed with granulomatous lesions by histopathological findings in a tertiary care hospital, Bhavnagar.

**Results:** Of the total 92 skin biopsies, 57.61% showed clinicopathological concordance. Out of 57 cases confirmed by histopathology, the highest number of granulomatous lesions (18) was seen in the age group of 31 to 40 years. In the present study, the most common granulomatous skin lesion is leprosy (n = 47, 82.46%). Leprosy is followed by cutaneous tuberculosis and granuloma annulare, with 2 cases (3.51%) each. There were cases of leishmaniasis, sarcoidosis, actinomycosis, pyoderma gangrenosum, secondary syphilis of the skin, and a case with necrobiosis, with 1 case of each in the present study. Among leprosy cases, most (n = 27, 57.45%) were multibacillary leprosy.

**Conclusion:** Our study showed that the most common etiology for granulomatous skin lesions is leprosy in the studied region, predominantly involving adult males. It demonstrated that etiology-specific diagnosis can be achieved through clinical evidence, morphology of granuloma, and special stains.

### Keywords:

*Cutaneous, granuloma, leprosy, Fite-Faraco stain*

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## Introduction

Granulomatous inflammation is a unique pattern within the range of chronic inflammatory processes that present differently both clinically and histopathologically [1].

Chronic inflammatory responses to a variety of organic and inorganic antigens result in granulomatous skin lesions. The inability of polymorphonuclear leukocytes and non-activated macrophages to fully break down and eliminate the offending agents causes

the cells to respond by activating macrophages, cell-mediated type IV hypersensitivity reaction, T and B lymphocytes, and the release of chemical mediators of inflammation, primarily cytokines, which causes the formation of granulomas.

The occurrence of granulomatous lesions varies significantly according to geographic regions [2]. In tropical countries, infectious causes are highly prevalent [3]. Endemic regions for particular infectious causes can also alter prevalence significantly. Environmental and occupational factors affect the prevalence of various non-infectious causes. Apart from these, genetic and ethnic predispositions increase the risk for various types of granulomas.

Thus, this study of granulomatous lesions for a defined region will identify highly prevalent etiology in specific regions. This will provide insight into the current status of health in the community. It will aid in developing cause-specific health programs, effective management of resources, and preventive steps with a high impact on the health status of the region.

## Materials and Methods

After institutional ethics committee approval, this two-year retrospective analysis took place at a tertiary care facility in Bhavnagar, Gujarat, India.

**Inclusion Criteria:** The study included all the biopsies collected within the study period from patients of all age groups and genders who were either clinically suspected of granulomatous lesions of the skin or were diagnosed as granulomatous lesions by histopathological findings.

**Exclusion Criteria:** Biopsies with insufficient clinical history, insufficient tissue, or degraded samples were excluded.

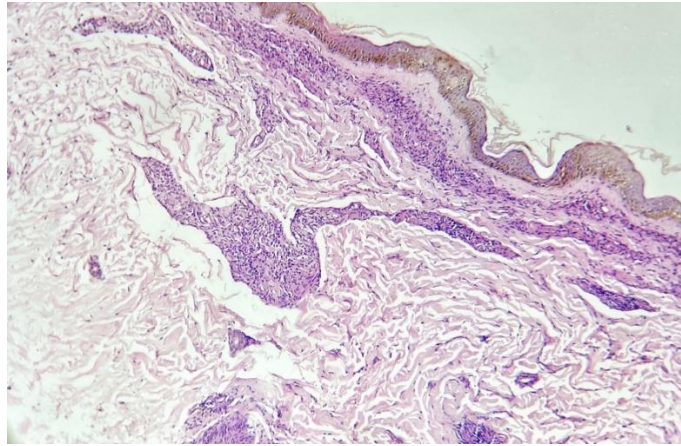
Patient particulars, brief history and clinical findings, provisional diagnosis, and differential diagnosis (if any) were mentioned in the biopsy requisition form. Special stains used were noted. The slides were reviewed and compared with various available previous studies. All these data were tabulated, and a clinico-histopathological correlation was attempted.

## Results

The present study included 92 skin biopsies from patients who were either clinically suspected of granulomatous lesions of the skin or were diagnosed as granulomatous lesions by histopathological findings.

Among 92 skin biopsies, 88 (95.65%) biopsies were clinically suspected as granulomatous lesions. Out of 88, 66 (75%) cases were suspected of infectious granuloma, and 10 (11.36%) were suspected of non-infectious granuloma. The remaining 12 (13.63%) were of non-specific causes, with suspicion of both infectious and non-infectious origins. This suggests the predominance of infectious etiology in the studied region.

Among 92 biopsies, based on histopathological analysis, a total of 57 (61.96%) biopsies were granulomatous lesions, while 35 (38.04%) were non-granulomatous lesions of the skin. The highest concordance between clinical suspicion and histopathological confirmation was seen in cases of leprosy. Out of 60 cases with suspected leprosy, 46 (76.67%) were confirmed by histopathological features [Figure 1]. The least concordance was seen in fungal granuloma, where out of 6 suspected cases, none were confirmed by histopathology. Other lesions showed variable concordance, e.g., out of 2 suspected cases of sarcoidosis, 1 case (50%); out of 6 suspected cases of tuberculosis, 2 cases (33.33%); out of 5 suspected cases of pyoderma gangrenosum, 1 case (20%); out of 11 suspected cases of granuloma annulare, 2 cases (18.18%) were confirmed by histopathology. This finding emphasizes that granulomatous lesions may present clinically similar to non-granulomatous lesions.



**Figure 1: Biopsy showing atrophic epidermis, grenz zone and area of lymphohistiocytic infiltrate (Hematoxylin & Eosin X 100).**

Out of 57 cases confirmed by histopathology, the highest number of granulomatous lesions (18) were seen in the age group of 31 to 40 years, followed by 15 in the 41 to 50 years age group, 9 in the 51 to 60 years age group, 8 in the 21 to 30 years age group, 3 in the 11 to 20 years age group, 2 in the 61 to 70 years age group, and 1 case each in the 71 to 80 and under 10 years age groups. The youngest case was a 3-year-old female with granuloma annulare, presenting with a lesion on her upper extremity. This suggests a higher prevalence of granulomatous skin lesions in adults in their 3rd and 4th decades, potentially due to chronic exposure to infectious agents during adulthood.

A slight male preponderance of 54.38% was observed in the present study, with a male-to-female ratio of 1.19:1.

These granulomatous lesions were predominantly present on the trunk (n = 23, 40.35%) and upper extremities (n = 20, 35.09%). The remaining 11 (19.30%) lesions were present on the lower extremities, and 3 (5.26%) on the face. The anatomical distribution suggests prolonged exposure to environmental triggers, which may occur more frequently on the trunk and upper extremities compared to other regions of the body.

In the present study, actinomycosis, granuloma annulare, and lupus vulgaris were present exclusively on the upper extremities, while pyoderma gangrenosum, sarcoidosis, secondary syphilis, and leishmaniasis were found on the lower extremities. Leprosy lesions were distributed predominantly on the trunk, followed by the upper extremities.

Out of 57 granulomatous lesions, most cases (49, 86%) presented with multiple lesions, while only 8 cases (14%) presented with single lesions.

In the present study, most cases (n = 36, 63.16%) with granulomatous lesions presented within a short duration of 6 months. Only 9 (15.79%) cases presented within a duration of 6 to 12 months, while 12 (21.05%) cases presented after 1 year.

On histopathological examination, the highest number of cases (n=50, 87.72%) were related to the tuberculoid type of granuloma, followed by 3 cases (5.26%) related to necrobiotic granuloma. Sarcoidal granuloma and suppurative granuloma were each related to 2 cases. Thus, in the present study, tuberculoid granuloma was highly prevalent among cases.

Out of 50 cases related to tuberculoid granuloma, 47 cases were diagnosed as leprosy, being the most common (94%) cause of tuberculoid granuloma as well as the most common cause (82.46%) of granulomatous lesions of the skin in the present study. The

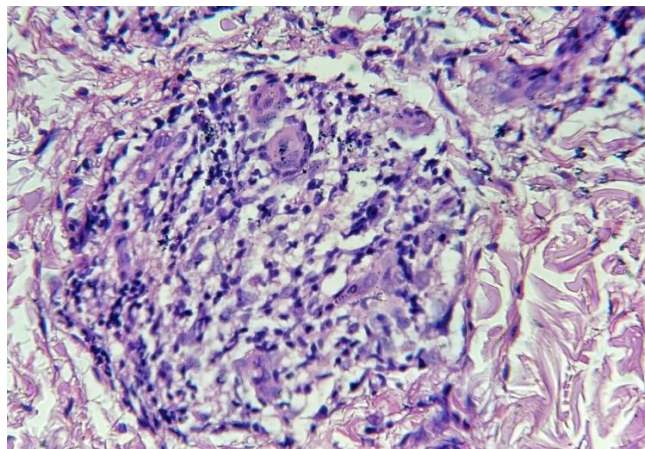
remaining 2 cases were due to tuberculosis, and 1 case was due to leishmaniasis. Out of 3 cases of necrobiotic granuloma, 2 cases were due to granuloma annulare.

In the present study, the most common granulomatous skin lesion is leprosy (n=47, 82.46%). Leprosy is followed by cutaneous tuberculosis and granuloma annulare, with 2 cases (3.51%) each. There were cases of leishmaniasis, sarcoidosis, actinomycosis, pyoderma gangrenosum, secondary syphilis of the skin, and necrobiosis, with 1 case of each in the present study. This shows that leprosy remains a major cause of granulomatous inflammation in the studied region.

Among 47 cases of leprosy, further classification was made into lepromatous leprosy (LL), borderline lepromatous leprosy (BL), borderline leprosy (BB), borderline tuberculoid leprosy (BT), and tuberculoid leprosy (BT). An early form of leprosy, indeterminate leprosy, is also classified in the present study.

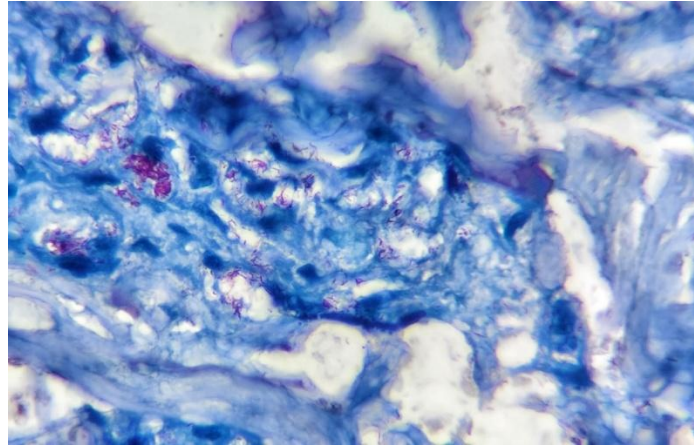
Among leprosy cases, the most common type was indeterminate leprosy, with 11 cases (23.41%), followed by 10 cases (21.28%) of borderline leprosy, 9 cases (19.15%) of borderline tuberculoid leprosy (Figure 2), 6 cases (12.76%) of lepromatous leprosy, 6 cases (12.76%) of borderline lepromatous leprosy, and 5 cases (10.64%) of tuberculoid leprosy. The predominance of indeterminate leprosy in this study represents early-stage leprosy, which may evolve into other forms later depending on immune response.

In the present study, among leprosy cases, most cases (n=27, 57.45%) were of multibacillary leprosy (Figure 3). The remaining 20 cases (42.55%) were of paucibacillary leprosy (Figure 4). This shows a predominance of multibacillary leprosy in the studied region.

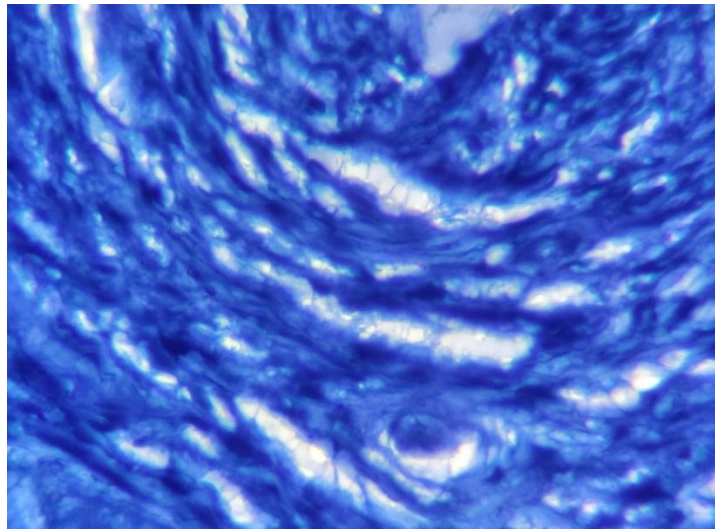


**Figure 2: Well-formed granuloma having epithelioid cells, Langhans giant cell and lymphocytes. (Hematoxylin & Eosin X 400)**

Among leprosy cases, the correlation of bacillary index and subtypes of leprosy showed that all cases of tuberculoid leprosy were of the paucibacillary type. In the borderline tuberculoid type, cases were distributed among 0, 1+, and 2+ bacillary indices, with most cases of the multibacillary type. Borderline leprosy cases were distributed among 0, 4+, and 5+ bacillary indices, with most cases of the multibacillary type. Borderline lepromatous leprosy cases were predominantly distributed among 4+, 5+, and 6+. Only one case of borderline lepromatous leprosy was of the paucibacillary type. Lepromatous leprosy cases were distributed among 5+ and 6+ bacillary indices only. No case of lepromatous leprosy was of the paucibacillary type. Indeterminate leprosy cases were distributed among 0 and 1+ bacillary indices.



**Figure 3:** Section shows a large number of lepra bacilli (Fite Faraco stain under Oil Immersion)



**Figure 4:** Section is negative for bacilli. (Fite Faraco stain under Oil Immersion)

## Discussion

The age incidence of granulomatous lesions ranged from the youngest case of 3 years to the oldest case of 75 years in the present study, with a mean age of 40.70 years. The highest cases of granulomatous lesions (18) were seen in the age group of 31 to 40 years.

Studies conducted by Chug J et al. [1], Queirós CS et al. [4], and Lin IT et al. [5] found the mean age to be 32.44 years, 54.1 years, and 53.5 years, respectively. This shows mild variation in mean age, which can be due to changes in the geographical location of the study population. However, all studies show a high incidence in the adult population, similar to this study.

In the present study, we observed that males are affected more than females. This result is similar to the study conducted by Nijhawan M et al. [6], Khalili M et al. [7], Choudhury M et al. [3], Chakrabarti S et al. [8], and Rajbhandari A et al. [9]. (Table 1) This is because males are more prone to exposure than females due to the outdoor life they lead. The slight variability in gender distribution across studies could be attributed to regional demography and exposure to various causative agents. It also may be due to different sample sizes in the study.

**Table 1: Gender-wise Distribution**

Studies	M: F Ratio	Male	Female	Total
<b>Present study</b>	1.19: 1	31(54.39%)	26(45.61%)	57(100%)
<b>Nijhawan M et al.</b> <sup>[6]</sup>	1.77 : 1	99 (63.87%)	56 (36.13%)	155 (100%)
<b>Khalili M et al.</b> <sup>[7]</sup>	1.05 : 1	119 (51.29%)	113 (48.71%)	232 (100%)
<b>Choudhury M et al.</b> <sup>[3]</sup>	1.26 : 1	29 (55.77%)	23 (44.23%)	52 (100%)
<b>Chakrabarti S et al.</b> <sup>[8]</sup>	1.24 : 1	103 (55.38%)	83 (44.62%)	186 (100%)
<b>Rajbhandari A et al.</b> <sup>[9]</sup>	1.32 : 1	62 (56.88%)	47 (43.11%)	109 (100%)
<b>M: F Ratio – Male: Female Ratio</b>				

In the present study, out of 88 suspected granulomatous lesions, 53 were confirmed as granulomatous lesions by histopathology, showing that 60.23% of cases correlated with clinical suspicion of granulomatous lesions. There were 4 cases with no clinical suspicion of granulomatous lesions, but histopathology revealed granulomatous lesions. Thus, the overall clinicopathological correlation was seen in 53 out of 92 cases, showing a 57.61% correlation.

Chug J et al. [1] found that the overall level of concordance between clinical and histopathological diagnosis was 78%. Nijhawan M et al. [6] found that among 155 cases, 117 cases (75.48%) were fully consistent with the clinical diagnosis, 30 (19.35%) cases were corroborative, and 8 (5.16%) were inconsistent. Choudhury M et al. [3] found that among 52 cases presented as cutaneous granulomatous lesions, 40 cases were confirmed by histopathology, showing a 76.92% correlation. The present study shows a lower clinicopathological correlation compared to the other mentioned studies. This can be due to variations in inclusion or exclusion criteria and the methods used for clinical diagnosis.

In the present study, based on etiology, out of 88 cases, 66 (75%) were suspected of infectious granuloma, and 10 (11.36%) were suspected of non-infectious granuloma. The remaining 12 (13.63%) were of non-specific causes, with suspicion of both infectious and non-infectious causes. Choudhury M et al. [3] found that out of 52 cases, 46 cases (88.46%) had infectious etiology. The remaining 6 cases (11.54%) had non-infectious etiology. Thus, our study has also found similar results, showing a high proportion of infectious etiology among clinical suspicions. This finding shows a comparatively high prevalence of infectious granulomatous lesions in Bhavnagar and the surrounding region, from where all the biopsy specimens were received.

In the present study, granulomatous lesions were predominantly present on the trunk (n = 23, 40.35%) and upper extremities (n = 20, 35.09%). The remaining 11 (19.30%) lesions were present on the lower extremities, and 3 (5.26%) were on the face. Khalili M et al. [7], in their study, found that the most common site of involvement was the upper limb (39.9%); other sites in descending order were the head and neck (35.5%), lower limbs (18.4%), trunk (3.9%), and genitalia (2.2%).

In contrast to our study, the study by Khalili M et al. [7] showed a slightly higher number of lesions over the upper limb, while in our study, slightly more lesions were found on the trunk, followed by the upper extremities. This variation can be explained by differences in the prevalent type of granulomatous lesion.

In the present study, on histopathological examination, the highest number of cases (n=50, 87.72%) were related to the Tuberculoïd type of granuloma, followed by 3 cases (5.26%) related to Necrobiotic granuloma. Sarcoid granuloma and suppurative granuloma were both related to 2 cases each. Slight variation was seen in other studies (Table 2). Regional variation may cause differences in the prevalence of infectious and non-infectious diseases, which may alter the frequency of various types of granulomas. This can also be due to endemic conditions. Population demographics also alter frequency. Study-related factors like inclusion or exclusion criteria may also impact the results.

**Table 2: Various types of granulomas**

Studies	Sarcoidal	Tuberculoid granuloma	Necrobiotic	Suppurative	Foreign body	others
<b>Present study</b>	3.51%	87.72%	5.26%	3.51%	-	-
<b>Choudhury M et al. [3]</b>	2.5%	57.5%	2.5%	7.5%	2.5%	27.5%
<b>Chug J et al. [1]</b>	8%	68%	8%	4%	2%	10%
<b>Chakrabarti S et al. [8]</b>	1.53%	69.39%	11.73%	4.59%	6.12%	6.63%
<b>Nijhawan M et al. [6]</b>	0.64%	74.67%	5.19%	18.18%	-	1.29%

In the present study, the most common granulomatous skin lesion is Leprosy (n=47, 82.46%). Leprosy is followed by cutaneous tuberculosis and granuloma annulare, with 2 cases (3.51%) each. There were cases of leishmaniasis, sarcoidosis, actinomycosis, pyoderma gangrenosum, secondary syphilis of the skin, and necrobiosis, with 1 case each in the present study.

In a study by Nijhawan M et al. [6], 98 (63.23%) cases were of leprosy. In a study by Rajbhandari A et al. [9], the most common cause of cutaneous granulomas was leprosy (n=25; 23%), followed by tuberculosis (n=16; 15%). In a study by Dutta B et al. [10], the most common cutaneous granuloma encountered was leprosy (69.33%), followed by fungal (11.33%) and tubercular (8%) granulomas. As found in various studies, granulomatous lesions were predominantly due to leprosy, and similar results were observed in our study. This shows a high prevalence of leprosy in the studied regions.

In our study, among leprosy cases, the most common type was indeterminate leprosy, with 11 cases (23.41%), followed by 10 cases (21.28%) of borderline leprosy, 9 cases (19.15%) of borderline tuberculoid leprosy, 6 cases (12.76%) of lepromatous leprosy, 6 cases (12.76%) of borderline lepromatous leprosy, and 5 cases (10.64%) of tuberculoid leprosy. Other studies showed borderline tuberculoid leprosy as the predominant subtype (Table 3). The variation in leprosy subtypes occurs due to geographic differences. It may also occur due to variations in methodology, such as sample size and diagnostic criteria.

**Table 3: Frequency of subtypes of leprosy.**

Different studies	Chakrabarti S et al. [8]	Kumar L et al. [11]	Present study
<b>Types of leprosy</b>			
<b>Tuberculoid leprosy</b>	13.08%	15%	10.64%
<b>Borderline tuberculoid leprosy</b>	57.94%	32.50%	19.15%
<b>Mid borderline</b>	-	12.50%	21.28%
<b>Borderline lepromatous leprosy</b>	6.54%	17.50%	12.76%
<b>Lepromatous leprosy</b>	9.35%	17.50%	12.76%
<b>Early indeterminate leprosy</b>	12.14%	5%	23.14%
<b>Others</b>	0.93%	-	-

In the present study, among leprosy cases, most cases (n=27, 57.45%) were of multibacillary leprosy. The remaining 20 cases (42.55%) were of paucibacillary leprosy. All cases of tuberculoid leprosy were of the paucibacillary type, and lepromatous leprosy cases were distributed among 5+ and 6+ bacillary index only.

In a study by Kumar L et al. [11], most cases (n=23, 57.5%) were of paucibacillary leprosy. The remaining 17 cases (42.5%) were multibacillary leprosy. In their study, Kumar L et al. [11] also found that all cases of tuberculoid leprosy were of the paucibacillary type, and lepromatous leprosy cases were distributed among high bacillary index, similar to our study.

This finding shows a correlation with the literature suggesting that the tuberculoid leprosy spectrum presents with paucibacillary lesions, while the lepromatous leprosy spectrum presents with multibacillary lesions.

**Limitations:** Due to the study's single tertiary care hospital setting, it might not accurately reflect the variety of granulomatous lesions found in other geographic or demographic groups. Due to variation in clinical presentation of various granulomatous diseases, clinical correlation might have been impacted.

## Conclusion

Our study showed that the most common etiology for granulomatous skin lesions is leprosy in the studied region, predominantly involving adult males. Histopathological diagnosis can be substantially improved by using clinical correlation and special stains, which help establish a definitive diagnosis. Therefore, an etiology-specific diagnosis can be achieved through appropriate clinical evidence, laboratory work, morphology of granuloma, and special stains.

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