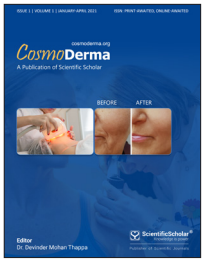
www.cosmoderma.org

ScientificScholar®
Knowledge is power
Publisher of Scientific Journals

CosmoDerma



Brief Report

Association of granuloma annulare with dyslipidemia: A case–control study from a tertiary care center

Durga Prasad Dubey[1], Swale Iftikhar[1], Deepak Agarwal[1], Raj Kumar[1], Vineet Kumar Patel[1], Anil Kumar Gupta[1]

[1]Department of Dermatology, Venereology and Leprology, Baba Raghav Das Medical College, Gorakhpur, Uttar Pradesh, India.

***Corresponding author:**
Durga Prasad Dubey,
Department of Dermatology,
Venereology and Leprology,
Baba Raghav Das Medical
College, Gorakhpur,
Uttar Pradesh, India.

drdpdubeyderma32@gmail.com

Received: 31 May 2025
Accepted: 16 June 2025
Published: 07 August 2025

DOI
10.25259/CSDM_87_2025

Quick Response Code:

ABSTRACT

Objectives: The objectives of the study are to evaluate the prevalence of dyslipidemia (DLP) in patients with granuloma annulare (GA) compared to age- and sex-matched healthy controls.

Materials and Methods: A case–control study was conducted on 30 histopathologically confirmed GA patients and 30 sex-matched healthy individuals. Fasting lipid profiles were analyzed and compared.

Results: GA patients had significantly higher levels of total cholesterol, triglycerides, and low-density lipoprotein cholesterol compared to controls ($P < 0.05$). Although low high-density lipoprotein was more common in GA cases, it was not statistically significant.

Conclusion: GA may be a clinical marker of underlying DLP, supporting metabolic evaluation in affected patients.

Keywords: Biomarkers, Dermatology, Dyslipidemia, Granuloma annulare, Lipid metabolism

INTRODUCTION

Granuloma annulare (GA) is a benign, self-limiting granulomatous skin disorder first described by Radcliffe Crocker in 1902. Characterized clinically by annular papules and histologically by palisading granulomas with mucin deposition, GA's precise etiology remains elusive. Epidemiological studies estimate a prevalence of 0.4–0.5% in the general population, affecting both children and adults in a bimodal distribution.[1,2]

Although traditionally considered idiopathic, GA has been associated with systemic conditions such as diabetes mellitus, thyroid dysfunction, infections, and malignancies. Recent focus has turned to the role of metabolic disturbances – particularly dyslipidemia (DLP) – as emerging evidence suggests higher lipid abnormalities in GA patients compared to healthy individuals.[3]

DLP is a well-established risk factor for atherosclerosis and systemic inflammation. Given the inflammatory and macrophage-rich histology of GA, an interplay between lipid metabolism and granulomatous response is biologically plausible. Dysregulated lipids may contribute to the immunopathogenesis of GA through mechanisms involving macrophage activation, oxidative stress, and cytokine release.[4,5]

This study was undertaken to investigate the association of DLP with GA in a North Indian population, with the goal of improving clinical vigilance and management strategies for this seemingly cutaneous disorder.

MATERIALS AND METHODS

A hospital-based, sex-matched case–control study was conducted at the Department of Dermatology, Baba Raghav Das Medical College, Gorakhpur, from January 2023 to May 2024. Thirty consecutive patients with clinically and histologically confirmed GA were enrolled. Thirty healthy individuals matched for age and sex served as controls. Exclusion criteria included known DLP, use of lipid-altering medications, uncontrolled diabetes, thyroid disorders, or systemic steroid use. Written informed consent was obtained from all participants. The study adhered to the Declaration of Helsinki (2008 revision) and received approval from the Institutional Ethics Committee. All cases underwent skin biopsy for histological confirmation. Clinical data, including age, sex, disease duration, and lesion distribution, were documented. Both groups underwent fasting lipid profile testing, including total cholesterol (TC), triglycerides (TG), high-density lipoprotein (HDL), and low-density lipoprotein (LDL). Statistical analysis was conducted using the Statistical Packages for the Social Sciences. Continuous variables were expressed as mean ± standard deviation, and categorical variables as percentages. Independent *t*-tests and Chi-square tests were used as appropriate. A $P < 0.05$ was considered statistically significant.

Table 1: Comparison of type of dyslipidemia in case and control.

		Case (*n*=30)		Control (*n*=30)		*P*-Value
		n	%	*n*	%	
Dyslipidemia	Present	20	66.67	8	26.67	0.001
	Absent	10	33.33	22	73.33	
Triglyceride	Elevated	18	60	2	6.67	<0.01
	Normal	12	40	28	93.33	
Cholesterol	Elevated	22	73.33	5	16.67	<0.01
	Normal	8	26.66	25	83.34	
LDL	Elevated	10	33.3	1	3.33	0.0026
	Normal	20	66.67	29	96.6	
HDL	Low	16	53.3	18	60	0.206
	Normal	14	46.67	12	40	

LDL: Low-density lipoprotein, HDL: High-density lipoprotein.

Table 2: Comparison of level of serum lipid (mg/dL) in case and controls.

Level of serum lipids (mg/dL)	Case (*n*=30)		Control (*n*=30)		*P*-value
	Mean	SD	Mean	SD	
Triglycerides	177.37	64.28	140.2	63.19	0.027
Cholesterol	214.33	39.66	190.21	39.15	0.018
LDL	137.37	31.93	118.2	30.82	0.021
HDL	55.24	24.76	46.44	14.22	0.096

SD: Standard deviation, LDL: Low-density lipoprotein, HDL: High-density lipoprotein.

RESULTS

The findings of this study indicate a significant association between GA and lipid abnormalities. The incidence of DLP, characterized by abnormal lipid levels, was markedly higher in the case group compared to the control group. Specifically, a significantly increased prevalence of hypertriglyceridemia, hypercholesterolemia, and elevated LDL cholesterol levels was observed among patients diagnosed with GA ($P < 0.05$). These results suggest a potential link between lipid metabolism disturbances and the pathogenesis of this dermatological condition.

In addition to the elevated levels of TC, TG, and LDL cholesterol, the study also assessed HDL cholesterol levels. Although the incidence of reduced HDL cholesterol was higher in the case group than in the control group, the difference did not reach statistical significance ($P = 0.206$) [Table 1]. This indicates that while there is a trend toward lower HDL levels in affected individuals, the study sample may not have been large enough to establish a conclusive correlation.

Further analysis of lipid parameters demonstrated that the mean levels of TC, TG, and LDL cholesterol were significantly higher in the case group when compared to the control group ($P < 0.05$) [Table 2]. This suggests that patients with GA may have an underlying predisposition to lipid metabolism disorders. However, when assessing HDL cholesterol levels, no statistically significant difference was noted between the two groups ($P = 0.096$). This finding implies that while GA appears to be associated with DLP, not all lipid parameters are equally affected.

DISCUSSION

The present case–control study highlights a statistically significant association between GA and DLP, particularly with elevated TC, TG, and LDL levels. These findings underscore the potential role of lipid metabolism disturbances in the pathogenesis of GA.

Our findings are in alignment with those of Wu *et al.*, who demonstrated a high prevalence of DLP (79.3%) in GA patients compared to controls (51.9%) and identified GA as an independent risk factor for DLP with an adjusted odds ratio of 4.04 (95% confidence interval: 2.53–6.46).[6] Similar to

our study, they reported statistically significant elevations in TC, TG, and LDL cholesterol in the GA group. Notably, they also found that annular morphology was more frequently associated with hypercholesterolemia and DLP, a finding that correlates with our observation of elevated cholesterol levels, particularly in annular GA subtypes.

Dabski and Winkelmann also observed lipid deposition (microdroplet staining) in 80% of annular GA lesions, suggesting a potential histopathological link between lipid accumulation and annular lesion morphology.[7] This lends further support to the hypothesis that specific morphological variants of GA may have stronger associations with lipid dysregulation. Although our study found reduced HDL cholesterol levels more frequently in GA patients, this did not reach statistical significance ($P = 0.206$). This is consistent with several earlier studies, including Fornons-Servent *et al*., who reported a 48% prevalence of hypercholesterolemia in GA cases versus 35% in controls ($P = 0.007$), but concluded that the clinical relevance of such associations remains uncertain due to the high background prevalence of metabolic conditions.[8] Moreover, Watanabe *et al*. documented improvement in GA lesions following the correction of hyperlipidemia, suggesting a possible causal or contributory role of DLP in disease persistence or progression.[9] Such therapeutic outcomes further reinforce the importance of evaluating and managing lipid abnormalities in GA patients.

Inflammation has been proposed as a mechanistic link between GA and DLP. Chronic low-grade inflammation seen in metabolic syndrome and lipid disorders may contribute to granuloma formation through macrophage activation and lipid deposition in the dermis. Khovidhunkit *et al*. and Esteve *et al*. have elaborated on how systemic inflammation alters lipid metabolism by influencing hepatic lipoprotein synthesis and catabolism.[10,11]

In recent literature, the expression of adipophilin – a lipid droplet-associated protein – was found to be significantly correlated with DLP in GA patients. Antoñanzas *et al*. reported a 10-fold increase in DLP risk in GA patients with positive adipophilin staining, and these individuals also demonstrated a higher incidence of developing DLP during follow-up.[12] These findings support the notion that GA may be a dermatological manifestation of underlying lipid metabolism disorders. While our study corroborates the association between GA and DLP, the causal direction remains speculative. It is plausible that shared immunoinflammatory pathways or lipid-mediated skin inflammation could play contributory roles. However, the lack of a significant difference in HDL levels and the absence of other systemic metabolic abnormalities (e.g., diabetes and thyroid disease) in our cohort suggest that DLP may act as an independent risk factor rather than a byproduct of broader metabolic syndrome.

Limitations

Our study is limited by its relatively small sample size, which may have constrained the statistical power to detect subtler associations – particularly regarding HDL cholesterol. In addition, the lack of histological lipid staining limit the mechanistic insights. Future prospective studies incorporating adipophilin expression and long-term follow-up are warranted to clarify causality and explore therapeutic implications.

CONCLUSION

Our study adds to the growing body of evidence linking GA with DLP. Screening for lipid abnormalities in patients with GA – especially those with annular or generalized forms – may be clinically warranted. Understanding this association may not only aid in more holistic patient care but may also open avenues for adjunctive metabolic interventions in recalcitrant cases of GA.

Ethical approval: Ethical approval was provided by the Institutional Human Ethical Committee, Baba Raghav Das Medical College, Gorakhpur, dated December 28, 2022, number 213/IHEC/2022.
Declaration of patient consent: The authors certify that they have obtained all appropriate patient consent.
Financial support and sponsorship: Nil.
Conflicts of interest: There are no conflicts of interest.
Use of artificial intelligence (AI)-assisted technology for manuscript preparation: The authors confirm that there was no use of artificial intelligence (AI)-assisted technology for assisting in the writing or editing of the manuscript, and no images were manipulated using AI.

REFERENCES

1. Muhlbauer JE. Granuloma annulare. J Am Acad Dermatol 1980;3:217-30.
2. Leung AK, Barankin B, Hon KL. Granuloma annulare. Int J Pediatr Child Health 2013;1:15-8.
3. Piette EW, Rosenbach M. Granuloma annulare: Pathogenesis, disease associations and triggers, and therapeutic options. J Am Acad Dermatol 2016;75:467-79.
4. Cyr PR. Diagnosis and management of granuloma annulare. Am Fam Physician 2006;74:1729-34.
5. Lukács J, Schliemann S, Elsner P. Treatment of generalized granuloma annulare-a systematic review. J Eur Acad Dermatol Venereol 2015;29:1467-80.
6. Wu W, Robinson-Bostom L, Kokkotou E, Jung H, Kroumpouzos G. Dyslipidemia in granuloma annulare: A case-control study. Arch Dermatol 2012;148:1131-6.
7. Dabski K, Winkelmann RK. Generalized granuloma annulare: Histopathology and immunopathology. Systematic review of 100 cases and comparison with localized granuloma annulare. J Am Acad Dermatol 1989;20:28-39.
8. Fornons-Servent R, Bauer-Alonso A, Llobera-Ris C, Penín RM, Marcoval J. Granuloma annulare: A case-control study

of possible associated diseases. Dermatol Pract Concept 2022;12:e2022173.
9. Watanabe S, Tanaka M, Kobayashi K, Sawada M, Ishizaki S, Tsurui K, *et al*. Remission of generalized erythematous granuloma annulare after improvement of hyperlipidemia and review of the Japanese literature. Dermatol Pract Concept 2014;4:97-100.
10. Khovidhunkit W, Kim MS, Memon RA, Shigenaga JK, Moser AH, Feingold KR, *et al*. Effects of infection and inflammation on lipid and lipoprotein metabolism: Mechanisms and consequences to the host. J Lipid Res 2004;45:1169-96.
11. Esteve E, Ricart W, Fernández-Real JM. Dyslipidemia and inflammation: An evolutionary conserved mechanism. Clin Nutr 2005;24:16-31.
12. Antoñanzas J, Núñez-Córdoba JM, Salido-Vallejo R, Álvarez-Gigli L, Robledano R, España A. Association between adipophilin expression and risk of dyslipidaemia in patients with granuloma annulare. Med Clin (Barc) 2024;163:232-7.

How to cite this article: Dubey DP, Iftikhar S, Agarwal D, Kumar R, Patel VK, Gupta AK. Association of granuloma annulare with dyslipidemia: A case–control study from a tertiary care center. CosmoDerma. 2025;5:82. doi: 10.25259/CSDM_87_2025