BENHA MEDICAL JOURNAL bmj
Print ISSN 1110-208X.
Online ISSN 2357-0016

original article

Assessment of Serum Level of Amyloid A in Patients with Acne Vulgaris

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Received:24 June 2024

Accepted:23 March 2025

Abstract:

Background: Serum Amyloid A (SAA) is a major acute phase protein produced in large quantity during Acute Phase Reactant (APR). The rise of SAA concentration in blood circulation during APR has been a clinical marker for active inflammation. This study aim to evaluate serum levels of Amyloid A in patients with acne and its correlation with the disease severity. **Methods:** This prospective case-control study included 60 patients suffering from acne vulgaris. Patients were divided into 3 equal groups: Group A: patients with mild acne vulgaris. Group B: patients with moderate acne vulgaris. Group C: 20 patients with severe acne vulgaris. In addition, 30 apparently healthy, age and sex matched individuals were included as control group. **Results:** Serum Amyloid A level was significantly higher in the acne vulgaris group when compared to the control (mean=4.89 versus 1.08, p<0.001). There was statistically significant increase in serum level of Amyloid A in relation to increased severity of acne. Serum Amyloid A showed significant positive correlation with BMI (p=0.005), duration of acne (p<0.001), and acne vulgaris scores (P<0.001). **Conclusion:** Serum amyloid A1 is increased in AV patients, and this elevation may play a role in the inflammatory milieu of AV. Serum amyloid A had significant correlation with severity of AV. Serum amyloid A had significant correlation with development of acne scars.

Keywords: Serum Level; Amyloid A; Disease Severity; Acne Vulgaris.

Introduction

Acne, one of the most common skin diseases, affects approximately 85% of the adolescent population, and occurs most prominently at skin sites with a high density of sebaceous glands such as the face, back, and chest. [(1)]

Acne can present as non-inflammatory comedones (black heads, white heads), inflammatory papules, pustules, nodules and cysts, or a mixture of lesions. This can result in symptoms of local tenderness and erythema [(2)].

The main pathogenic factors of acne are high sebaceous gland secretion, follicular hyperproliferation, high androgen effects, propionibacterium acnes, colonization and inflammation [(3)].

Propionibacterium acne activates the innate immunity via the expression of protease activated receptors (PARs), tumour necrosis factor Alpha (TNF α) and toll-like receptors (TLRs), and the production of interferon Gama (INF γ), interleukins IL (1, 8, 12), Tumor Growth Factor (TGF), and matrix metalloproteinases (MMPs) by keratinocytes [(4)].

Serum Amyloid A (SAA) is a major acute phase protein produced in large quantity during Acute Phase Reactant (APR). The rise of SAA concentration in blood circulation during APR has been a clinical marker for active inflammation [(5)].

Serum Amyloid A is a highly conserved acute-phase protein, released in response to inflammation or infection. Production of acute-phase SAA is stimulated by proinflammatory cytokines, such as IL-1, IL-6, TNF, IFN-γ, and TGF. The concentration of SAA increases dramatically during acute inflammation and injury, reaching within 5-6 hours levels that are 1000-fold greater than normal [(6)].

Serum Amyloid A increases moderately to markedly in bacterial and fungal infections, invasive malignant diseases, tissue injuries in the acute myocardial infarction and autoimmune diseases such as rheumatoid arthritis and vasculitis. Mild elevation is often seen in viral infections, systemic lupus erythematosus and localized inflammation or tissue injuries in cystitis and cerebral infarction [(7)].

The purpose of this study was to evaluate serum levels of Amyloid A in patients with acne and its correlation with the disease severity.

Patients and methods

This prospective case-control study included 60 patients suffering from acne vulgaris All patients were selected from the Outpatient Clinic of Dermatology and Andrology Department of Benha University Hospitals from January 2021 to December 2021.

A written informed consent was obtained from all participants. The study was approved by the Local Ethics Committee on research involving human subjects of Benha Faculty of Medicine. **Approval code: Ms.8.10.2018**

Inclusion criteria were both gender and age from 16 to 35 years

Exclusion criteria were patients with inflammatory disease, e.g.: rheumatoid arthritis, with bacterial, fungal, and viral infections, e.g.: Herpes Zoster, invasive malignant disease, autoimmune disease, e.g. familial mediterranean fever, and pregnant and lactating women.

Grouping: Patients were divided into 3 equal groups: Group A: patients with mild acne vulgaris. Group B: patients with moderate acne vulgaris. Group C: 20 patients with severe acne vulgaris. In addition, 30 apparently healthy, age and sex matched individuals were included as control group.

All studied cases were subjected to the following: Full history taking, including [age, sex, duration of acne, family history and previous treatments.]. Full clinical examination: Complete clinical examination to exclude any systemic disease, complete dermatological examination to evaluate the clinical type and severity of acne. Routine laboratory

investigations [serum level of amyloid A by ELISA technique].

Blood sampling:

Serum sample collection and storage: Venous blood samples (5 ml) were taken from patients and controls. Samples were left to clot at room temperature in a sterile, clean and dry tube. After clotting, the samples were centrifuged for 20-min at the speed of 2000-3000 r.p.m. and the supernatant was removed. The serum was separated and stored immediately at -20°C in the laboratory. After collecting serum samples from all participants, the serum samples were used to determine Amyloid A.

Statistical analysis

Statistical analysis was done by SPSS v25 (IBM Corp. Released 2017. Armonk, NY: IBM Corp.). Quantitative variables were presented as mean and standard deviation (SD) and compared between the two groups utilizing unpaired Student's t- test and ANOVA (F) test. Qualitative variables were presented as frequency and percentage (%) and were analyzed utilizing the Chi-square test. One Way ANOVA test was used to assess the statistical significance of the difference between more than two study group parametric variables. Correlation analysis assesses the strength of association between two quantitative variables. The ROC Curve (receiver operating characteristic) provides a useful way to evaluate the sensitivity and specificity for quantitative diagnostic measures that categorize cases into one of two groups A two tailed P value < 0.05 was considered statistically significant.

Results

There was no significant difference between the studied groups regarding demographic and anthropometric data. **(Table 1)**

There were no significant relations between acne grades and age, sex and BMI. Among all cases studied, only severe grades were significantly associated with the family history of acne scars. There was a statistically significant relation between disease duration and severity of acne as patients with severe acne had significant increase in disease duration. Acne scars were significantly associated with increased severity ($p<0.001$). No significant differences were found regarding acne scar types with severity grades ($p>0.05$). **(Table 2)**

Serum Amyloid A level was significantly higher in the acne vulgaris group when compared to the control (mean=4.89 versus 1.08, $p<0.001$). There was a statistically significant increase in serum level of Amyloid A in relation to increased severity of acne. ($P<0.05$)**. (Table 3)**

Serum Amyloid A level was significantly higher in cases with acne scars compared to those without acne scars ($p<0.001$). No significant relations were found between Serum Amyloid A level and gender, family history of acne scars, relation to stress, sun exposure, and type of scar ($p>0.05$ for each).

Serum Amyloid A showed significant positive correlation with BMI ($p=0.005$), duration of acne ($p<0.001$), and acne vulgaris scores ($P<0.001$).

ROC curve of Serum Amyloid A was conducted for prediction of severe AV grades. Serum Amyloid A showed high accuracy AUC (AUC=0.991), for prediction of severe grades of acne vulgaris. At cut off point >5.32, sensitivity was 95%, specificity was 95%, PPV was 90.5% and NPV was 97.4%. **(Figure 1)**

This ROC curve of SAA was conducted for prediction of AV scar formation. Serum Amyloid A showed high accuracy AUC (AUC=0.974) for prediction of AV scar formation. At cut off point >5.01, sensitivity was 95%, specificity was 82.5%, PPV was 73.1% and NPV was 97.1%.**(Figure 2)**

Table 1: Comparison of AV patients and control groups regarding demographic and anthropometric data and distribution of different variables in patients with AV

	Acne Vulgaris n = 60		Control n = 30		P value
	No.	**%**	**No.**	**%**	
Gender					
Male	30	50.0	15	50.0	1.000
Female	30	50.0	15	50.0	
Age (years)	22.70 ± 3.54		21.63 ± 3.70		0.188
Family history of acne scars	8	13.3	2	6.7	0.486

		AV N=60	
		No.	**%**
Onset	Gradual	60	100
Course	Progressive	60	100
Duration in years		3.55 ± 1.29	
Acne scars		20	33.3
Type of scar			
Ice pick		8	40.0
Box car		11	55.0
Rolling		1	5.0
Relation to sun exposure		5	8.3

Data are represented as Mean ± SD or frequency (%),

Table 2: Relations between acne vulgaris severity and clinical variables, disease duration and acne scars.

	Acne vulgaris severity						P value
	Mild n=20		**Moderate n=20**		**Severe n=20**		
	No.	**%**	**No.**	**%**	**No.**	**%**	
Gender							
Male	8	40.0	9	45.0	13	65.0	0.247
Female	12	60.0	11	55.0	7	35.0	
Age (years)	21.60 ± 3.62		22.95 ± 3.07		21.55 ± 2.89		0.211
BMI (kg/m^2)	21.15 ± 1.50		21.75 ± 1.68		22.60 ± 1.64		0.121
Family history of acne scars	0	0.0	0	0.0	8	40.0	<0.001*
Relation to sun	2	10.0	3	15.0	0	0.0	0.352
Duration in years	2.35 ± 0.813		3.40 ± 0.821		4.90 ± 0.641		<0.001*
Acne scars	0	0	2	10	18	90	<0.001*
Scar type							
Ice pick	-	-	2	100	6	33.3	0.245
Box car	-	-	0	0	11	61.1	
Rolling	-	-	0	0	1	5.6	

Data are represented as Mean ± SD or frequency (%),, *: statistically significant as P value <0.05

Table 3: Comparison of serum amyloid A level among AV patients and control groups and Relation between AV severity grades and serum amyloid A level.

	Acne Vulgaris n = 60	Control n = 30	P value	
Serum Amyloid A (ng/ml)	4.89 ± 1.36	1.08 ± 0.61	<0.001*	
	Acne vulgaris severity			
	Mild N=20	**Moderate N=20**	**Severe N=20**	
Serum Amyloid A (ng/ml)	3.309 ± 0.657	5.020 ± 0.266	6.338 ± 0.614	P1<0.001*	P_2<0.001*, p_3<0.001*, p_4<0.001*

Data are represented as Mean ± SD *: statistically significant as P value <0.05

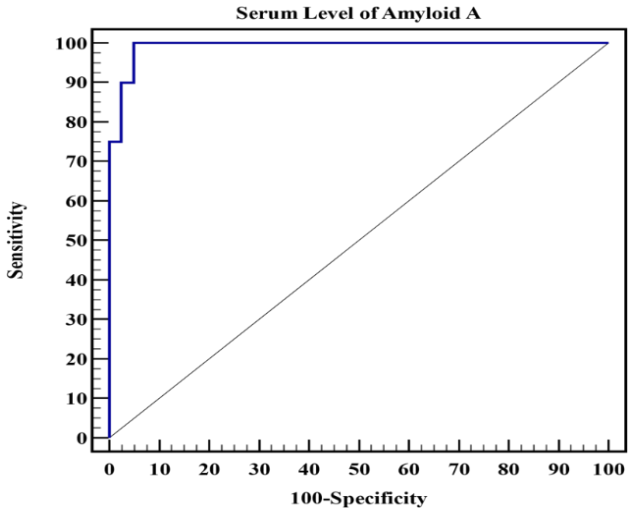

Figure 1: ROC Curve of serum amyloid A level for prediction severe AV grades

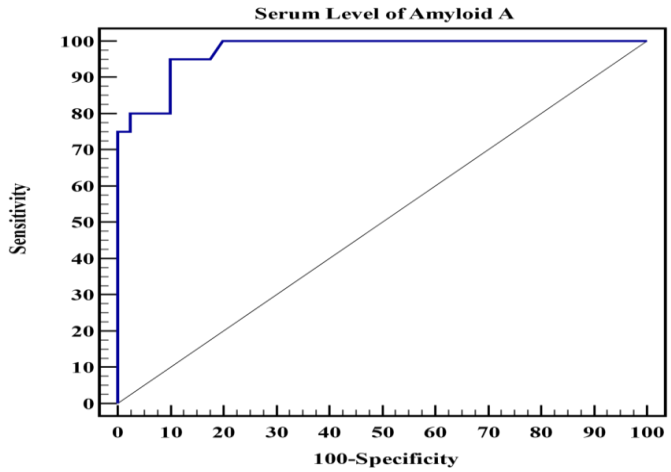

Figure 2: ROC Curve of serum amyloid A level for prediction of AV scar formation.

Discussion

The present study revealed that serum Amyloid A level was significantly higher in the acne vulgaris group when compared to the control. There was a statistically significant increase in serum levels of SAA in relation to increased severity of acne. Serum levels of SAA showed significant positive correlation with duration of acne and acne vulgaris scores.

The acute-phase response markers reflect the changes occurring secondary to inflammation or infection. Among these markers, the expression of the amyloid A family is prominent [9]. The expression of amyloid A proteins is induced by several inflammatory cytokines and lipopolysaccharide, and even systemic glucocorticoids. SAA1 is increased in different disorders linked with AV such as polycystic ovary, insulin resistance, and hyperandrogenism [10, 11].

The exact role of SAA in AV has not been previously investigated. Serum amyloid A1 may have a role in AV pathogenesis through different mechanisms, it is known for its lipophilicity, with a strong effect on sebocyte activation. In addition, SAA can maintain tissue inflammation and can induce remolding through metalloproteinase release [12].

Cutibacterium acne can also increase the release of SAA and the effect of SAA1 is also mediated through activation of Toll-like receptors, especially Toll-like receptor 2. SAA can increase the expression of peroxisome proliferator-activated receptor γ and subsequent induction of inflammation. Furthermore, SAA is a strong initiator of Akt/mTOR inflammatory cascade. All these are involved in the pathophysiological process of AV [13, 14].

In the present study, the serum level of amyloid A showed significant positive correlation with BMI. According to the SAA gene has been associated with obesity in humans [16]. Also a relationship was reported between obesity and the SAA gene [17]. In addition, obesity has been found to affect systemic inflammatory responses, leading to increased serum levels of the acute phase protein SAA, which may contribute to insulin tolerance.

The association between psoriasis and SAA was also reported, SAA would be a more specific marker of psoriasis rather than CRP [19]. Serum levels of amyloid A were significantly increased in other inflammatory diseases like atopic dermatitis, CTCL [20], urticaria [21] and lichen planus patients [22].

The present study showed that SAA level was significantly higher in cases with acne scars compared to those without acne scars. These results could be explained as SAA has a direct effect on dermal fibroblast [23], and its serum level is elevated in diseases characterized by fibrosis like sarcoidosis [24].

In the present work, logistic regression analysis was conducted for the prediction of acne scar formation, using age, gender, BMI, family history of acne scars, relation to stress, relation to sun exposure, duration, severity and serum level of Amyloid A as covariates. Higher serum level of Amyloid A was considered as a risk predictor for acne scar formation. This was in agreement with other researchers, who suggested that SAA1 delays normal murine dermal wound healing [25]. Also, SAA induces inflammatory phenotype and promotes cell proliferation in activated hepatic stellate cells, the major scar forming cells in the liver [26]. SAA assays of sera from keloid patients (these patients form greatly exaggerated dermal scars) showed normal levels of SAA, as the fibrocyte assay on keloid patient showed that these cells are relatively insensitive to SAA [27].

Conclusion

Serum amyloid A1 is increased in AV patients, and this elevation may play a role in the inflammatory milieu of AV. Serum amyloid A had significant correlation with severity of AV severity. Serum amyloid A

had significant correlation with the development of acne scars.

References

1. Picardo M, Eichenfield LF, Tan J. Acne and Rosacea. Dermatol Ther (Heidelb). 2017;7:43-52.
2. Mahto A. Acne vulgaris. Medicine. 2017;45:386-9.
3. Emiroğlu N, Cengiz FP, Kemeriz F. Insulin resistance in severe acne vulgaris. Postepy Dermatol Alergol. 2015;32:281-5.
4. Dréno B. What is new in the pathophysiology of acne, an overview. J Eur Acad Dermatol Venereol. 2017;31 Suppl 5:8-12.
5. Ye RD, Sun L. Emerging functions of serum amyloid A in inflammation. J Leukoc Biol. 2015;98:923-9.
6. Targońska-Stępniak B, Majdan M. Serum amyloid A as a marker of persistent inflammation and an indicator of cardiovascular and renal involvement in patients with rheumatoid arthritis. Mediators Inflamm. 2014;2014:793628.
7. Jovanović DB. [Clinical importance of determination of serum amyloid A]. Srp Arh Celok Lek. 2004;132:267-71.
8. Jia W, Li X, Lei F, Hu F, Li F, Zhang X, et al. Diagnostic Predictive Value of Tryptase, Serum Amyloid A and Lipoprotein-Associated Phospholipase A2 Biomarker Groups for Large Atherosclerotic Cerebral Infarction. Emerg Med Int. 2022;2022:5784909.
9. Sorić Hosman I, Kos I, Lamot L. Serum Amyloid A in Inflammatory Rheumatic Diseases: A Compendious Review of a Renowned Biomarker. Front Immunol. 2020;11:631299.
10. De Buck M, Gouwy M, Wang JM, Van Snick J, Proost P, Struyf S, et al. The cytokine-serum amyloid A-chemokine network. Cytokine Growth Factor Rev. 2016;30:55-69.
11. Sun L, Ye RD. Serum amyloid A1: Structure, function and gene polymorphism. Gene. 2016;583:48-57.
12. De Buck M, Gouwy M, Struyf S, Opdenakker G, Van Damme J. The ectoenzyme-side of matrix metalloproteinases (MMPs) makes inflammation by serum amyloid A (SAA) and chemokines go round. Immunol Lett. 2019;205:1-8.
13. Li H, Ooi SQ, Heng CK. The role of NF-κB in SAA-induced peroxisome proliferator-activated receptor γ activation. Atherosclerosis. 2013;227:72-8.
14. Chu PY, Tung SL, Tsai KW, Shen FP, Chan SH. Identification of the Novel Oncogenic Role of SAAL1 and Its Therapeutic Potential in Hepatocellular Carcinoma. Cancers (Basel). 2020;12.
15. Kim B, Elzinga SE, Henn RE, McGinley LM, Feldman EL. The effects of insulin and insulin-like growth factor I on amyloid precursor protein phosphorylation in in vitro and in vivo models of Alzheimer's disease. Neurobiol Dis. 2019;132:104541.
16. Deram S, Villares SM. Genetic variants influencing effectiveness of weight loss strategies. Arq Bras Endocrinol Metabol. 2009;53:129-38.
17. Zhang X, Tang QZ, Wan AY, Zhang HJ, Wei L. SAA1 gene variants and childhood obesity in China. Lipids Health Dis. 2013;12:161.
18. Ahlin S, Olsson M, Olsson B, Svensson PA, Sjöholm K. No evidence for a role of adipose tissue-derived serum amyloid a in the development of insulin resistance or obesity-related inflammation in hSAA1(+/-) transgenic mice. PLoS One. 2013;8:e72204.
19. Dogan S, Atakan N. Is serum amyloid A protein a better indicator of inflammation in severe psoriasis? Br J Dermatol. 2010;163:895-6.
20. Suzuki H, Sugaya M, Nakajima R, Oka T, Takahashi N, Nakao M, et al. Serum amyloid A levels in the blood of patients with atopic dermatitis and cutaneous T-cell lymphoma. J Dermatol. 2018;45:1440-3.
21. Lu W, Chen B, Wang C, Yang X, Zhou C. Serum amyloid A levels in acute and chronic urticaria. An Bras Dermatol. 2019;94:411-5.
22. Metwalli M, Ibraheem A. Abu bakr H, Fathia MK. Serum Amyloid A as an Inflammation Marker in Lichen Planus. J Clin Investigat Dermatol. 2021;9:3.
23. O'Reilly S, Cant R, Ciechomska M, Finnigan J, Oakley F, Hambleton S, et al. Serum amyloid A induces interleukin-6 in dermal fibroblasts via Toll-like receptor 2, interleukin-1 receptor-associated kinase 4 and nuclear factor-κB. Immunology. 2014;143:331-40.
24. Zhang Y, Zhang J, Sheng H, Li H, Wang R. Acute phase reactant serum amyloid A in inflammation and other diseases. Adv Clin Chem. 2019;90:25-80.
25. Naik-Mathuria B, Pilling D, Crawford JR, Gay AN, Smith CW, Gomer RH, et al. Serum amyloid P inhibits dermal wound

healing. Wound Repair Regen. 2008;16:266-73.
26. Yuan ZY, Zhang XX, Wu YJ, Zeng ZP, She WM, Chen SY, et al. Serum amyloid A levels in patients with liver diseases. World J Gastroenterol. 2019;25:6440-50.
27. Naylor MC, Lazar DA, Zamora IJ, Mushin OP, Yu L, Brissett AE, et al. Increased in vitro differentiation of fibrocytes from keloid patients is inhibited by serum amyloid P. Wound Repair Regen. 2012;20:277-83.

To cite this article: Neveen E. Sorour, Ahmad M. Hamed, Asmaa A. Elfallah, Mariam M. Abd Elwahed. Assessment of Serum Level of Amyloid A in Patients with Acne Vulgaris. BMFJ 2025;42(7):860-867.