DIAGNOSTIC VALUE OF SERUM MMP-9 AND GRANZYME B IN BULLOUS PEMPHIGOID: A CASE–CONTROL STUDY

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ABSTRACT

Background: Bullous pemphigoid (BP) is a common autoimmune blistering disease in the elderly. Proteases like matrix metalloproteinase-9 (MMP-9) and granzyme B contribute to dermal–epidermal separation, but their circulating levels and clinical relevance remain unclear. **Objectives:** To compare serum levels of MMP-9 and granzyme B in BP patients versus healthy controls, and evaluate their correlations with disease severity and clinical features. **Methods:** This single-center case–control study in Hanoi, Vietnam (June 2024–June 2025) included 17 newly diagnosed BP patients and 17 age-matched healthy controls. Serum MMP-9 and granzyme B were measured by ELISA and normalized to total protein. Clinical parameters including BPDAI scores were recorded. Associations and diagnostic value were assessed using correlation and ROC analysis. **Results:** Serum MMP-9 levels were significantly lower in BP than controls (median 375.2 vs. 728.1 pg/µg protein; p = 0.0376), while granzyme B levels were higher but not statistically significant (p = 0.454). MMP-9 positively correlated with BPDAI (r = 0.47, p = 0.03), unlike granzyme B. MMP-9 and granzyme B showed moderate correlation (r = 0.66, p = 0.002). BP patients with diabetes had higher levels of both markers. Combining MMP-9 and granzyme B improved diagnostic accuracy (AUC = 0.844). **Conclusions:** Circulating MMP-9 levels are reduced in BP patients but correlate with disease severity. Granzyme B alone has limited value. Combined measurement enhances diagnostic performance and may aid in disease monitoring.

Keywords: *bullous pemphigoid; MMP-9; granzyme B; serum biomarkers; proteases.*

I. INTRODUCTION

Bullous pemphigoid (BP) is the most common autoimmune subepidermal blistering disease in the elderly (7), marked by autoantibodies against BP180 and BP230 at the dermal–epidermal junction (7). These autoantibodies trigger complement activation, immune cell infiltration, and release of proteolytic enzymes that disrupt basement membrane integrity (7). Neutrophils and eosinophils are key players, releasing enzymes like neutrophil elastase and MMPs (notably MMP-2 and MMP-9), as well as granzyme B (1,7). These proteases damage adhesion molecules (e.g., collagen XVII, integrin α6β4) and amplify inflammation (1).

MMP-9 (gelatinase B) degrades type IV collagen and is abundant in BP lesions (5). Secreted as an inactive proenzyme, it requires activation by proteases like chymase or plasmin (4). Active MMP-9 can cleave BP180 and potentiate neutrophil elastase (1,4), promoting blister formation. In BP models, MMP-9 deficiency reduces blistering, while its reintroduction restores disease (4). However, most research has focused on lesional MMP-9, with limited data on its circulating levels in BP patients (5).

Granzyme B, a serine protease from $CD8^+$ T and NK cells, also contributes to BP pathogenesis. Beyond inducing apoptosis, it cleaves structural proteins (collagen VII, XVII, integrin α6β4) (3) and activates cytokines like IL-1α (8). It is found in BP lesions and blister fluid, and granzyme B inhibition reduces blistering in animal models (3). Yet, few studies have quantified circulating granzyme B in BP (2). This study aimed to assess serum MMP-9 and granzyme B levels in BP patients vs. healthy controls, and evaluate their clinical significance.

II. MATERIALS AND METHODS

Study design and population

We conducted a single-center case–control study at the National Hospital of Dermatology and Venereology, Hanoi (June 2024–June 2025), enrolling 17 newly diagnosed BP patients and 17 healthy controls. BP diagnosis was based on clinical features (pruritic, tense blisters with negative Nikolsky sign), histopathology (subepidermal bulla), and direct immunofluorescence (linear IgG and C3 at the basement membrane). Patients on immunosuppressives within 4 weeks were excluded. Controls had no autoimmune/ dermatologic disease or recent immunosuppressive use.

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Date of receipt: 13.1.2026
Date of scientific judgment: 3.3.2026
Reviewed date: 14.4.2026

Clinical data collection

Demographic and clinical data-including age, sex, disease duration, comorbidities, and treatments-were recorded. BP severity was assessed using BPDAI, with disease categorized as mild (BPDAI < 19), moderate (19–56), or severe (> 56) (6). Matched data were collected for controls.

Serum sampling and protease quantification

Peripheral blood (2 mL) was collected from each participant into a clot-activator tube. Samples were allowed to clot (2 hours at room temperature or overnight at 4 °C) and then centrifuged at 1,000 × g for 15 minutes. The serum (approximately 0.5–0.8 mL) was aliquoted and stored at –80 °C until analysis.

Serum samples were analyzed for MMP-9 and granzyme B levels using enzyme-linked immunosorbent assay (ELISA). MMP-9 was measured with a human MMP-9 ELISA kit following the manufacturer's instructions (absorbance read at 450 nm on an Agilent BioTek ELx808 microplate reader; BioTek Instruments, VT, USA). Granzyme B was measured with a human Granzyme B ELISA kit (Cusabio, Wuhan, China; CSB-E08718h) on the same instrument (450 nm). To normalize for sample protein content, total serum protein was quantified by BCA assay (Abcam, Cambridge, UK; ab102536) with absorbance at 562 nm (Allsheng AMR-100 microplate reader, Hangzhou, China). MMP-9 and granzyme B concentrations were normalized and expressed as picograms per microgram of total protein (pg/μg). All BP patient and control samples were assayed in parallel under identical conditions to ensure comparability.

Statistical analysis

Data distribution was assessed by the Shapiro–Wilk test. Continuous variables are presented as mean ± standard deviation (SD) if normally distributed, or median (interquartile range, IQR) if skewed. Between-group comparisons were made using the Student's t-test for normally distributed data or the Mann–Whitney U test for non-normal data. Categorical variables were compared by the chi-square test or Fisher's exact test. Correlation and linear regression analyses were performed to examine associations between serum biomarker levels (MMP-9, granzyme B) and clinical or laboratory parameters (e.g., BPDAI score, blood cell counts, disease duration). Variables with no variability (present in 0% or 100% of subjects, such as methotrexate use or presence of pruritus) were excluded from regression analyses. The diagnostic performance of MMP-9 and granzyme B was evaluated using ROC curve analysis. ROC curves and area under the curve (AUC) values were generated for each biomarker individually and for a combined logistic regression model including both markers. Optimal cutoff values were determined by Youden's index, and the corresponding sensitivity and specificity were calculated. A two-tailed $p < 0.05$ was considered statistically significant. All statistical analyses were performed using GraphPad Prism (v10.1) and R (v4.3).

Ethical statement

The study was approved by Hanoi Medical University's IRB (HMUIRB#1346-GCN), with written informed consent from all participants, and adhered to STROBE (Strengthening the Reporting of Observational Studies in Epidemiology) guidelines.

III. RESULTS

Baseline characteristics

A total of 17 BP patients (8 males, 9 females) and 17 healthy controls (5 males, 12 females) were included. The BP patients were older on average than controls (mean age 69.8 ± 15.3 years vs. 51.6 ± 4.8 years; $p < 0.001$). There was no significant difference in sex distribution between the groups ($p = 0.76$). Among BP patients, common comorbidities included hypertension (23.5%), diabetes (11.8%), and prior stroke (11.8%). Before admission, 64.7% used topical corticosteroids, 47.1% systemic corticosteroids, and 17.6% doxycycline. No patients received methotrexate or other immunosuppressants. Clinically, 88.2% reported pruritus, 70.6% had urticarial lesions, and 82.4% developed bullae. Lesions frequently involved the trunk (82.4%) and limbs (76.5%), with mucosal involvement in only 17.6%. Disease severity varied: 9 mild, 5 moderate, and 3 severe (BPDAI medians: 9.5, 39, 68). Key baseline characteristics of the patients and controls are summarized in **Table 1**.

Table 1. Baseline characteristics of BP patients and healthy controls.

Characteristic	BP patients (n = 17)	Healthy controls (n = 17)
Age (years, mean ± SD)	69.8 ± 15.3	51.6 ± 4.8
Sex, No. (%)		
- Male	10 (58.8)	5 (29.4)
- Female	7 (41.2)	12 (70.6)
Concomitant medical conditions, No. (%)		
- Hypertension	4 (23.5)	NA
- Diabetes	2 (11.8)	NA
- Stroke	2 (11.8)	NA
Current medications, No. (%)		
- Topical corticosteroids	11 (64.7)	NA
- Systemic corticosteroids	8 (47.1)	NA
- Doxycycline	3 (17.6)	NA
- Methotrexate	0	NA
Clinical manifestations in BP, No. (%)		
- Pruritus	15 (88.2)	NA
- Truncal lesions	14 (82.4)	NA
- Vesicles/bullae	14 (82.4)	NA
- Extremity lesions	13 (76.5)	NA
- Urticarial papules/wheals	12 (70.6)	NA
- Mucosal erosions/bullae	3 (17.6)	NA
BPDAI, median [IQR]		
- Mild (<19)	9.5 [5 - 14]	NA
- Moderate (19-56)	39 [22 - 49]	NA
- Severe (>56)	68 [59 - 75.3]	NA

Abbreviations: BP, bullous pemphigoid; BPDAI, bullous pemphigoid disease area index; NA, Not Applicable.

Serum levels of MMP-9 and Granzyme B

As shown in **Figure 1**, serum MMP-9 levels in BP patients were significantly lower than in healthy controls (median 375.2 vs. 728.1 pg/µg, p = 0.0376). While both groups had similar upper ranges, the BP group showed a left-skewed distribution with most patients presenting low MMP-9 levels. In contrast, serum granzyme B levels showed a non-significant trend toward being higher in BP patients (median 0.00933 vs. 0.00658 pg/µg, p = 0.47), but with much greater variability. A small subset of BP patients exhibited highly elevated granzyme B, whereas most had levels similar to controls.

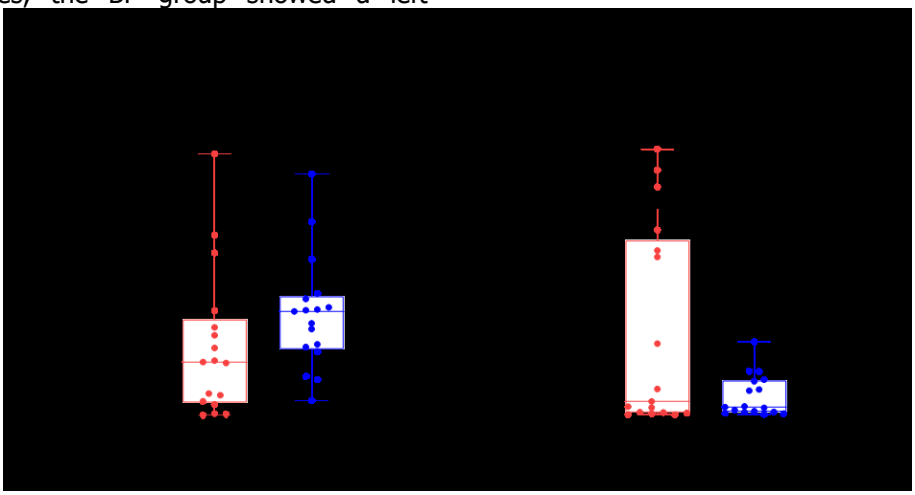
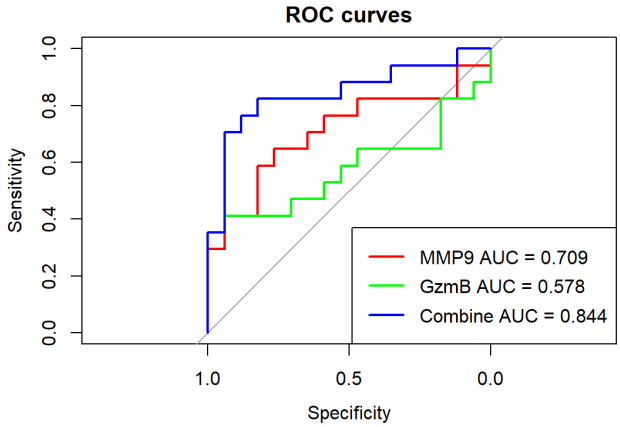


Figure 1. Normalized serum concentrations of MMP-9 and granzyme B in bullous pemphigoid patients and healthy donors.

Abbreviations: BP, bullous pemphigoid; MMP-9, Matrix Metalloproteinase-9.

Serum levels of MMP-9 (A) and granzyme B (B) are shown as box-and-whisker plots (boxes indicate interquartile range; horizontal line indicates median; whiskers show minimum and maximum; individual data points are plotted). p = 0.0376; ns = not significant (p > 0.05).

Diagnostic performance of MMP-9 and granzyme B



ROC analysis (**Figure 2**) showed that serum MMP-9 moderately distinguished BP patients from controls (AUC = 0.709; 95% CI: 0.53–0.89; p = 0.037), with 64.7% sensitivity and 76.5% specificity at a cutoff of 477.1 pg/µg. Granzyme B alone had limited diagnostic value (AUC = 0.578; p = 0.389), showing high specificity (94.1%) but low sensitivity (41.2%). Combining both markers significantly improved diagnostic performance (AUC = 0.844), achieving 82.4% sensitivity and specificity.

	MMP-9	Gran-zyme B	Combine
AUC	0.709	0.578	0.844
p-value	***0.037****	0.389	***0.0006****
95% CI	0.53 - 0.89	0.38 - 0.79	0.70 - 0.98
Thres-hold	477.136	0.03	0.439
Sensi-tivity	0.647	0.412	0.823
Speci-ficity	0.765	0.941	0.823
Youden's Index	1.412	1.353	1.646

Figure 2. Differential performance of MMP-9, Granzyme B, and their combination in BP.

Abbreviations: ROC, receiver operating characteristic; BP, bullous pemphigoid; MMP9, Matrix Metalloproteinase-9; GzmB, granzyme B; AUC, area under the curve.

ROC curves are shown for serum MMP-9 (red curve; AUC = 0.709; optimal cutoff 477.1 pg/µg), serum granzyme B (green curve; AUC = 0.578; optimal cutoff 0.030 pg/µg), and a logistic model combining MMP-9 and granzyme B (blue curve; AUC = 0.844; optimal cutoff probability = 0.439). The gray diagonal line represents random chance (AUC = 0.5). The table on the right summarizes the AUC, p-value, 95% confident interval, optimal cutoff, sensitivity, specificity, and Youden's index for each case.

Factors associated with serum levels of MMP-9/Granzyme B in BP patients

Table 2 and **Table 3** present correlations between clinical variables and biomarkers. Serum MMP-9 and granzyme B showed a moderate positive correlation (r = 0.66, p = 0.002), suggesting co-elevation during active inflammation. MMP-9 also correlated with disease severity (BPDAI; r = 0.47, p = 0.03), indicating its potential as a marker of disease activity. Although not specific to BP, elevated MMP-9 levels were associated with more severe disease.

BP patients with type 2 diabetes (n = 2) had higher levels of both MMP-9 (r = 0.59, p = 0.01) and granzyme B (r = 0.50, p = 0.04), though the sample was small. Those with prior topical corticosteroid use had significantly lower MMP-9 (r = –0.49, p = 0.04), likely due to systemic anti-inflammatory effects. Other variables-including age at onset, disease duration, blood counts, CRP, and total IgE-were not significantly associated with MMP-9 (all p > 0.05).

Although granzyme B moderately correlated with MMP-9 (r = 0.66), it showed no association with disease severity (BPDAI; r = 0.04, p = 0.45), suggesting limited value in reflecting clinical activity-possibly due to low serum concentrations or rapid clearance. Granzyme B tended to be higher in BP patients with diabetes (r = 0.50, p = 0.04), though variability was high. Treatment (systemic corticosteroids, doxycycline) had no significant effect on granzyme B levels (all p > 0.1).

Doxycycline use was associated with lower BPDAI scores (r = –0.44, p = 0.03), although this may reflect prescription patterns in less

severe cases. Diabetic patients also showed a trend toward higher BPDAI (r = 0.31, p = 0.05), supporting a link between metabolic comorbidity and disease severity. Other variables-including age, disease duration, blood counts, and lesion distribution-showed no significant association with MMP-9, granzyme B, or BPDAI (all p > 0.05). Overall, inflammation intensity appeared more influenced by disease severity and comorbidities than by baseline characteristics.

Table 2. Correlation Between Serum MMP-9, Granzyme B, and BPDAI Score With Clinical Parameters in Bullous Pemphigoid Patients.

Clinical feature	Sample size	IQR	MMP9 (pg/ug protein)		Granzym B (pg/ug protein)		BPDAI score	
			r	P	r	P	r	P
MMP9 (pg/ug protein)	17/17	[91.02-674.1]	1.00	NA	0.66	***0.002****	0.47	***0.03****
Granzym B (pg/ug protein)	17/17	[0.004-0.08]	0.66	***0.002****	1.00	NA	0.04	0.45
BPDAI score	17/17	[36.5-69]	0.47	***0.03****	0.04	0.45	1.00	NA
Age of onset	17/17	[62.5-81.5]	-0.21	0.21	-0.06	0.41	0.11	0.33
Time of onset (month)	15/17	[2-9]	0.05	0.43	-0.04	0.44	-0.13	0.33
Hemoglobin (g/L)	14/17	[123.3-145.3]	-0.09	0.38	0.06	0.42	-0.18	0.26
Leucocyte (g/L)	14/17	[8.325-13.5]	0.41	0.08	0.11	0.35	-0.04	0.44
Neutrophil (g/L)	14/17	[5.58-9.21]	0.29	0.16	0.06	0.42	0.23	0.21
Eosinophil (g/L)	13/17	[0.16-0.81]	0.16	0.30	-0.42	0.08	0.03	0.47
Weight (kg)	11/17	[50-60]	0.44	0.09	0.35	0.14	-0.18	0.29
Height (cm)	8/17	[152.5-168.8]	0.10	0.42	-0.33	0.21	-0.07	0.44
BMI	8/17	[19.51-23.99]	0.33	0.21	0.62	0.06	0.33	0.21
CRP (mg/L)	8/17	[1.59-55.55]	-0.21	0.31	-0.40	0.16	-0.02	0.49
Pulse (bpm)	6/17	[76-85]	0.62	0.11	0.26	0.31	-0.26	0.31
Temp (°C)	6/17	[36.65-37]	0.15	0.38	0.15	0.38	0.37	0.23
Highest arterial tension (mmHg)	6/17	[107.5-130]	-0.18	0.38	0.09	0.47	0.53	0.16
Lowest arterial tension (mmHg)	6/17	[68.75-80]	-0.68	0.07	-0.22	0.33	0.31	0.28
Breathing rate (bpm)	6/17	[16.75-19.25]	-0.03	0.49	-0.29	0.29	-0.44	0.21

Abbreviations: BMI, body mass index; BPDAI, bullous pemphigoid disease activity index

Values represent linear regression coefficients (r), and corresponding p-values for each correlation. *p < 0.05 was considered statistically significant.

Table 3. Association of Serum MMP-9, Granzyme B, and BPDAI Score With Immunopathological and Treatment Characteristics in Bullous Pemphigoid.

Characteristic	Number (percentage %)	MMP9 (pg/ug protein)		Granzym B - (pg/ug protein)		BPDAI score	
		r	*p*	*r*	*p*	*r*	*p*
Gender	10 Male / 7 Female	0.27	0.16	-0.12	0.33	0.25	0.26
Hypertension	4/15 (26.67%)	0.07	0.43	-0.14	0.33	0.22	0.41
Diabetes	2/15 (13.33%)	0.59	***0.01****	0.50	***0.04****	0.31	***0.05****
Stroke	2/15 (13.33%)	0.14	0.34	0.41	0.09	0.31	0.12
Topical corticosteroids	11/15 (73.33%)	-0.49	***0.04****	-0.21	0.24	0.04	0.39
Systemic corticosteroids	8/15 (53.33%)	-0.25	0.20	-0.03	0.48	-0.05	0.42
Doxycycline	3/15 (20%)	-0.08	0.42	0.31	0.15	-0.44	***0.03****
Truncal lesions	14/15 (93.33%)	0.19	0.33	-0.19	0.33	-0.21	0.53
Vesicles/bullae	14/15 (93.33%)	0.00	0.53	-0.25	0.27	0.25	0.27
Extremity lesions	13/15 (86.67%)	-0.05	0.47	-0.14	0.34	0.52	0.06
Urticarial papules/wheals	12/15 (80%)	-0.08	0.42	0.12	0.37	0.02	0.41
Mucosal erosions/bullae	3/15 (20%)	0.12	0.37	0.12	0.37	-0.31	0.11

Abbreviations: BPDAI, bullous pemphigoid disease activity index

Values represent linear regression coefficients (r), and corresponding p-values for each association. *p < 0.05 was considered statistically significant.

IV. DISCUSSION

Our study is the first in Vietnam to quantify serum MMP-9 and granzyme B in BP patients versus healthy controls, providing novel but partly consistent insights into BP pathogenesis.

We found serum MMP-9 levels significantly lower in BP patients than controls, despite MMP-9 being elevated in BP lesional skin (5). This likely reflects local rather than systemic production, as blister fluid contains much higher MMP-9 than blood (5). Over 60% of BP patients had used topical corticosteroids before sampling, possibly reducing serum MMP-9. Additionally, our controls were younger (mean 51.6 vs. 69.8 years), and MMP-9 tends to increase with age (8). Individual variation also contributed: some healthy controls had high MMP-9, while some BP patients had extremely low levels. Consequently, MMP-9 showed only modest diagnostic accuracy (AUC ~0.71).

Nonetheless, serum MMP-9 positively correlated with BPDAI scores, suggesting that more severe disease may cause increased MMP-9 spillover into the bloodstream. Prior studies also showed higher MMP-9 in active disease versus remission (2), indicating that while not diagnostic, MMP-9 may reflect disease activity. Although serum MMP-9 levels were lower in BP patients than in controls, the positive correlation with BPDAI can still be explained. Pre-sampling use of topical corticosteroids in most patients likely suppressed circulating MMP-9, reducing overall group values. In contrast, several healthy controls-who were younger-showed naturally higher baseline MMP-9, raising the control median. Moreover, MMP-9 in BP is produced mainly at lesional sites, and serum reflects only minimal spillover. Thus, within the BP group, patients with more active disease still show relatively higher serum MMP-9, resulting in a positive correlation despite lower absolute levels compared with controls.

Serum MMP-9 and granzyme B levels were moderately correlated (r ~ 0.66), indicating overlap in innate and adaptive immune activation, possibly via cytokine pathways like IL-17/IL-23(2,8).

Serum granzyme B levels did not differ significantly between BP patients and controls, which is consistent with its predominantly localized activity in lesional skin and its rapid inactivation in circulation. Previous studies have similarly reported higher granzyme B concentrations in blister fluid rather than serum (3), suggesting that circulating levels may only partially reflect its biological role in BP. While granzyme B alone showed limited diagnostic value, the combined model of MMP-9 and granzyme B yielded a higher AUC (0.844). This improvement should be interpreted cautiously, as the sample size was small, but it indicates that integrating multiple inflammatory markers may enhance diagnostic performance. Larger studies are needed to confirm this potential.

Interestingly, BP patients with type 2 diabetes (2 of 17) had higher BPDAI scores and higher MMP-9 and granzyme B levels, aligning with chronic low-grade inflammation in diabetes (8). This systemic inflammation may worsen BP or slow healing. Prior studies also suggest that BP patients with metabolic comorbidities respond less well to therapy.

We found that corticosteroid use was associated with lower serum MMP-9, likely due to anti-inflammatory suppression (2). This underscores the need to consider prior treatment when interpreting biomarker levels. Doxycycline use was linked to higher BPDAI scores, but had no clear impact on biomarker levels (only 3 patients received it).

Our main limitation was small sample size (17 BP patients), limiting power, especially for correlation and ROC analyses. Some trends (p ~ 0.05–0.1) might reach significance in larger cohorts. Additionally, our single-center design and unmatched age between groups may affect generalizability. However, we found no significant age correlation with MMP-9 or granzyme B.

We did not measure MMP-9 or granzyme B in blister fluid due to technical constraints. Prior studies show MMP-9 levels are much higher in blisters than in serum (5), and granzyme B likely follows this pattern (3). Future work will compare local vs. systemic levels and increase sample size.

Despite limitations, our study offers the first Vietnamese data on serum MMP-9 and granzyme

B in BP. MMP-9 may reflect disease activity, while circulating granzyme B is less informative. We also observed a possible link between metabolic disease and BP inflammation. These findings may inform future research on BP biomarkers and pathogenesis.

V. CONCLUSION

Serum MMP-9 was significantly lower in BP patients, while granzyme B showed a non-significant increase. Only MMP-9 correlated with disease severity (BPDAI). The two markers were positively correlated and tended to rise in diabetic BP patients; MMP-9 was lower in those on topical corticosteroids. MMP-9 showed moderate diagnostic utility (AUC ~0.71), granzyme B was poor (~0.58), but their combination improved accuracy (~0.84). MMP-9 may help monitor BP activity, pending further validation.

REFERENCES

1. **Cirillo N**, Prime SS. *A Scoping Review of the Role of Metalloproteinases in the Pathogenesis of Autoimmune Pemphigus and Pemphigoid*. Biomolecules. 2021;11(10):1506. DOI: 10.3390/biom11101506.
2. **Gleave A**, Granville DJ. *Granzyme B in Autoimmune Skin Disease*. Biomolecules. 2023;13(2):388. DOI: 10.3390/biom13020388.
3. **Hiroyasu S**, Zeglinski MR, Zhao H, *et al. Granzyme B inhibition reduces disease severity in autoimmune blistering diseases*. Nat Commun. 2021;12(1):302. DOI: 10.1038/s41467-020-20604-3.
4. **Liu Z**, Li N, Diaz LA, *et al. Synergy between a plasminogen cascade and MMP-9 in autoimmune disease*. J Clin Invest. 2005;115(4):879–87. DOI: 10.1172/JCI23977.
5. **Niimi Y**, Pawankar R, Kawana S. *Increased expression of MMP-2, MMP-9 and MMP-13 in lesional skin of bullous pemphigoid*. Int Arch Allergy Immunol. 2006;139(2):104–13. DOI: 10.1159/000090385.
6. **Masmoudi W**, Vaillant M, Vassileva S, et al. *International validation of the Bullous Pemphigoid Disease Area Index severity score and calculation of cut-off values for defining mild, moderate and severe types of bullous pemphigoid*. Br J Dermatol. Jun 2021;184(6):1106-1112.
7. **Schmidt E**, Zillikens D. *Pemphigoid diseases*. Lancet. 2013;381(9863):320–32. DOI: 10.1016/S0140-6736(12)61140-4.
8. **Velotti F**, Barchetta I, Cimini FA, Cavallo MG. *Granzyme B in Inflammatory Diseases: Apoptosis, Inflammation, Extracellular Matrix Remodeling, Epithelial-to-Mesenchymal Transition and Fibrosis*. Front Immunol. 2020;11:587581. DOI: 10.3389/fimmu.2020.587581