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Research Article

Evaluation of Apoptotic Pathways in Psoriatic Skin Using Immunohistochemical Expression of p53 and Bcl-2

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Abstract

Background: Psoriasis is a chronic, immune-mediated inflammatory skin disease characterized by hyperproliferation and incomplete differentiation of keratinocytes. Aberrant apoptosis has been proposed as one of the key pathogenetic mechanisms contributing to epidermal hyperplasia. Among the regulatory molecules, Bcl-2 and p53 play crucial but contrasting roles in cell survival and programmed death. ***Aim***: To evaluate apoptotic changes in psoriatic skin by analyzing the immunohistochemical expression patterns of Bcl-2 and p53 and to interpret their combined role in regulating epidermal apoptosis and inflammatory persistence. ***Materials and Methods:*** This prospective study included 50 biopsy-proven cases of psoriasis vulgaris from the Department of Pathology, Hind Institute of Medical Sciences, Barabanki. Formalin-fixed paraffin-embedded sections were stained using monoclonal antibodies against Bcl-2 and p53 (Dako, 1:200 dilution). The proportion and localization of immunopositive cells were recorded in epidermal, basal, and lymphocytic compartments and correlated with histopathological findings and clinical variables. Statistical analysis was performed using SPSS version 13.0, applying Chi-square and Pearson correlation tests. ***Results***: The mean age of patients was concentrated between 31–40 years (28%), with a male predominance (64%). p53 positivity was observed in epidermal hyperplasia (68%) and lymphocytes (66%), while Bcl-2 expression was strongest in lymphocytes (72%) and epidermal cells (60%). Overexpression (≥26%) was noted in 28% for p53 and 24% for Bcl-2. No significant correlation was found between the two markers ($r = -0.02$; $p = 0.88$). p53 expression correlated weakly with epidermal hyperplasia, whereas Bcl-2 showed limited association with disease duration. ***Conclusion***: The findings suggest that p53 plays a more prominent role than Bcl-2 in the apoptotic regulation of psoriatic keratinocytes. The concurrent yet independent activation of both pro- and anti-apoptotic mechanisms highlights a dynamic imbalance between cellular proliferation and programmed death. Combined evaluation of Bcl-2 and p53 provides valuable insight into the molecular basis of psoriasis and supports the concept of apoptosis resistance as a central event in its pathogenesis.

Keywords: Psoriasis, Apoptosis, Bcl-2, p53, Immunohistochemistry, Epidermal hyperplasia.

Introduction:

Psoriasis is a chronic, relapsing inflammatory skin disorder with a recognized immune-mediated and genetic basis. It affects approximately 2–3% of the global population, manifesting as well-demarcated erythematous plaques with adherent silvery scales and variable extents of induration and recurrence [1]. The lesions typically involve extensor surfaces and the scalp, and the disease course shows fluctuations in severity, duration, and remission periods.

Histopathologically, psoriatic skin exhibits acanthosis, parakeratosis, hypogranulosis, elongation of rete ridges, dilated dermal capillaries, and dense mononuclear infiltration [2]. While the precise trigger remains uncertain, environmental factors such as infections, stress, drugs, and alcohol are known to exacerbate disease in genetically predisposed individuals [3]. A central role of activated T-lymphocytes and cytokine-mediated inflammation has been firmly established [4]. The pathophysiology involves epidermal hyperproliferation, enhanced Th1/Th17 cytokine activity, and angiogenesis, leading to accelerated epidermal turnover [5].

Psoriatic keratinocytes demonstrate an aberrant resistance to apoptosis, contributing to sustained hyperplasia and chronic inflammation [6]. Apoptosis, described by Kerr et al., is a programmed mechanism of cell death critical for maintaining tissue homeostasis [7,8]. In normal epidermis, it regulates keratinocyte proliferation and stratum corneum formation [9]; impaired apoptosis disrupts this equilibrium, promoting uncontrolled epidermal growth.

The Bcl-2 family of proteins governs cell survival by modulating the balance between pro- and anti-apoptotic signals, whereas p53, a nuclear phosphoprotein, functions as a transcriptional regulator promoting apoptosis in response to cellular stress [10,11]. Previous studies on psoriasis have yielded conflicting results—some report increased Bcl-2 expression, while others note minimal or absent expression, and p53 immunoreactivity remains variably reported in psoriatic and other inflammatory dermatoses [10,11,12].

Given these inconsistencies, evaluating both markers concurrently offers insight into the interplay between keratinocyte proliferation and apoptosis resistance in psoriasis.

Aim and Objective

To assess the immunohistochemical expression patterns of Bcl-2 and p53 in psoriatic skin and to interpret their combined role in regulating epidermal apoptosis and inflammatory persistence

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Study Design and Setting

This prospective, cross-sectional study was conducted in the Department of Pathology, Hind Institute of Medical Sciences, Safedabad, Barabanki, Uttar Pradesh, over a period of one year (2016–2017). A total of 50 paraffin-embedded skin biopsy specimens from patients clinically and histologically diagnosed with psoriasis vulgaris were included. All procedures conformed to the principles of the Declaration of Helsinki, and informed consent was obtained from each participant prior to biopsy collection. Ethical approval was obtained from the institutional ethics committee.

Study Population

The study comprised patients of either sex and any age group who presented with clinically diagnosed psoriasis vulgaris. Diagnosis was confirmed histopathologically. To eliminate drug-induced variation, none of the patients had received systemic or topical therapy for at least one month before biopsy.

Inclusion criteria: all patients with clinically and histologically confirmed psoriasis vulgaris.

Exclusion criteria: cases with other clinical forms of psoriasis (such as psoriatic arthritis or isolated nail psoriasis) or with overlapping dermatoses and secondary infections.

Clinical and Histopathological Assessment

Detailed clinical information including age, gender, family history, socioeconomic background, disease duration, and distribution of lesions was recorded in a structured proforma. A complete general and dermatological examination was performed for each patient.

Punch biopsies were taken from representative psoriatic plaques to include a margin of perilesional skin. Specimens were fixed in 10% neutral buffered formalin, processed routinely, and embedded in paraffin. 4-µm sections were cut and stained with hematoxylin and eosin (H&E) for histopathological evaluation. Microscopic examination focused on characteristic features such as epidermal hyperplasia, parakeratosis, hypogranulosis, suprapapillary thinning, dilated capillaries, and mononuclear inflammatory infiltrate. For correlation with IHC findings, epidermal hyperplasia was selected as the representative histologic feature of psoriatic activity.

Immunohistochemical Procedure

Serial 4-µm-thick sections were prepared on poly-L-lysine-coated slides. Deparaffinization was carried out in xylene, followed by rehydration through graded alcohols. Antigen retrieval was achieved by immersing sections in citrate buffer (pH 6.0) and heating in a microwave oven for 15 minutes. Endogenous peroxidase activity was quenched using 3% hydrogen peroxide for 10 minutes.

Sections were incubated overnight at 4 °C with monoclonal mouse antibodies against p53 and Bcl-2 (Dako, Denmark) at a 1:200 dilution. Detection was performed using the standard peroxidase–antiperoxidase technique and visualized with diaminobenzidine (DAB) as chromogen. Counterstaining was done with hematoxylin.

For each slide, 500 keratinocytes were examined in three high-power (×400) fields showing maximal staining intensity, and the mean percentage of positive cells was calculated. Staining localization was categorized as epidermal, basal cell, or lymphocytic. Basal cell positivity was assessed separately to distinguish proliferative activity from suprabasal differentiation. Staining intensity and proportion of positive cells were recorded semi-quantitatively and expressed as low expression (0–25%) and overexpression (26–100%).

Statistical Analysis: Data were analyzed using SPSS version 13.0 (Statistical Package for the Social Sciences, Lead Technologies Inc., USA). Descriptive statistics were expressed as mean ± standard deviation for continuous variables and frequency with percentage for categorical variables. The Chi-square test was applied to assess associations between marker expression and clinical parameters such as age, gender, and disease duration. The Pearson correlation coefficient (r) was used to evaluate the relationship between p53 and Bcl-2 expression. A p-value < 0.05 was considered statistically significant

Results

Table 1. Demographic Summary of Psoriasis Patients (n = 50)

Variable	Category	n	%
Age (years)	10–20	8	16.0
	21–30	13	26.0
	31–40	14	28.0
	>40	15	30.0
Gender	Male	32	64.0
	Female	18	36.0
Predominant Site	Extensor	27	54.0
	Others	23	46.0
Duration of Disease (months)	≤12	23	46.0
	>12	27	54.0

Most patients were young to middle-aged (31–40 years: 28%) with a male predominance (64%). Extensor surfaces were most frequently affected (54%), and slightly more than half (54%) had disease duration exceeding one year, representing a balanced distribution of acute and chronic lesions suitable for IHC assessment.

Figure 1. Expression Profile of p53 and Bcl-2 in Psoriatic Lesions (n = 50)

Low-intensity expression dominated for both markers. p53 overexpression (≥26%) was seen in 14 patients (28%), while Bcl-2 overexpression occurred in 12 patients (24%), reflecting limited but distinct activation of apoptotic and anti-apoptotic mechanisms.

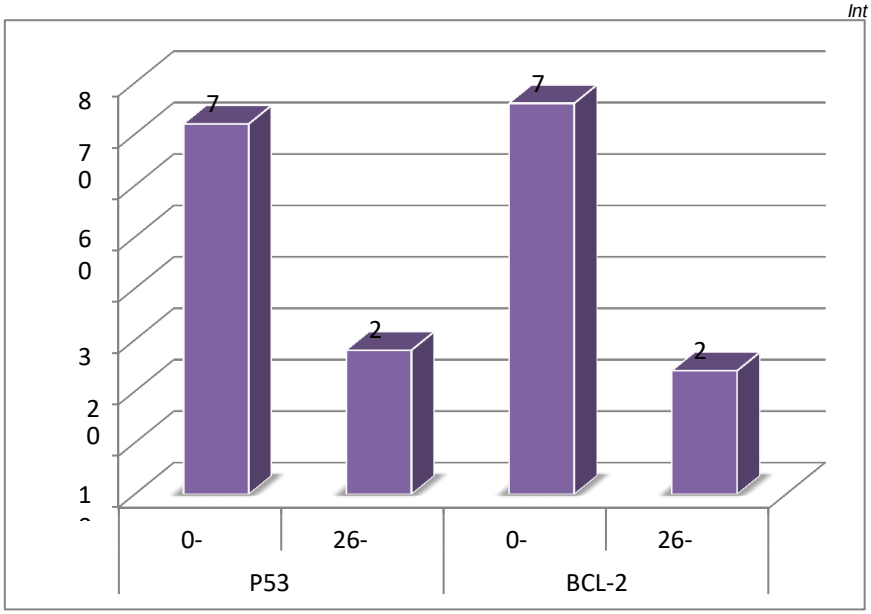

Table 3. Immunostaining Pattern of p53 and Bcl-2 in Lesional Tissue

Tissue Component	p53 Positive n (%)	Bcl-2 Positive n (%)
Basal cells	20 (40.0)	26 (52.0)
Mononuclear cells	28 (56.0)	12 (24.0)
Epidermal cells (diffuse)	32 (64.0)	30 (60.0)
Lymphocytes	33 (66.0)	36 (72.0)
Epidermal hyperplasia	34 (68.0)	29 (58.0)

p53 positivity was highest in epidermal hyperplasia (68%) and lymphocytes (66%), indicating proliferative stress in keratinocytes and immune activation. Bcl-2 was most expressed in lymphocytes (72%) and epidermal cells (60%), highlighting its role in prolonging inflammatory cell survival and protecting hyperplastic epidermis from apoptosis.

Figue 2. Correlation Between p53 and Bcl-2 Expression

No significant correlation ($r = -0.02$; $p = 0.88$) was observed between p53 and Bcl-2 expression, implying that apoptotic activation and anti-apoptotic inhibition act through independent regulatory pathways within psoriatic lesions.

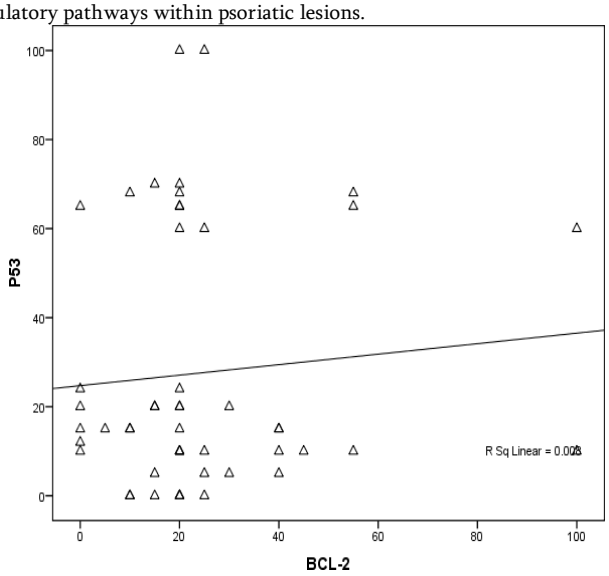

Fig.2 shows the correlation of p53 and BCL-2 expressions. There was poor the correlation of p53 and BCL-2 expression.

Table 5. Association of Marker Expression with Clinical Parameters

Parameter	Category	p53 ≥ 26% n (%)	Bcl-2 ≥ 26% n (%)	p-value
Age (years)	≤ 30	4 (19.0)	6 (28.6)	0.16
	31–50	8 (32.0)	4 (16.0)	
	> 50	2 (40.0)	2 (40.0)	
Gender	Male	9 (28.1)	8 (25.0)	0.82
	Female	5 (27.8)	4 (22.2)	
Duration of Disease	< 6 months	4 (25.0)	6 (37.5)	0.24
	> 24 months	3 (18.8)	3 (18.8)	

Neither marker showed a statistically significant relationship with demographic or duration variables ($p > 0.05$). However, p53 expression increased with age (from 19% in ≤30 years to 40% in >50 years), while Bcl-2 expression was relatively higher in early (<6 months) disease (37.5%), suggesting that p53 may be linked to chronic proliferative activity, whereas Bcl-2 predominates during early inflammatory phases.

Discussion

The present study was conducted in the Department of Pathology, Hind Institute of Medical Sciences, Barabanki, with the objective of evaluating apoptotic changes in psoriatic skin using immunohistochemical (IHC) expression of Bcl-2 and p53. Fifty biopsy-proven psoriasis vulgaris patients were included. The majority of cases were aged 31–40 years (28%), followed by 21–30 years (26%), 41–50 years (20%), 10–20 years (16%), and > 50 years (10%). Males constituted 64% of the cohort, confirming the usual male predominance reported in earlier series.

Typical histopathological features were consistently observed. Suprapapillary thinning and hypogranulosis were present in 92% of patients, dilated vascular channels in 90%, and hyperkeratosis and spongiform pustules of Kogoj in 78%. These findings are comparable to those of Younas and Haque (2004) [14], who reported hyperkeratosis, elongated rete ridges, and acanthosis in 100% of psoriatic lesions, and to Karumbaiah et al (2014) [15], who observed hyperkeratosis in 77%, parakeratosis in 73%, acanthosis in 86%, and suprapapillary thinning in 41% of cases. Similarly, Gordon and Johnson (1967) [16] described parakeratosis, Munro's microabscesses, vascular dilation, and basal cell degeneration as key microscopic hallmarks.

These results reaffirm that the present series represents the classical histologic spectrum of psoriasis.

Apoptosis, a form of programmed cell death characterized by cell shrinkage, nuclear condensation, and fragmentation (Moorchung et al, 2015) [16], is a critical regulatory mechanism in normal epidermis. Psoriasis is known for keratinocyte hyperproliferation with impaired apoptosis (Molès et al, 1993) [17]. In the present study, immunostaining demonstrated p53 positivity in 68% of cases within epidermal hyperplasia and 66% in lymphocytes, whereas Bcl-2 positivity was highest in lymphocytes (72%) and epidermal cells (60%). These results highlight parallel activation of apoptotic (p53) and anti-apoptotic (Bcl-2) pathways within the psoriatic epidermis.

Reports on Bcl-2 family protein expression in psoriasis have been controversial. Some investigators noted overexpression of Bcl-2, while others found it nearly absent (Adams and Cory, 1998) [18]. This contradiction may reflect the coexistence of anti-apoptotic Bcl-xL and pro-apoptotic Bax, both belonging to the same family. In our material, Bcl-2 expression in basal cells correlated with p53 expression in the epidermis, basal layer, and lymphocytes, suggesting that both pathways may operate concurrently rather than antagonistically, as also noted by Adams and Cory (1998) [18].

Despite its theoretical anti-apoptotic function, Bcl-2 overexpression did not correlate with epidermal hyperplasia in the present study, indicating that Bcl-2 plays a limited role in psoriatic epidermal kinetics. Similar weak or absent basal-cell expression has been reported earlier, implying its relative unimportance in psoriasis pathogenesis (Anton and Brandes, 1968; Raj et al, 2006) [6,19].

In contrast, p53 immunostaining correlated weakly but consistently with the grade of epidermal hyperplasia, suggesting that p53 is more directly implicated in regulating keratinocyte proliferation and apoptotic turnover. Baran et al (2005) [10] and Susana et al (2012) [20] also reported elevated p53 expression in lesional psoriatic epidermis compared with normal skin. Swanbeck et al (1994) [21] emphasized p53 overexpression as a compensatory response to DNA damage rather than a mutational event. Indeed, molecular studies show no p53 gene mutation in psoriasis, and the elevated expression reflects wild-type protein accumulation as a stress-induced cellular response (Thompson, 1995) [22].

The coexistence of both pro- and anti-apoptotic activity within the same lesions implies that psoriatic keratinocytes simultaneously undergo proliferative drive and apoptotic resistance, maintaining chronic epidermal hyperplasia (Raj et al, 2006) [19]. The linear correlation between p53 and Bcl-2, though paradoxical, indicates simultaneous activation of opposing pathways, possibly reflecting dynamic tissue remodeling rather than a simple on–off switch of apoptosis.

Apoptosis and cell-cycle control are fundamental to epidermal homeostasis. Disruption of these mechanisms, as observed in psoriasis, shares conceptual parallels with tumorigenesis, where imbalance between cell proliferation and programmed death contributes to uncontrolled growth. As emphasized by Adams and Cory (1998) [18], multi-gene interactions across apoptotic and cell-cycle pathways are more informative than single-marker analyses.

Our findings support the notion that p53 has a greater pathogenetic role than Bcl-2 in psoriatic apoptosis regulation, consistent with prior reports that describe enhanced p53 activity in the absence of p53 mutation (Susana et al, 2012; Thompson, 1995) [20, 22]. The combined evaluation of Bcl-2 and p53 provides a clearer picture of apoptotic balance, reaffirming the concept that psoriasis is a hyperproliferative yet apoptosis-resistant inflammatory dermatosis.

Conclusion

The present study demonstrates variable expression of p53 and Bcl-2 in psoriatic skin. p53 overexpression correlated with epidermal hyperplasia, indicating a role in keratinocyte turnover and DNA-damage response, whereas Bcl-2 expression was largely confined to lymphocytes, reflecting inflammatory cell survival. The lack of inverse correlation between the two suggests simultaneous but independent regulation of apoptosis and anti-apoptotic mechanisms. Multi-marker evaluation of apoptosis-related genes, rather than isolated protein analysis, may better elucidate disease mechanisms and ultimately complement clinicopathologic parameters in predicting disease behavior and therapeutic response.

Conflict of interest: Nil.

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