ORIGINAL RESEARCH

Role of Janus kinase 1 and signal transducer and activator of transcription 3 in vitiligo

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Background: Vitiligo is an acquired autoimmune skin disorder. The often-visible lesions of vitiligo have a major impact on patients' quality of life and the results of the treatment regimens on offer are unsatisfactory, so there is a need for new therapeutic regimens. Recent advances in vitiligo pathogenesis have led to recognition of the importance of the JAK–STAT pathway as an attractive therapeutic option.
Purpose: To evaluate role of JAK1 and STAT3 in vitiligo.
Methods: This prospective case–control study was carried out on 35 patients presenting with vitiligo and 20 apparently healthy age- and sex-matched volunteers. Skin biopsies from controls and cases were taken for histopathological and immunohistochemical JAK1 and STAT3 evaluation.
Results: Epidermal and dermal overexpression of STAT3 was noted in lesional skin compared to the other groups (P=0.02 and P<0.001, respectively). There was a positive correlation between dermal expression of JAK1 and dermal expression of STAT3 (r=0.52, P=0.004).
Conclusion: In conjunction, JAK1 and STAT3 might be involved in the pathogenesis of vitiligo. This could open the gate for the use of JAK1 and STAT3 inhibitors as new targeted therapy for vitiligo.
Keywords: JAK1, STAT3, vitiligo, immunohistochemical

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Introduction

Vitiligo is a chronic autoimmune disease that results from the destruction of melanocytes, causing white spots on the skin. Vitiligo affects approximately 1% of population and can affect both adults and children, causing diminished quality of life and marked psychological distress.[1]

The pathogenesis of vitiligo involves the destruction of melanocytes via cell-mediated immunity, and IFNγ and that CD8 T cells play a key role in this process.[2]

The JAK–STAT pathway mediates the intracellular signals of more than 60 cytokines, growth factors, and hormones.[3] The JAK family includes JAK1, JAK2, JAK3, and TYK2.[4] There are seven STAT genes in humans: *STAT1*, *STAT2*, *STAT3*, *STAT4*, *STAT5A*, *STAT5B*, and *STAT6*.[5]

Treatment with topical corticosteroids, calcineurin inhibitors, and narrowband ultraviolet B phototherapy are unsatisfactory, and poor response to treatment is common.[6]

Targeting the JAK–STAT pathway has gained huge attraction in various immunological diseases, especially T cell–mediated diseases.[7] Although few JAK inhibitors are US Food and Drug Administration–approved, other JAK and possible STAT inhibitors are being developed for vitiligo therapy.[8]

The aim of this work was to evaluate role of JAK1 and STAT3 in vitiligo.

Methods

This prospective case–control study was carried out on 35 patients presenting with vitiligo and 20 healthy age- and gender-matched individuals as a control group. They were selected from the Outpatient Clinic of Dermatology in Menoufia University Hospital spanning the period between January 2017 and January 2018. This study was approved by the Menoufia University ethics committee and conducted in accordance with the Declaration of Helsinki. All participants provided written informed consent after the procedure had been fully explained. Patients included in this study suffered from vitiligo, either segmental or nonsegmental, and had received no topical or systemic treatment for vitiligo within the last month. Patients with leukoderma secondary to other causes were excluded. Each patient was subjected to complete history-taking and general and dermatological examinations. Vitiligo area scoring index (VASI) scores were calculated for all patients to assess the severity of the disease,[9] and vitiligo disease activity (VIDA) scores calculated to assess disease activity.[10]

Skin biopsies

Two skin biopsies were taken with a 3 mm punch from each patient under 2% lignocaine local anesthesia. The first was from the center of the vitiliginous macule and the other from nearby apparently normal skin within a 5 cm radius of any vitiliginous macules.[11] They were fixed in 10% neutral buffered formalin and sent to the Pathology Department, Faculty of Medicine, Menofuia University for routine histochemical processing and sectioning. Skin sections were stained with H&E for routine histopathological examination. Other sections were mounted on positive-charged slides and stored at room temperature for JAK1 and STAT3 immunohistochemical staining.

Immunohistochemical staining

Sections were stained. They were dewaxed and rehydrated in graded alcohol solutions. For antigen retrieval, sections were placed in target-retrieval solution (pH 6.1 or 9, 97°C) for 10–30 minutes. Slides were blocked using a peroxidase-blocking reagent and incubated for 1 hour at room temperature with the primary diluted antibodies JAK1 (mouse monoclonal antibody, 0.1 mL, each vial containing 200 µg IgG_{2b} in 1 mL PBS, A9

sc1677; Santa Cruz Biotechnology) and STAT3 (mouse monoclonal antibody, 0.1 mL, each vial containing 200 µg IgG_1 in 1 ml PBS, F2 sc-8019; Santa Cruz Biotechnology). They were diluted 1:200 and 1:100 for JAK1 and STAT3, respectively. Deparaffinized sections were stained using immunohistochemistry products in Dako automatic immunohistochemistry apparatus. Detection was performed using the detection reagent and DAB. Slides were counterstained using Mayer's hematoxylin. Finally, sections were mounted and covered using distyrene, plasticizer and xylene. Positive-control slides were mouse-kidney tissue for JAK1 and human fallopian-tube tissue for STAT3. Negative-control slides were prepared by omitting primary antibodies from the staining procedure.

Interpretation of JAK1 and STAT3 expression

Stained JAK1 and STAT3 sections were scored: staining status positive or negative, localization:nucleocytoplasmic, cytoplasmic, or nuclear,[12] and histochemical score (H-score) applied to evaluate positive cases, where both the intensity and the percentage of positivity were considered using formula: H-score = + 3 (strong intensity) × % + 2 (moderate intensity) × % + 1 (mild intensity) × %. The score ranges between 0 and 300.[13]

Statistical analysis

Statistical analysis was conducted using SPSS version 20 on an IBM computer. Qualitative data are expressed as numbers and percentage. Quantitative data are expressed as mean ± SD, percentages, and medians. Fisher's exact test and χ^2 were used for comparing qualitative variables. Mann–Whitney U test was used in comparing two nonparametric quantitative variables. The Kruskal–Wallis test was used for testing equality of population medians among groups, as it is an extension of the Mann–Whitney test. ANOVA was used for comparison between three or more quantitative variables. The results were considered statistically significant where $P \leq 0.05$.

Results

Clinical criteria of vitiligo patients and demographic and histopathological data of lesional and perilesional vitiligo skin are given in Table 1.

Table 1 Clinical and demographic data and histopathological characteristics of the vitiligo patients

	Cases (n=35)
Age, years	
Mean ± SD	29.8±16.8
Median	24
Range	10–66
Sex, n (%)	
Male	12 (34.3)
Female	23 (65.7)
Family history, n (%)	
Positive	7 (20.0)
Negative	28 (80.0)
Occupation, n (%)	
Housewife	15 (42.9)
Worker	8 (22.9)
Student	12 (34.2)
Duration, months, n (%)	
Mean ± SD	46.6±47.0
Median	36
Range	1–192
Distribution, n (%)	
Nonsegmental	21 (60)
Segmental	14 (40)
VASI score	
Mean ± SD	17.9±22.2
Median	10
Range	3–100
VIDA, n (%)	
0	9 (25.7)
+1	6 (17.1)
+2	4 (11.4)
+3	7 (20)
+4	9 (25.7)
VIDA category, n (%)	
Old	19 (54.3)
Recent	16 (45.7)

	Lesional, n (%)	Perilesional, n (%)
Epidermal changes		
Epidermal thickness		
Atrophy	12 (34.3)	10 (28.6)
Normal	21 (60)	25 (71.4)
Acanthosis	2 (5.7)	0
Parakeratosis		
Present	0	0
Absent	35 (100)	35 (100)

(Continued)

Table 1 (Continued).

Melanin pigment		
Present	9 (25.7)	30 (85.7)
Absent	26 (74.3)	5 (14.3)
Density of melanin pigment (n=9)		
Few	6 (66.7)	15 (50)
Numerous	3 (33.3)	15 (50)
DEJ disruption		
Normal	15 (42.9)	25 (71.4)
Disrupted	20 (57.1)	10 (28.6)
Degree of DEJ disruption (n=20)		
Focal	18 (90)	9 (90)
Extensive	2 (10)	1 (10)
DEJ vacuolar alteration		
Present	25 (71.4)	13 (37.1)
Absent	10 (28.6)	22 (62.9)
Degree of DEJ vacuolar alteration (n=25)		
Focal	23 (65.7)	13 (100)
Extensive	2 (5.7)	0
Dermal changes		
Congested blood vessels, n (%)		
Present	0	0
Absent	35 (100)	35(100)
Perivascular inflammatory infiltrates, n (%)		
Present	25 (71.4)	17 (48.6)
Absent	10 (28.6)	18 (51.4)
Degree of perivascular inflammatory infiltrates (n=25), n (%)		
Mild	15 (60)	14 (82.4)
Moderate	9 (36)	3 (17.6)
Severe	1 (4)	0

Abbreviations: VASI, vitiligo area and severity index; VIDA, vitiligo disease activity; DEJ, dermoepidermal junction; BVs, blood vessels.

Comparison between controls and vitiligo skin (lesional and perilesional) regarding JAK1 and STAT3 tissue immunoreactivity

There were no significant differences between the studied groups regarding JAK1 expression. There were significant differences between the groups regarding epidermal and

Table 2 Comparison between controls and vitiligo skin (lesional and perilesional) regarding JAK1 and STAT3 tissue immunoreactivity

Immunoreactivity parameters	Controls, n=20	Perilesional, n=35	Lesional, n=35	*P*-value
Epidermal JAK1				
Expression, n (%)				(χ^2)
Positive	13 (65)	22 (62.9)	21 (60)	0.99
Negative	7 (35)	13 (37.1)	14 (40)	
Localization, n (%)				(χ^2)
Nuclear	0	2 (9.1)	4 (19)	0.49
Cytoplasmic	9 (69.2)	18 (81.8)	14 (66.7)	
Nucleocytoplasmic	4 (30.8)	2 (9.1)	3 (14.3)	
H score				(ANOVA)
Mean ± SD	80±32.5	60.0±36.5	81.9±40.9	0.12
Median	70	50	70	
Range	20–120	1–130	20–160	
Dermal JAK1				
Expression, n (%)				(χ^2)
Positive	14 (70)	22 (84.6)	19 (70.4)	0.39
Negative	6 (30)	4 (15.4)	8 (29.6)	
Localization, n (%)				(χ^2)
Nuclear	0	0	0	0.23
Cytoplasmic	13 (92.9)	22 (100)	19 (100)	
Nucleocytoplasmic	1 (7.1)	0	0	
H-score				(ANOVA)
Mean ± SD	48.9±19.5	35.4±18.7	38.9±19.7	0.13
Median	50	30	40	
Range	20–80	11–70	12–70	
Epidermal STAT3				
Expression, n (%)				(Fisher)
Positive	20 (100)	29 (82.9)	34 (97.1)	0.03*
Negative	0	6 (17.1)	1 (2.9)	
Localization, n (%)				(χ^2)
Nuclear	1 (5)	3 (10.3)	2 (5.9)	0.72
Cytoplasmic	7 (35)	8 (27.6)	7 (20.6)	
Nucleocytoplasmic	12 (60)	18 (62.1)	25 (73.5)	
H-score				(ANOVA)
Mean ± SD	169.1±80.5	127.9±68.9	175±27.2	0.02*
Median	180	130	170	
Range	20–290	20–280	140–230	
Expression, n (%)				(χ^2)
Positive	17 (85)	22 (62.9)	30 (85.7)	0.04*
Negative	3 (15)	13 (37.1)	5 (14.3)	
Localization, n (%)				(χ^2)
Nuclear	0	0	2 (6.7)	0.45
Cytoplasmic	6 (35.3)	6 (27.3)	6 (20)	
Nucleocytoplasmic	11(64.7)	16 (72.7)	22 (73.3)	

(*Continued*)

Table 2 (Continued).

Immunoreactivity parameters	Controls, n=20	Perilesional, n=35	Lesional, n=35	P-value
H-score				
Mean ± SD	136.7±64.0	122.7±36.9	196.5±46.9	(ANOVA)
Median	140	115	190	<0.001*
Range	10–260	70–210	120–270	

Note: *Significant.
Abbreviation: H-score, histochemical score.

dermal STAT3 expression (P=0.03 and P=0.04, respectively). Epidermal and dermal H-scores for STAT3 expression were significantly higher in lesional skin than the other groups (P=0.02 and P<0.001, respectively; Table 2, Figures 1 and 2).

Relationships among lesional H-scores of JAK1 and STAT3 and demographic and clinical parameters (sex, occupation, family history, distribution, and VIDA score)

There was a significant relationship between epidermal H-score for JAK1 expression and the occupation of patients (P=0.05). There were significant relationships between high epidermal and dermal H-scores for JAK1 expression and family history of patients (P=0.02 and P=0.04, respectively). There was no significant relationship between epidermal and dermal H-scores for STAT3 expression and demographic and clinical parameters (Table 3).

Relationships among lesional H-scores for JAK1 and STAT3 and histopathological parameters

There was a significant association between high epidermal H -scores for JAK1 expression and epidermal atrophy (P=0.03). Also, dermal H- scores for JAK1 expression had significant relationships with focal DEJ disruption and vacuolar alteration (P=0.008 and P=0.01, respectively). There were significant associations between epidermal H- scores for STAT3 expression and focal DEJ disruption and vacuolar alteration (P=0.008 and P=0.01, respectively; Table 4).

Correlation between JAK1 and STAT3 (lesional and perilesional)

There was a positive correlation between lesional expression of JAK1 in dermis and lesional expression of STAT3 in dermis (r=0.52, P=0.004; Figure 3).

Discussion

Vitiligo is a common skin and mucous-membrane depigmenation disorder[14] that is characterized by well-circumscribed depigmented macules and patches.[15]

The JAK–STAT) pathway is utilized bysuchcytokines as interleukins and interferons to transmit signals from the cell membrane to the nucleus. Upon engagement of extracellular ligands, intracellular JAK proteins become activated and phosphorylate STAT proteins, which dimerize, and then phospo-STAT (pSTAT), which is the active form, translocates to the nucleus to directly regulate gene expression.[16]

JAK1 is involved in IFNγ signals through binding of IFNγ to the IFNγ receptor, which initiates phosphorylation of STAT1 and translocates it to the nucleus, where IFNγ–dependent genes, including *CXCL9* and *CXCL10*, are transcribed. Then, CXCL9 and CXCL10 recruit CD8 T cells to the skin, where they attack melanocytes.[17]

STAT3 is involved in the pathogenesis of vitiligo through its activation, possibly in response to Langerhans cell activation, which induces the recruitment and differentiation of T_H17 cells in vitiligo and may downregulate melanogenic activity.[18]

IFNγ signaling, which has a role in the pathogenesis of vitiligo through targeted destruction of melanocytes by CD8 T cells, utilizes the JAK–-STAT pathway;[19] therefore, vitiligo may be susceptible to treatment with JAK and STAT inhibitors.

Significant repigmentation is reported in patients after oral administration of tofacitinib (JAK1/3 inhibitor),[20] ruxolitinib (JAK1/2 inhibitor),[21] and topical ruxolitinib, particularly on the face.[22]

To the best of our knowledge, there have been few studies to investigate immunohistochemical expression of JAK1 and STAT3 in vitiligo and correlate this with clinical and histopathological parameters.

In the present study, the immunohistochemical expression of JAK1 in the epidermis and dermal adnexa showed
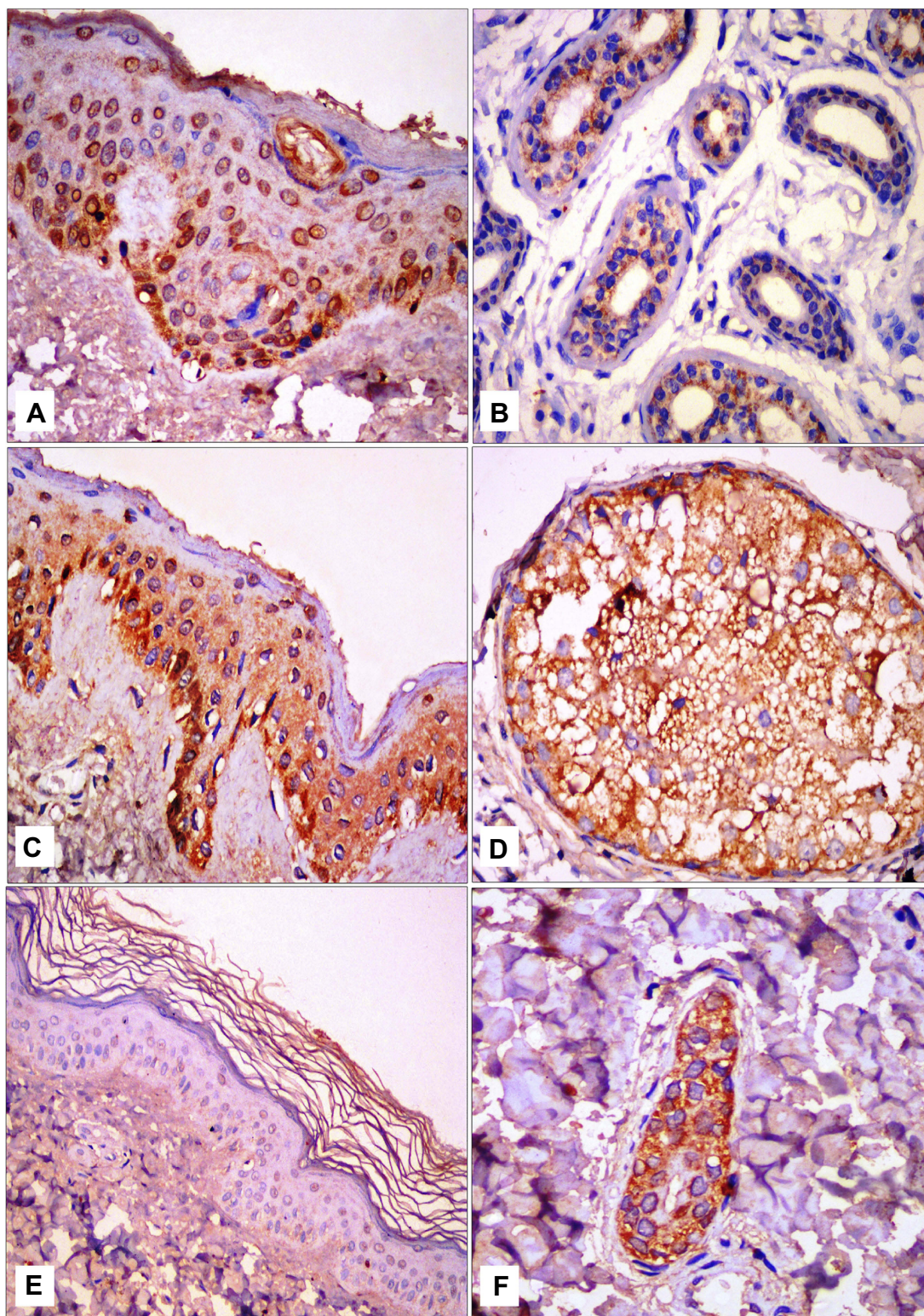
Figure 1 JAK1 immunohistochemical staining.

Notes: (**A**) Nucleocytoplasmic JAK1 expression in epidermis in control skin; (**B**) cytoplasmic expression of JAK1 in eccrine and sweat-gland ducts in control skin; (**C**) Epidermal cytoplasmic JAK1 expression with focal nucleocytoplasmic localization in perilesional vitiligo skin sections; (**D**) cytoplasmic JAK1 expression in pilosebaceous unit in perilesional skin; (**E**) nucleocytoplasmic JAK1 expression in epidermis in lesional skin sections; (**F**) cytoplasmic JAK1 expression in eccrine and sweat-gland ducts and dermal fibroblasts in lesional vitiligo skin sections. 200× (**A–C**); 100× for (**E**); 400× (**D,F**).
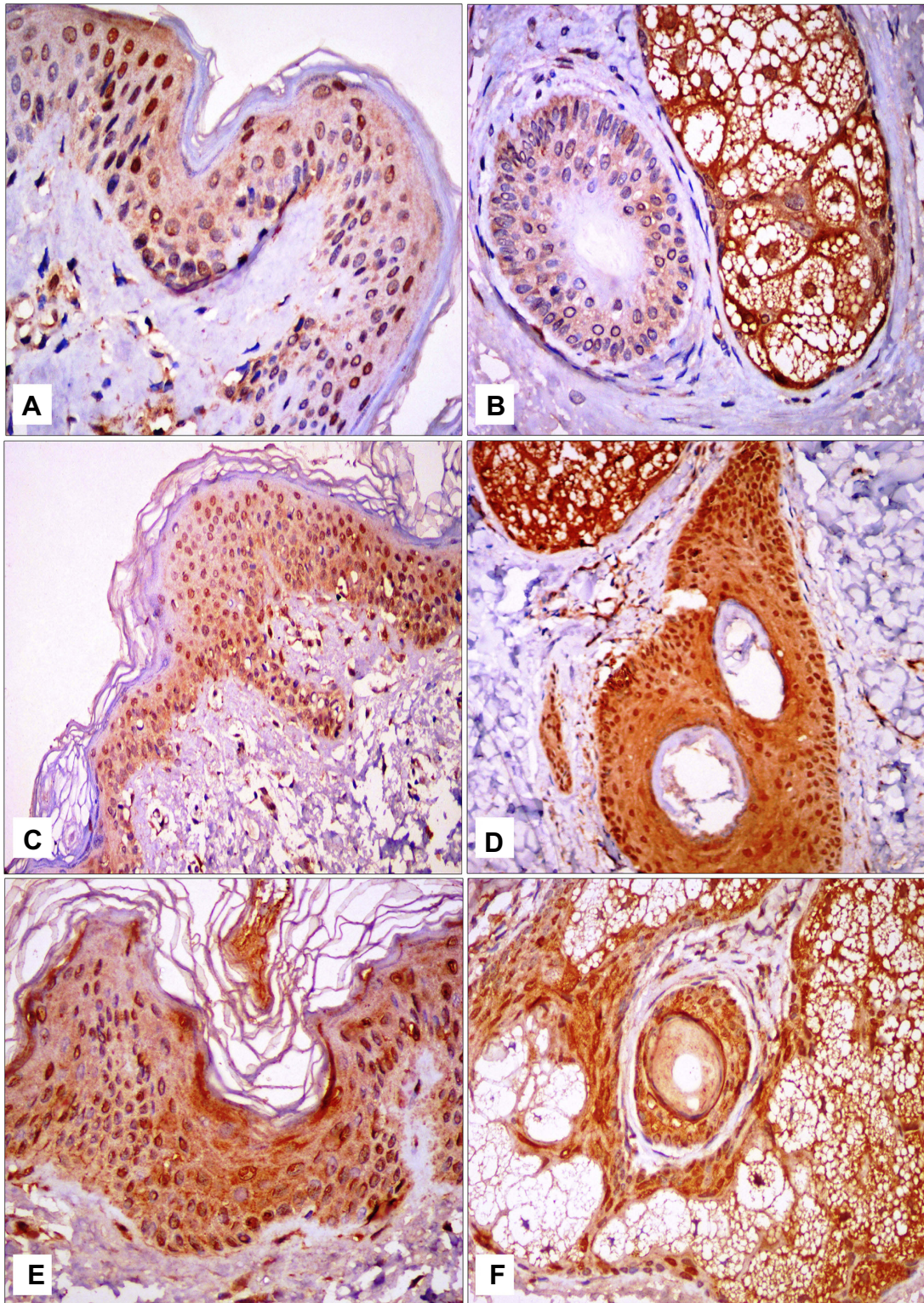
Figure 2 STAT3 immunohistochemical staining.
Notes: (**A**) Epidermal nucleocytoplasmic STAT3 expression in control skin; (**B**) nucleocytoplasmic STAT3 expression in pilosebaceous unit in control skin; (**C**) perilesional vitiligo skin showed epidermal nucleocytoplasmic STAT3 expression; (**D**) perilesional nucleocytoplasmic STAT3 expression in sebaceous gland and dermal fibroblasts; (**E**) epidermal nucleocytoplasmic STAT3 expression in lesional skin sections; (**F**) nucleocytoplasmic STAT3 expression in pilosebaceous unit in lesional skin sections. 200× for all.

Table 3 Relationship between lesional H-scores of JAK1 and STAT3 with demographic and clinical parameters

	JAK1 H-score in epidermis	JAK1 H-score in dermis	P-value	STAT3 H-score in epidermis	STAT3 H-score in dermis	P-value
	Mean ± SD	Mean ± SD		Mean ± SD	Mean ± SD	
Sex			U			U
Male	95±51.3	62.5±43.5	0.37[P1]	168.2±77.2	133.3±45.3	0.96[p3]
Female	76.7±36.8	62.0±34.1	0.98[P2]	169.6±83.7	138.1±71.5	0.86[P4]
Occupation			(Kruskal–Wallis)			(Kruskal–Wallis)
Housewife	90±41.8	90.0±41.8	0.05*[P1]	178.7±61.6	147.1±58.4	0.8[P3]
Worker	106±48.8	106.0±48.8	0.67[P2]	155.0±89.9	110.0±54.8	0.46[P4]
Student	54.3±13.9	54.3±13.9		166.4±100.5	141.1±78.9	
Family history			U			U
Positive	160±0	130.0±0	0.02*[P1]	176.7±83.9	136.7±37.9	0.87p3
Negative	73.7±33.4	58.3±31.7	0.04*[P2]	168.4±81.6	136.7±66.8	0.87[P4]
Distribution			U			U
Segmental	68.6±29.1	73.3±40.3	0.24[P1]	160.8±90.2	147.3±72.7	0.66[p3]
Nonsegmental	88.6±45.2	85.3±42.1	0.56[P2]	174.3±75.7	130.5±59.7	0.53[P4]
VIDA			(Kruskal–Wallis)			(Kruskal–Wallis)
0	80±48.7	66.7±41.3	0.93[P1]	205.6±47.5	150.0±48.9	0.96[p3]
+1	86.7±20.8	40.0	0.28[P2]	186.7±57.2	145.0±58.9	0.79[P4]
+2	75±45.1	120		150±124.6	133.3±120.6	
+3	70±36.1	42.0±13.0		118.3±85.2	104.0±82.0	
+4	97.5±51.9	68.3±36.0		163.3±90.6	137.1±56.2	
VIDA			U			U
Old	80±40.6	70.0±41.4	0.78[P1]	187.9±70.5	123.3±66.8	0.8[p3]
Recent	85.7±44.7	56.4±30.1	0.42[P2]	145.3±88.3	145.6±62.4	0.36[P4]

Note: *Significant. [P1]JAK1 H score in epidermis, [P2]JAK1 H score in dermis, [P3]STAT3 H score in epidermis, [P4]STAT 3 H score in dermis.
Abbreviations: VIDA, vitiligo disease activity; H-score, histochemical.

Table 4 Relationship between lesional H-scores of JAK1 and STAT3 with histopathological parameters

	JAK1 H-score in epidermis Mean ± SD	JAK1 H-score in dermis Mean ± SD	Test of significance	P-value	STAT3 H-score in epidermis Mean ± SD	STAT3 H-score in dermis Mean ± SD	Test of significance	P-value
Epidermal changes								
Epidermal thickness							Kruskal–Wallis	
Atrophy	82.5±44.9	82.5±44.9	U / 2.36[P1]	0.03*[P1]	155.0±52.3	155.0±52.3	0.06[P3]	0.97[P3]
Normal	47.0±14.9	47.0±14.9	Kruskal–Wallis / 2.57[P2]	0.29[P2]	130.0±68.4	130.0±68.4	1.35[P4]	0.51[P4]
Acanthosis		50.0±0			105.0±91.9	105.0±91.9		
Melanin pigment			U				U	
Present	73.3±38.8	167.8±83.5	0.89[P1]	0.39[P1]	167.8±83.5	154.3±50.3	0.06[P3]	0.96[P3]
Absent	56.9±33.3	169.6±81.2	Kruskal–Wallis / 0.06[P2]	0.96[P2]	169.6±81.2	131.3±67.7	0.83[P4]	0.52[P4]
Density of melanin pigment			U				U	
Few	72.5±34.0	195.0±51.3	0.05[P1]	0.97[P1]	195.0±51.3	153.3±55.0	1.48[P3]	0.18[P3]
Numerous	75.0±63.6	113.3±120.9	Kruskal–Wallis / 1.12[P2]	0.36[P2]	113.3±120.9	160.0±0	0.11[P4]	0.92[P4]
DEJ disruption			U				U	
Normal	67.8±35.3	167.1±85.4	0.66[P1]	0.52[P1]	167.1±85.4	135.8±57.9	0.12[P3]	0.91[P3]
Disrupted	57.0±35.6	170.5±79.0	Kruskal–Wallis / 0.12[P2]	0.91[P2]	170.5±79.1	137.2±69.4	0.06[P4]	0.96[P4]
Degree of DEJ disruption			1.11[P1]	0.3[P1]			U	
Focal	61.1±35.2	180.0±77.5	Kruskal–Wallis		180.0±77.6	135.9±71.3	4.02[P3]	0.008[P3]*
Extensive	20.0±0	85.0±21.21	4.02[P2]	0.008[P2]*	85.0±21.2	160.0±0	0.33[P4]	0.75[P4]
DEJ vacuolar alteration			U				U	
Present	56.7±32.3	170.0±76.8	0.84	0.42	170.0±76.8	133.9±68.0	0.11[P3]	0.92[P3]
Absent	71.4±39.8	166.7±95.1	Kruskal–Wallis / 0.09	0.93	166.7±95.1	145.7±52.2	0.42[P4]	0.68[P4]
Degree of DEJ vacuolar alteration			U				U	
Focal	60.0±31.6	177.4±75.5	1.21	0.25	177.4±75.5	132.7±69.4	4.25[P3]	0.01[P3]*
Extensive	20.0±0.0	85.0±21.2	Kruskal–Wallis / 4.25	0.01*	85.0±21.2	160.0±0	0.39[P4]	0.7[P4]

(*Continued*)

Table 4 (Continued).

	JAK1 H-score in epidermis Mean ± SD	JAK1 H-score in dermis Mean ± SD	Test of significance	P-value	STAT3 H-score in epidermis Mean ± SD	STAT3 H-score in dermis Mean ± SD	Test of significance	P-value
Dermal changes								
Perivascular inflammatory infiltrates			U 1.01[P1] Kruskal–Wallis 0.48[P2]	0.34[P1] 0.64[P2]			U 0.46[P3] 1.39[P4]	0.65[P3] 0.19[P4]
Present	56.2±32.0	165.0±84.1			165.0±84.1	125.7±60.8		
Absent	75.0±40.4	179.0±74.3			179.0±74.3	162.2±67.6		
Degree of perivascular inflammatory infiltrates			Kruskal–Wallis 3.10[P1] 0.01[P2]	0.21[P1] 0.93[P2]			Kruskal–Wallis 0.14[P3] 3.46[P4]	0.93[P3] 0.18[P4]
Mild	67.8±35.6	164.3±94.4			128.5±63.4	66.0±38.4		
Moderate	101.7±42.6	161.1±74.7			104.3±39.5	58.0±24.9		
Severe	110±0	210.0±0			240.0±0	130.0±0		

Notes: *Significant.
Abbreviations: H score, histochemical score; DEJ, dermo-epidermal junction.

no significant differences between patients and controls, although Nada et al[23] found that that JAK1 levels on Western blot assay were significantly higher in vitiligo patients than controls. This discrepancy in results could be attributed to different techniques used and fewercontrols.

There were significant relationships between epidermal and dermal H- scores for JAK1 expression and family history of patients. Hu et al[24] found that three single-nucleotide polymorphisms (rs310230, rs310236, and rs310241) in JAK1 were associated with susceptibility to Vogt–Koyanagi–Harada syndrome, which is a rare presentation of vitiligo.

In the current study, there was a significant relationship between epidermal H-scores for JAK1 expression and the occupation of patients. This could be explained by exposure to such chemicals as *para-tert*-butylphenol, which can be found in adhesive resins and other products that were presumed to cause vitiligo in genetically susceptible patients.[25]

There were significant associations between overexpression of JAK1 and epidermal atrophy, degree of DEJ disruption, and degree of DEJ vacuolar alteration. This could be explained by oxidative damage and autoimmune mechanisms that cause damage to skin lipids, DNA, and proteins, leading to pathological alterations and separation at the DEJ.[26]

There were significant differences between studied groups regarding epidermal and dermal STAT3 expression. Overexpression of STAT3 was noted more in lesional skin than the other groups. This is in agreement with Tanemura et al,[27] who reported that there was much more pSTAT3 in lesional skin than perilesional skin, as pSTAT3 is located in the nuclei of keratinocytes and/or dermal inflammatory cells, suggesting the significance of STAT3 activation.[12]

There were significant associations between overexpression of STAT3 and focal DEJ disruption and vacuolar alteration. These relationships have not previously been reported, and further studies are recommended to investigate these correlations.

In the current study, there was a positive correlation between dermal expression of JAK1 and dermal expression of STAT3, which suggests arole of JAK1 and STAT3 in the pathogenesis of vitiligo upon activation of the JAK–STAT pathway. Further studies are recommended to assess this correlation.

Limitation

There were fewer controls than patients.
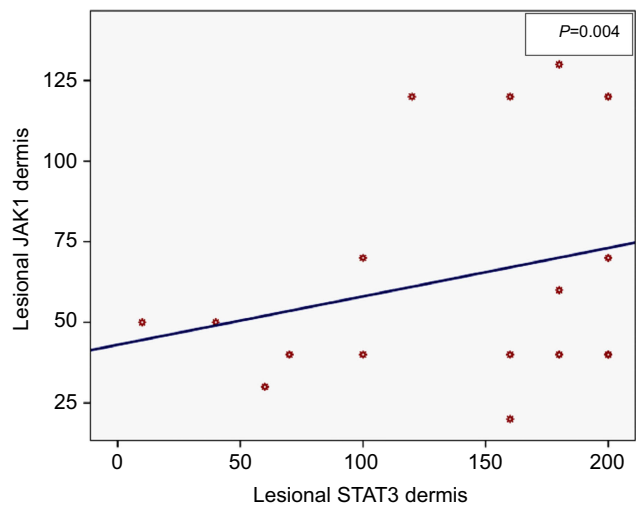
Figure 3 Positive correlation between lesional expression of JAK1 in dermis and lesional expression of STAT3 in dermis (r=0.52, P=0.004).

Conclusion

In conjunction, JAK1 and STAT3 might be involved in the pathogenesis of vitiligo. This could open the gate for the use of JAK1 and STAT3 inhibitors as new targeted therapy for vitiligo.

Disclosure

The authors report no conflicts of interest in this work.

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