Hindawi
Dermatologic Therapy
Volume 2023, Article ID 6689580, 6 pages
https://doi.org/10.1155/2023/6689580

Research Article

Correlation between LRG1 and Adipokines in Psoriasis

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Received 31 May 2023; Revised 28 August 2023; Accepted 20 September 2023; Published 3 October 2023

Academic Editor: Imran Majid

Background and Objective. Patients with psoriasis may exhibit abnormal changes in serum adipokine levels, which are often related to disease severity of the disease. Leucine-rich alpha-2-glycoprotein 1 (LRG1) is an acute-phase inflammatory protein that may be linked to adipokines in psoriasis. In this study, we evaluated the differences in the expression of adipokines and LRG1 between patients with psoriasis and healthy individuals, analyzed the correlation between the expression of LRG1 and adipokines, and explored their relationship with psoriatic lesions. *Methods*. In this cross-sectional study, patients with psoriasis ($n = 54$) and healthy controls ($n = 26$) were enrolled, and their clinical characteristics were recorded. Fasting venous blood samples were collected from each participant. The serum concentrations of leptin, resistin, adiponectin, and LRG1 in each sample were measured using the enzyme-linked immunosorbent assay. *Results*. The study included 54 patients with psoriasis vulgaris and 26 healthy controls. The serum levels of LRG1, leptin, and resistin were significantly higher in patients with psoriasis than in healthy controls. Conversely, adiponectin levels were significantly lower in patients with psoriasis. The study showed that LRG1 expression was positively correlated with leptin and resistin expression but negatively correlated with adiponectin expression. Interestingly, only leptin, resistin, and LRG1 expression showed a linear correlation with the Psoriasis Area and Severity Index (PASI). When we categorized patients with psoriasis based on their LRG1 levels, we observed that the group with high LRG1 levels showed a higher PASI. *Conclusions*. We observed a significant correlation between LRG1 and adipokine expression in patients with psoriasis. In addition, the expression levels of LRG1, leptin, and resistin were observed to be correlated with the severity of psoriasis. We believe that the occurrence and development of psoriasis are collectively influenced by LRG1 and leptin/resistin expression.

1. Introduction

Psoriasis is a chronic skin disease that affects over 60 million people worldwide. Its overall prevalence ranges from 0.1% in East Asia to 1.5% in Western Europe [1]. The occurrence and development of psoriasis are driven by T cell dysfunction and a complex imbalance in the network of inflammatory cytokines, including tumor necrosis factor-α (TNF-α), interleukin-23 (IL-23), and the IL-17 family [2]. Findings from several studies have demonstrated the involvement of adipokines, including leptin, resistin, and adiponectin, in the pathogenesis of psoriasis. Elevated levels of leptin and resistin, as well as decreased levels of adiponectin, have been observed in patients with psoriasis, which may contribute to the severity of skin lesions [3]. Chronic subclinical low-grade inflammation could result from the abnormal secretion of adipokines and cytokines in the skin and adipose tissue. This inflammation could contribute to the stimulation, differentiation, and proliferation of keratinocytes and immune cells [4]. Leucine-rich α-2 glycoprotein 1 (LRG1) is an acute-phase inflammatory protein that has been linked to cancer, infection, and autoimmune diseases [5, 6]. Studies have shown that patients with psoriasis have significantly higher serum levels of LRG1, and LRG1 could be a valuable biomarker for monitoring disease activity and treatment efficacy [7, 8]. Furthermore, the sensitivity of LRG1 as a biomarker is considerably higher than that of C-reactive protein [8]. LRG1 is synthesized primarily by the liver and

neutrophils and is involved in various biological processes such as inflammation, lipid metabolism, and glucose metabolism [9]. However, the correlation between LRG1 and adipokine expression in patients with psoriasis remains unclear.

In this study, we investigate the association between the aberrant expression of adipokines and LRG1 in patients with psoriasis as well as their relationship with disease severity.

2. Materials and Methods

2.1. Selection of Patients. This study was a two-center observational cross-sectional investigation that included patients with psoriasis who visited the Department of Dermatology of Dongzhimen Hospital and the Air Force Medical Center of PLA from December 2022 to February 2023. The inclusion criteria were patients with psoriasis vulgaris who were 18 to 64 years old. Participants were required to refrain from using systemic antipsoriasis drugs for at least 1 month before the study. In addition, all participants were informed and agreed to blood sampling. The exclusion criteria included pustular psoriasis, other types of psoriasis, coinfection, tumor, other autoimmune diseases, severe cardiovascular disease, and blood system disease. In addition, 26 healthy controls were recruited as baseline controls for each serological index. Participants were informed and agreed to blood sampling. This study was approved by the Dongzhimen Hospital and Air Force Medical Center of PLA Ethics Committee (Registration Number: 2022DZMEC-287-02).

2.2. Clinical and Serological Variables. The basic clinical data included were gender, age, BMI, disease duration, and PASI score at the time of enrollment. BMI was calculated by dividing the body weight of each patient in kilograms by the square of their height in centimeters. The levels of the biochemical indicators were measured by collecting venous blood from each participant on an empty stomach. The blood sample was then centrifuged at 2500 rpm for 20 min to collect the serum, which was stored in a −80°C freezer for future use.

The expression of leptin, resistin, adiponectin, and LRG1 proteins was measured using the Elabscience® Human LEP (leptin) ELISA Kit (Catalog No: E-EL-H6017), Elabscience® Human RETN (resistin) ELISA Kit (Catalog No: E-EL-H1213c), Elabscience® Human ADP/Acrp30 (adiponectin) ELISA Kit (Catalog No: E-EL-H5811c), and Elabscience® Human LRG1 (Leucine Rich Alpha-2-Glycoprotein 1) ELISA Kit (Catalog No: E-EL-H6067). The detection sensitivities were 9.38 pg/mL, 18.75 pg/mL, 46.88 pg/mL, and 0.38 ng/mL, respectively. The detection ranges were 15.63–1000 pg/mL, 31.25–2000 pg/mL, 78.13–5000 pg/mL, and 0.63–40 ng/mL, respectively. The coefficient of variation for each measurement was less than 10%. The number of dilutions used during the process was 40 times for leptin, 500 times for resistin, 20,000 times for adiponectin, and five times for LRG1.

2.3. Statistical Analysis. Descriptive statistical analysis was performed on all variables using IBM SPSS Statistics 24.0 and Microsoft Excel 2016. For continuous variables that conformed to a normal distribution, the mean ± standard deviation was used to express data, and the difference between groups was expressed using an unpaired *t*-test. Variables that did not adhere to a normal distribution were expressed using the median (25th percentile and 75th percentile) values. We used nonparametric rank-sum tests to compare groups. Dichotomous variables were expressed as percentages, and we used chi-square tests to compare groups. We conducted linear regression analyses among variables and drew graphs using GraphPad Prism 8. Statistical significance was set at P value <0.05.

3. Results

The study included 54 patients with psoriasis vulgaris and 26 healthy controls. Eighty serum samples were collected from the participants. The results showed significant differences in age and BMI between the two groups. Patients with psoriasis were younger but had higher BMI values than healthy controls. We observed notable variations in the serum levels of leptin, resistin, adiponectin, and LRG1 in the two groups. Specifically, patients with psoriasis had significantly higher levels of leptin, resistin, and LRG1 than healthy controls ($P < 0.001$). Conversely, the levels of adiponectin were lower in patients with psoriasis than in healthy controls ($P < 0.001$) (Figure 1). To minimize the impact of age and BMI variations on adipokine and LRG1 expression, we conducted a 1 : 1 matching based on age and BMI in the groups. Despite this, the results indicated significant differences between the groups ($P \leq 0.001$). Basic clinical data and serological indicator differences are shown in Table 1.

Linear regression was used to examine the association between the expression patterns of LRG1 and leptin, resistin, or adiponectin. Simultaneously, we analyzed the correlation of these expression patterns with the PASI. Results indicated a significant linear correlation between PASI and LRG1 ($F = 6.17$, $P = 0.0163$), leptin ($F = 5.511$, $P = 0.0227$), and resistin expression ($F = 6.054$, $P = 0.0172$) but showed no correlation with adiponectin ($P = 0.1045$) (Figure 2). There was a significant positive correlation between LRG1 and leptin ($F = 3643$, $P < 0.0001$) and resistin ($F = 2647$, $P < 0.0001$), while a negative correlation was found between LRG1 and adiponectin ($F = 96.01$, $P < 0.0001$) (Figure 3). Meanwhile, a linear correlation was also observed between LRG1 and leptin ($F = 253.5$, $P < 0.0001$) and resistin ($F = 12.50$, $P = 0.0017$) expression in healthy controls. However, this correlation was weaker compared to that in patients with psoriasis. In addition, the association of LRG1 expression with adiponectin expression was not observed in healthy participants. To further investigate the correlation between LRG1 expression and psoriasis, we categorized patients based on their serum levels of LRG1. Patients with higher serum levels of LRG1 (≥15 ng/mL) had a significantly higher PASI score than patients with lower levels of LRG1 ($P < 0.05$). Although patients with lower levels of LRG1 appeared to have had psoriasis for a longer duration, no statistically significant difference was observed between the groups ($P > 0.05$) (Figure 4).

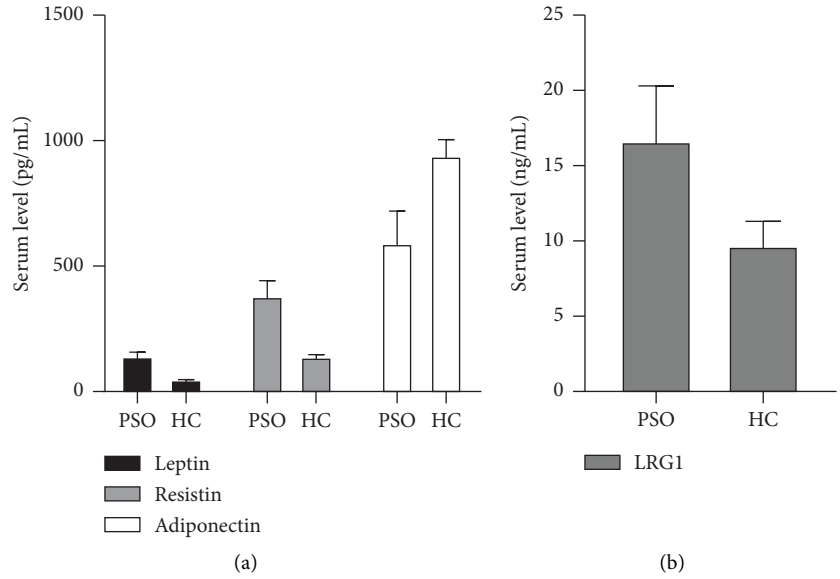

Figure 1: The serum levels of leptin and resistin in patients with psoriasis were significantly higher than in healthy controls ($P < 0.001$), whereas adiponectin levels were lower ($P < 0.001$) (a). Additionally, the serum levels of LRG1 were significantly higher in patients with psoriasis ($P < 0.001$) (b).

Table 1: Clinical characteristics of patients with psoriasis and healthy controls.

Variables	Psoriasis	Healthy control	P
Gender			
Male	40 (74.07%)	20 (76.92%)	$P > 0.05$
Female	14 (25.93%)	6 (23.08%)	
Age (years)	41.46 ± 14.45	48.81 ± 13.69	$P = 0.033$
BMI	30.08 (22.27, 32.25)	22.51 (20.66, 23.95)	$P < 0.001$
Duration (years)	10.00 (4.00, 17.25)	—	
PASI	15.90 (11.10, 23.10)	—	
LRG1 (ng/mL)	16.71 ± 3.88	9.74 ± 1.71	$P < 0.001$
LRG1 (adjusted)	13.25 ± 1.40	9.71 ± 2.19	$P = 0.001$
Leptin (pg/mL)	142.04 ± 27.46	49.07 ± 10.64	$P < 0.001$
Leptin (adjusted)	117.75 ± 11.60	47.16 ± 12.61	$P < 0.001$
Resistin (pg/mL)	382.50 ± 73.04	140.19 ± 18.94	$P < 0.001$
Resistin (adjusted)	320.95 ± 26.07	136.21 ± 20.87	$P < 0.001$
Adiponectin (pg/mL)	596.14 ± 137.99	945.03 ± 75.87	$P < 0.001$
Adiponectin (adjusted)	663.51 ± 92.88	967.75 ± 89.92	$P < 0.001$

4. Discussion

Psoriasis is a chronic skin disease caused by the abnormal proliferation of keratinocytes and the release of pro-inflammatory cytokines [10]. Recent studies have revealed that adipokines contribute significantly to the pathological progression of psoriasis [11]. Adipokines are a group of biologically active proteins primarily produced by adipocytes. There are various types of adipokines, including leptin, resistin, adiponectin, visfatin, and chemerin [12]. Adipokines play a significant role in various cellular signal transductions during metabolic processes, and they also exert a significant impact on immune inflammation regulation [11, 13]. Our research findings indicated that, compared to healthy individuals, patients with psoriasis showed significantly abnormal levels of leptin, resistin, and adiponectin. These abnormal levels persisted even after controlling for age and BMI and were closely correlated with the severity of skin lesions. The relationship may be attributed to an abnormal increase in the levels of proinflammatory adipokines, such as leptin and resistin, and a decrease in the levels of antiinflammatory adipokines, such as adiponectin [12].

Leptin is primarily produced by adipocytes in white fat and plays a crucial role in regulating the body's energy balance. Its levels are often elevated in patients with psoriasis and obesity and are closely associated with BMI [14]. In psoriasis, leptin has been shown to exert a stimulating effect on angiogenesis and the production of inflammatory factors such as IL-6, TNF-α, IL-8, and IL-17 [15, 16]. Under normal conditions, leptin is only detected in the basal layer of the skin. However, in individuals with psoriasis, it can be overexpressed in all layers of the epidermis, particularly in

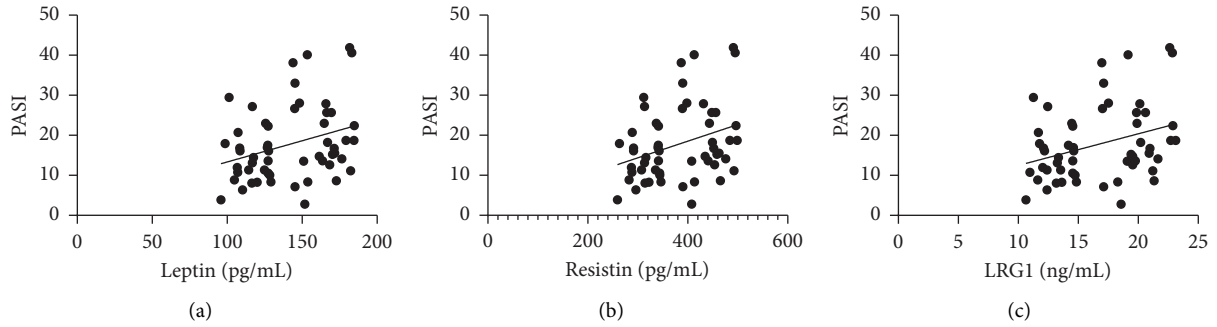

Figure 2: A positive linear correlation between the serum levels of leptin (a), resistin (b), and LRG1 (c) and PASI ($P < 0.05$).

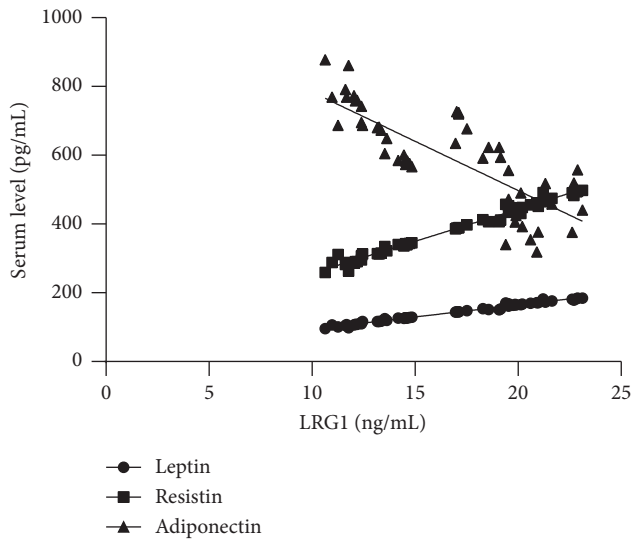

Figure 3: Correlation between LRG1 and adipokine expression in patients with psoriasis.

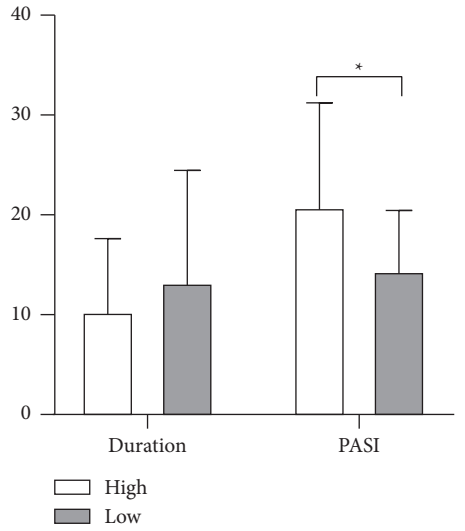

Figure 4: Differences in PASI and duration of disease between patients with high and low serum levels of LRG1.

inflammatory cells [17]. Research has indicated that leptin can aggravate the inflammatory response of keratinocytes, a process that is mediated by TNF-α and IL-17A. This can lead to the worsening of psoriatic lesions [18]. Resistin, like leptin, is closely associated with an individual's BMI and can promote inflammation by activating the nuclear factor kappa-B (NF-κB) signaling pathway in human macrophages and peripheral monocytes. This leads to the production of proinflammatory cytokines such as IL-6, IL-12, and TNF-α [19]. A positive correlation exists between the elevation of resistin levels and the severity of psoriasis, suggesting that resistin may play a role in the pathogenesis of psoriasis [20]. Adiponectin exhibits antiinflammatory effects, and its secretion levels are significantly low in patients with psoriasis [21]. It inhibits the expression of NF-κB and retinoid-related orphan receptor-γt (ROR-γt) while upregulating IL-10 secretion, which also inhibits the differentiation of Th17 cells and regulates toll-like receptors (TLRs). In response to this, TLRs exhibit antiinflammatory effects [15]. Our findings indicate a strong positive linear correlation between leptin and resistin expression and PASI. However, we did not observe a significant linear relationship between PASI and adiponectin expression, which may be attributed to sample size and other factors. These results provide sufficient evidence to support the strong association between adipokine expression and psoriasis.

LRG1 is a member of a highly conserved protein family that contains leucine-rich repeat domains. It is primarily synthesized by the liver and neutrophils and can be rapidly secreted in response to infection or inflammatory stimulation [5]. Increased levels and the ectopic expression of LRG1 are typically associated with disease pathology [5, 6]. In a recent study, the use of bio-orthogonal noncanonical amino-acid tagging (BONCAT) and mass spectrometry facilitated the characterization of LRG1 as a novel adipokine [22]. Another study showed that LRG1 mRNA and protein levels were significantly higher in adipose tissue than in liver tissue [9]. LRG1 has been shown to exert a beneficial impact on the survival and function of adipocytes. This can be attributed to its ability to inhibit adipocyte apoptosis through the RAS oncogene family member (RAB31) protein [23]. Currently, limited research is available on the connection between LRG1 and other adipokines. However, our findings revealed that LRG1 expression exhibited a significant positive linear correlation with leptin and resistin expression but a strong negative linear correlation with adiponectin expression. This suggested a close relationship between the expression of LRG1 and these three adipokines. Currently, LRG1 is being used as a marker to measure disease activity in rheumatoid arthritis and inflammatory bowel disease. Some researchers have suggested that it may also be useful in assessing and treating patients with psoriasis [8]. In our study, we found a positive correlation between LRG1 expression and PASI. Patients with higher serum LRG1 levels (≥15 ng/mL) also had a more active form of psoriasis and severe skin lesions ($P < 0.05$) compared to individuals with lower serum levels of LRG1. However, patients with lower serum levels of LRG1 tended to have a longer disease duration, although the difference in this parameter between the two groups was not statistically significant ($P > 0.05$). This may be because LRG1, as an acute-phase inflammatory protein, induces the production of inflammatory factors such as transforming growth factor-β (TGF-β), IL-1β, TNF-α, and IL-6. As a result, liver cells synthesize more LRG1, thus participating in a feedback mechanism that exacerbates psoriatic lesions and inflammation in the skin [7]. Another research has demonstrated that LRG1 plays a crucial role in enhancing the migration of keratinocytes and expediting the healing of skin injuries. This finding holds significant implications for the restoration of the skin barrier [24]. In conclusion, our findings suggest that LRG1 may work in conjunction with leptin/resistin to enhance the impact of psoriatic inflammatory factors. This mechanism highlights the potential role of adipokines in the pathogenesis of psoriasis.

The limitations of this study include its cross-sectional design, which only allowed for the analysis of correlations between variables and not causal relationships. In addition, the sample size may restrict the generalizability of our findings, and future studies with larger sample sizes are necessary to confirm our results. Further research is necessary to fully understand the mechanism of action and potential applications of LRG1 in treating psoriasis.

5. Conclusion

This study provides valuable insights into the relationship between psoriasis and adipokine expression. Patients with psoriasis often have higher levels of LRG1, leptin, and resistin as well as lower levels of adiponectin than healthy controls. The elevation of LRG1 levels was found to be closely associated with the development of psoriatic skin lesions and the expression of other adipokines, suggesting that LRG1 may work in conjunction with leptin/resistin to exacerbate psoriatic inflammation. This study is among the first to investigate the relationship between the expression of LRG1 and adipokines in individuals with psoriasis.

Data Availability

All data and figures are included within this paper, and further data are available upon request to the author by e-mail.

Ethical Approval

All participants were informed and agreed to blood sampling. This study has been approved by the Dongzhimen Hospital and Air Force Medical Center of PLA ethics committee (Registration number: 2022DZMEC-287-02).

Disclosure

Keshuai Liu and Lanzhi Li are the co-first authors.

Conflicts of Interest

The authors declare that there are no conflicts of interest.

Authors' Contributions

The article was authored by Keshuai Liu and Lanzhi Li with the assistance of Xingwu Duan. Yue Li, Hailing Dong, and Ziqing You were involved in data collation, validation, and review. Keshuai Liu and Lanzhi Li contributed equally to this work. All authors participated in the scientific discussion of the manuscript and approved of the submitted version.

Acknowledgments

We express our gratitude to those who have provided constructive comments to enhance the quality of this paper. In addition, we acknowledge the linguistic assistance provided by KetengEdit (https://www.ketengedit.com) in refining the language of this manuscript. This work was supported by the National Natural Science Foundation of China (Num: 82074436).

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