Journal of Advanced Zoology

ISSN: 0253-7214
*Volume **44** Issue **S-3 Year 2023** Page **1408:1416***

Study the Serum Levels of IL-17, IL-23, TLR-4, and TLR-7 Role in Immunopathogenesis in Patients with Moderate and Severe Psoriasis

Abdulla Hamad Abood[1*], Hassan Ali Hussein Al-Saadi[2]

[1,2]Department of Clinical Laboratories/College of Applied Medical Sciences/University of Iraq/Iraq.
Email: hassan.a@uokerbala.edu.iq[2]

**Corresponding author's E-mail: Abdullah.alhassnawi@gmail.com*

Article History

Received: 06 June 2023
Revised: 05 Sept 2023
Accepted: 13 Nov 2023

Abstract

Objective: *Psoriasis is an immune-mediated disease* (a disease with an unclear cause that is characterized by inflammation caused by dysfunction of the immune system) that causes inflammation in the body. This study examined the relationship between immunological markers (IL-17 and TLR-4) and several socio-demographic parameters, including age, sex, disease severity, stress, smoking behaviours, BMI classification, and dietary preferences, in patients with psoriasis.* ***Methods:*** *Psoriasis on patients at the Imam Al-Hussein City Hospital in Karbala Province, Iraq, psoriasis from December 2022 to April 2023. The participants were healthy individuals and newly diagnosed, untreated psoriasis patients. Pregnant women, those with chronic conditions, and those receiving psoriasis medication were excluded. A case-control observational study was conducted, using convenience sampling to select participants. The PASI scoring method was used to evaluate four body areas, and the sandwich ELISA method was used for immunomarker analysis.* ***Results:*** *The study found significant dispirited in the severity of psoriasis among individuals, with 54.44% presenting with intermediate symptoms and 45.56% showed severe manifestations. The moderate and severe psoriasis patients were classified into five age cohorts. The severity of psoriasis correlates with age, with those with severe psoriasis being older. Socio-demographic features revealed a greater prevalence of moderate patients than those with severe psoriasis. The study also found a significant association between greater BMI values and severe symptoms, smoking behaviours, elevated stress levels, and higher consumption of processed foods. Immunological markers such as IL-17, IL-23, TLR-4, and TLR-7 were also examined, showed significant variations between control participants and those with moderate and severe forms of the condition. These findings contributed to understanding the determinants impacting psoriasis severity and its clinical implications for patient care and therapeutic interventions.* ***Conclusion:*** *Psoriasis patients make up a significant part of the study population, with higher smoking, stress, and healthy food habits. There was no significant difference in BMI, disease severity. of immunological markers IL-17, IL-23, TLR-4, and TLR-7 showed a significantly increase.*

Keywords: *IL-17, IL-23, TLR-4, TLR-7, BMI, Severity, Artificial food*

1. Introduction

Psoriasis is an autoimmune disease with a prevalence of roughly 2-3% among the worldwide populace (1). Extensive research efforts have been dedicated to investigating this intricate illness; nonetheless, a comprehensive understanding of its precise aetiology and pathophysiology is still lacking. The role of immunological dysregulation in the pathogenesis and advancement of psoriasis has been well acknowledged. Several cytokines and innate immune receptors have been identified as significant contributors within the complex network of immune responses associated with this condition (2,3).

Psoriasis is a skin condition characterised by erythematous plaques coated with white-silver scales, most often on the extensor surfaces of the body (e.g., elbow, knee, lumbosacral areas, scalp). Psoriasis comes in many different manifestations, the most common of which is plaque psoriasis (psoriasis vulgaris), but others include flexural or inverse Psoriasis, guttate Psoriasis, pustular psoriasis, erythrodermic Psoriasis, and psoriatic arthritis. Nearly 90% of all instances of psoriasis are caused by

plaque psoriasis. The condition affects both sexes equally, with an incidence of 1%-3% depending on the community. There is an increased chance of psoriasis among first-degree relatives of those with the condition. Although its precise cause is unknown, genetic, environmental, and autoimmune variables are all thought to have a role in the development of Psoriasis (4,5).

The significance of Interleukin-17 (IL-17) and Interleukin-23 (IL-23) has been the subject of much research in recent times, primarily owing to their crucial involvement in regulating immunological responses and their correlation with the development of autoimmune disorders, such as psoriasis (6). The cytokines mentioned in this context have been identified as agents that facilitate the stimulation and attraction of inflammatory cells towards the skin, resulting in the distinctive inflammation and excessive growth of keratinocytes observed in psoriatic lesions (7).

Besides IL-17 and IL-23, Toll-like receptors (TLRs), particularly TLR-4 and TLR-7, play a crucial role as integral constituents of the innate immune system, responsible for the recognition of pathogen-associated molecular patterns (PAMPs) and damage-associated molecular patterns (DAMPs). An increasing body of data indicates that these receptors may play a role in the immunopathogenesis of Psoriasis by initiating abnormal immune responses to endogenous ligands. The activation of Toll-like receptor 4 (TLR-4) and Toll-like receptor 7 (TLR-7) has been implicated in the promotion of inflammatory cytokine production, which in turn contributes to the persistent inflammation observed in psoriatic lesions (8,9).

The primary aim of this study is to provide a comprehensive understanding of the role played by IL-17, IL-23, TLR-4, and TLR-7 in the immunopathogenesis of Psoriasis.

2. Materials And Methods

This study is an observational case-control study with consecutive sampling containing 40 healthy controls and 50 psoriasis patients. The subjects for this study consist of patients undergoing Psoriasis in the unit of Dermatology in the Hospital of Imam Al-Hussein City in Karbala province, Iraq, from December 2022 to April 2023. The postgraduate committee of the Clinical Laboratories Department, College of Applied Medical Sciences of Kerbala University, Karbala, Iraq, approved the study. Patients were taken for this study after the dermatologist diagnosed them. The patients were divided into two groups. All patients performed an ethical consent to enrolls in this study. The inclusion criteria were Healthy patients who underwent the clinical dermatology department, were newly diagnosed with Psoriasis, and were not under any treatment. The exclusion criteria were pregnant women, Patients with chronic diseases (celiac + autoimmune), and Patients who received treatment for Psoriasis.

The collected data was analyzed using the Statistical Packages for Social Sciences- version 28 (SPSS-28), a widely used statistical software package. Statistical tests such as the student's t-test were employed for independent means to determine the significance of differences in means for quantitative data. In contrast, the paired t-test was utilized for paired observations or dependent means. For qualitative data, the chi-square test was used. Spearman's rank correlation coefficient (Spearman rho) was calculated to examine the correlation between variables. The scattering distribution curve was employed to visualize the correlation pattern. In assessing statistical significance, a p-value ≤ 0.05 was considered the threshold (10).

3. Results and Discussion

The statistical analysis indicated a significant variation in disease severity among psoriasis patients, with the majority (54.44%) exhibiting moderate symptoms and the remainder (45.56%) displaying severe signs, as shown in Figure (1). Despite this disparity in illness severity distribution, the study revealed a statistically significant difference between the two groups ($p = 0.0461$). These results had significant implications for comprehending the severity range of Psoriasis in afflicted people. The substantially more significant proportion of moderate instances highlighted the prevalence of milder symptoms, which may have had significant consequences for patient management and treatment strategies. On the other hand, severe instances necessitate heightened vigilance since patients with more severe symptoms may need more intense and specialist treatment.

Analysing several variables that may have contributed to this result was crucial. A bigger sample size might have more solid insights into the illness severity distribution. In addition, the psoriasis patients' variety of psoriasis symptoms complicates the categorisation of individuals into various severity categories, resulting in the possibility of overlapping symptomatology. In addition, the absence of statistical significance does not undermine the clinical importance of the observed heterogeneity in illness severity. It is essential to recognised the possible effect of other variables on psoriasis severity, including genetic predisposition, environmental triggers, lifestyle, and treatment history. Unaccounted-for confounding factors may have contributed to the reported results (11).

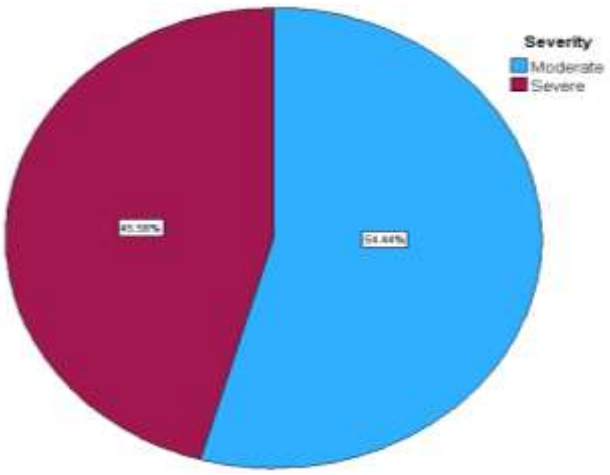

Figure (1): Comparison between the severity of psoriasis patients

The age range of psoriasis patients was divided into five age groups for moderate and severe cases, as illustrated in Table (1). These groups were divided into 2-15 years, 16-25 years, 26-35 years, 36-51 years, and Above 51 years. A significant difference was found between the moderate and severe psoriasis patients for all groups. There was a significant difference between the psoriasis severity groups for total psoriasis patients (moderate and severe). From observation, the severe psoriasis patients were older than moderate in the age groups of 16 -25 years and 36 – 51 years, while the moderate psoriasis patients were older than severe in the age groups of 2 – 15 years, 26 - 36 years, and above 51 years.

Table (1): Age group distribution of psoriasis patients

Age groups	Patients	N	Mean± SD	*p*-value
2-15 year	**Moderate**	2	13.50 ± 0.50	NA
	Sever	1	13	
16-25 year	**Moderate**	5	18.40 ± 1.12	0.13845
	Sever	7	21.14 ± 1.28	
26-35 year	**Moderate**	3	30.00 ± 2.08	0.230698
	Sever	3	27.00 ± 0.12	
36-51 year	**Moderate**	10	44.50 ± 1.42	0.788874
	Sever	14	45.00 ± 1.16	
Above 51 years	**Moderate**	3	63.33 ± 5.66	0.423887
	Sever	2	57.50 ± 2.50	
Total	**Moderate**	23	36.69 ± 3.45	< 0.001*
	Sever	27	36.55 ± 2.58	< 0.001*
*** Independent T-Test is significant at the 0.05 level**				

The socio-demographic characteristics of psoriasis patients were distributed according to the disease severity and presented in Table (2). The moderate patients were more than the severe psoriasis patients. The moderate percentage was higher than the severe patients. The severe patients were older than moderate with no significant difference, as shown in Figure (2). The moderate psoriasis patients had a higher minimum and maximum age than the severe psoriasis patients.

The body mass index comparison between the severe and moderate psoriasis patients classified according to obesity into underweight, healthy weight, overweight, and obese. It was shown that the psoriasis patients with severe symptoms had a significantly higher BMI than those with moderate symptoms. Moreover, the psoriasis patients with smoking habits were significantly higher in severe patients than those with moderate symptoms. As previously mentioned, the severe psoriasis patients had more significant stress and tended to consume artificial foods than moderate psoriasis patients.

Table (2): Socio-demographic characteristics of moderate and severe psoriasis patients.

Socio-demographic Characteristics		Moderate	Severe	*p*-value
Sex	**Male**	9	10	0.879192
	Female	14	17	
BMI	**Underweight**	17.23 ± 1.21	17.72	<0.001*
	Healthy Weight	23.78 ± 0.56	22.47 ± 1.66	

	Overweight	27.34 ± 1.17	26.85 ± 0.95	
	Obesity	33.73 ± 3.90	36.96 ± 5.91	
	Total	26.47 ± 6.01	27.51 ± 6.95	
Smoking	**Smoker**	13 %	33 %	<0.001*
	Non-Smoker	87 %	67 %	<0.001*
Stress	**Stressful**	43%	55%	<0.001*
	Non-Stressful	57%	45 %	<0.0321*
Consuming Artificial Food	**Yes-consumed**	48 %	63 %	<0.001*
	No-consumed	52 %	37 %	<0.001*
*** Significant at the ≤0.05 level.**				

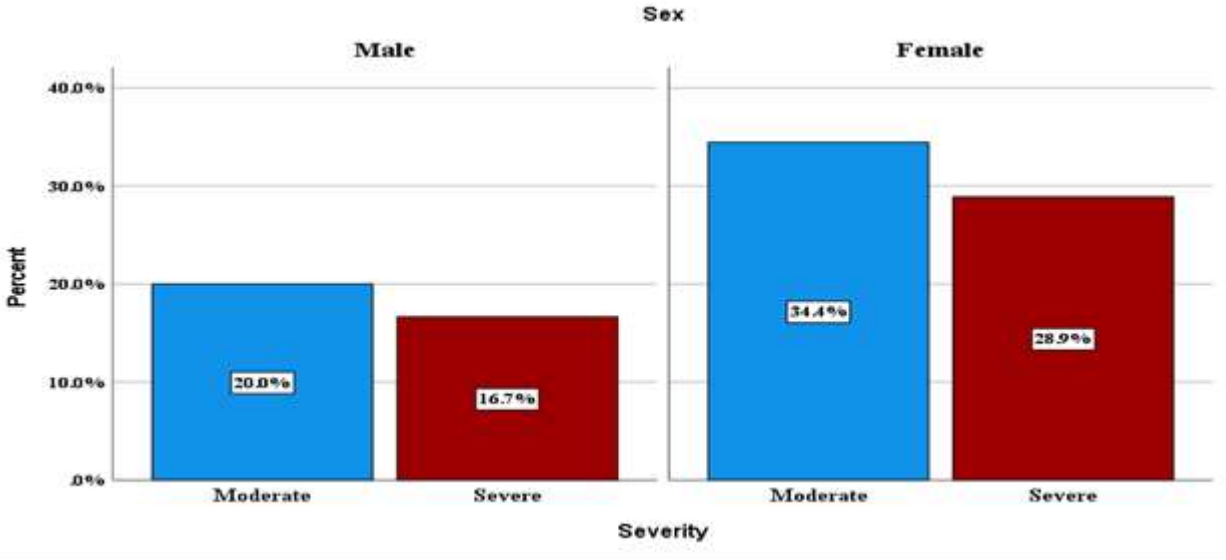

Figure (2): Sex distribution comparison between the moderate and severe psoriasis patients

This study showed that the age differences between people with severe and mild Psoriasis may be attributable to genetic predisposition, lifestyle decisions, and environmental variables. Also, the severity of Psoriasis may change with age, which may explain the age-related discrepancies (12,13).

The higher BMI in individuals with severe psoriasis might be attributable to several variables. Due to their illness, people with severe psoriasis may engage in less physical activity, leading to weight gain. In addition, obesity and severe Psoriasis may share some risk factors (14). Li et al.'s study compared the clinical features of two groups of Chinese psoriasis patients who differed mainly by their BMI (BMI). The study included a comprehensive data review from 208 people diagnosed with Psoriasis. Patients who were overweight or obese were placed in one group, while those with a healthy weight were placed in another. Also, compared to psoriasis patients with normal BMI levels (p>0.05), those with overweight or obesity had a significantly greater incidence of comorbidities such as fatty liver, hyperlipidaemia, hyperuricemia, and impaired liver function. Using linear regression analysis, the authors found a clear correlation between PASI scores and body mass index (p=0.016). This statistical evidence highlighted the connection between psoriasis severity and increased body mass index. Patients with Psoriasis who are overweight or obese are at a higher risk for acquiring metabolic comorbidities and have psoriatic lesions that are more severe on average. Therefore, it is inferred that a thorough assessment of patients' body mass index (BMI) is necessary for those with psoriasis. People who are overweight or obese and have psoriasis may need to lose weight or use other weight management strategies to reduce their risk of metabolic problems. These results add much to our understanding of how psoriasis, body mass index, and health outcomes are interconnected (15).

This study indicated that the increased incidence of smoking among psoriasis patients with severe psoriasis may be attributable to the fact that smoking is a risk factor for psoriasis and may aggravate the illness. Individuals with severe psoriasis may be more likely to engaged in harmful behaviours like smoking.

The scholarly review by Naldi explored the complex relationship between smoking and various health conditions, highlighting the role of genetic, environmental, and social factors. The main addictive component in tobacco, nicotine, is responsible for the habit-forming nature of tobacco products. Smoking is a significant risk factor for various diseases, including cardiovascular ailments, respiratory

disorders, cancer, and global mortality. The review also highlights the association between smoking and immune-related inflammatory conditions, such as Psoriasis. Smoking influences the onset of Psoriasis, with a higher risk for smokers consuming 1-14 cigarettes per day and more for those consuming 25 or more. Smoking also affects the clinical severity of Psoriasis and its treatment responsiveness and contributes to comorbidities like cardiovascular disease, inflammatory bowel disease, and various cancers. The review explores potential pathophysiological mechanisms underlying the association between Psoriasis and smoking, including oxidative stress, interactions with signalling pathways, and vascular influences (16).

In this study, the increased stress experienced by individuals with severe Psoriasis may result from the psychological load of managing a more severe and possibly debilitating skin disease. Stress was a recognised cause of psoriasis flare-ups, so it may aggravate the severity of the illness in certain instances.

Rigas *et al.* (17) reported that 3-5% of individuals in affluent nations have psoriasis. In addition, it is among the top dermatological complaints seen in primary care settings. Stress and depression have been linked to psoriasis' development, aggravation, and treatment resistance. They want to investigate the massive amount of study investigating Psoriasis's devastating effects on people's mental health. We are also looking to make a direct relationship between the disease's severity and its emotional aftereffects. The idea is to get people thinking about how their mental health is connected to their skin health so that they may take preventive actions. People living with Psoriasis may benefit from a multidisciplinary approach to therapy if the complex relationship between a person's mental health and skin condition is better understood. This review demonstrates that the psychological effects of Psoriasis should be considered an essential part of patient care and treatment (17).

An agreement was found in a study conducted by Tribó *et al*., 2019. According to the studies conducted by Tribó *et al.*, 2019 (18), Psoriasis is more than just an annoying skin illness; it is also associated with severe psychological and physiological complications. The role of stress and emotional disturbances in developing and exacerbating Psoriasis has come into focus. A total of 300 people with Psoriasis were evaluated to see if there was an association between the severity of the condition and their levels of stress and mood changes. Validated questionnaires that assessed things like stress and emotional state. The effect that Psoriasis has on the lives of those who have it was also measured in this study. The study's results revealed a correlation between the severity of Psoriasis and emotional distress and negative impacts on participants' quality of life ratings. The severity of the disease was found to be directly correlated with the increased risk of depression as measured by several essential depression assessment tools, including the Montgomery-Asberg Depression Rating Scale, the Hamilton Rating Scale, and the Hospital Anxiety and Depression Scale for Depression. The relevance of the correlation between depressive symptoms, anxious states, self-perceived stress, and psoriasis severity cannot be overstated. It highlights the need to consider patients' mental health when developing a care plan for Psoriasis. To improve the well-being and results of people dealing with Psoriasis, it is crucial to identify and treat the psychological elements of the illness (18).

In this study, psoriasis may influence patients' healthy habits and food choices; for example, those with severe Psoriasis may consume more processed foods. People with severe Psoriasis may react to their illness or manage stress by making poor food choices.

The study by Garbicz *et al*. focused on Psoriasis, a chronic inflammatory skin condition with multiple etiological factors, including dietary considerations. The study suggests that dietary modifications can improve a patient's quality of life by reducing skin lesions and mitigating the risk of concurrent health issues. One recommendation is a low-energy diet for overweight patients, which can help manage psoriasis symptoms. The study also emphasises the importance of dietary fat composition, suggesting a reduction in saturated fatty acids and a preference for polyunsaturated fatty acids from the omega-3 family. Another study also recommended the inclusion of antioxidants like vitamin A, vitamin C, vitamin E, carotenoids, flavonoids, and selenium in diet therapy. Vitamin D supplementation is also recommended, as it affects immune regulation. The study also explores alternative dietary approaches, such as gluten-free, vegetarian, and Mediterranean diets, which could positively impact psoriasis treatment (19).

Kanda et al.'s review focused on Psoriasis, a persistent inflammatory skin condition with comorbidities like obesity, diabetes, dyslipidemia, cardiovascular disorders, and inflammatory bowel diseases. Psoriasis patients often have dietary imbalances, with increased fat consumption and reduced fish and dietary fibre intake. Nutrition plays a crucial role in psoriasis development and progression.

Consumption of saturated fatty acids, simple sugars, red meat, and alcohol can exacerbate Psoriasis by activating pathways involved in inflammation. Conversely, certain nutrients and dietary elements, such as n-3 polyunsaturated fatty acids, vitamin D, vitamin B12, short-chain fatty acids, selenium, genistein, dietary fibres, and probiotics, can mitigate Psoriasis by suppressing inflammatory pathways or promoting regulatory T cell induction. Imbalances in gut microbiota and vitamin D and selenium deficiencies further contribute to psoriasis progression (20).

Muzumdar and Rothe's literature review examined the use of nutrition and dietary supplements in psoriasis management. While these interventions are widely used, their effectiveness is not uniformly conclusive. The review indicated that caloric restriction, particularly in overweight or obese individuals, has a consistent positive impact on reducing psoriatic activity. However, the evidence surrounding other dietary supplements and interventions was less clear and lacked consistency. The review emphasises the need for more extensive, extended study studies to establish a more comprehensive understanding of how dietary interventions can effectively manage psoriasis and alleviate symptoms. While caloric restriction shows promise, further study is needed to better understand nutrition's role in psoriasis management and potentially offer alternatives to pharmaceutical treatments (21).

The comparative study between the control and psoriasis patients of moderate and severe diseases for immune markers IL-17, IL-23, TLR-4, and TLR-7 were shown in tables (3), (4), (5), and (6), respectively. The analysis showed a significant difference in the levels of immune markers (IL-17, IL-23, TLR-4, and TLR-7) between the control and psoriasis patients of moderate and severe psoriasis patients. The control always showed a lower level, while the levels increased in moderate, and higher levels were shown in severe psoriasis patients.

Table (3): The IL-17 levels for control, moderate, and severe psoriasis patients.

		N	Mean ± SD	*p*-value
IL 17	Control	40	178.82 ± 6.03	<0.001*
	Moderate Psoriasis	23	506.16 ± 31.52	
	Severe Psoriasis	27	514.09 ± 20.77	
	Total	90	363.06 ± 20.31	
* Significant at the ≤0.05 level.				

Table (4): The IL-23 levels for control, moderate, and severe psoriasis patients.

		N	Mean	*p*-value
IL 23	Control	40	344.28 ± 8.32	<0.001*
	Moderate Psoriasis	23	753.12 ± 24.36	
	Severe Psoriasis	27	778.51 ± 28.36	
	Total	90	577.90± 24.65	
* Significant at the ≤0.05 level.				

Table (5): The TLR-4 levels for control, moderate, and severe psoriasis patients.

		N	Mean ± SD	*p*-value
TLR 4	Control	40	233.71 ± 5.64	<0.001*
	Moderate Psoriasis	23	647.03 ± 37.02	
	Severe Psoriasis	27	657.93 ± 19.13	
	Total	90	463.60 ± 24.49	
* Significant at the ≤0.05 level.				

Table (6): The TLR-7 levels for control, moderate, and severe psoriasis patients.

		N	Mean	*p*-value
TLR 7	Control	40	1.47 ± 0.03	<0.001*
	Moderate Psoriasis	23	3.35 ± 0.11	
	Severe Psoriasis	27	3.38 ± 0.13	
	Total	90	2.52 ± 0.11	
* Significant at the ≤0.05 level.				

This study showed a significant difference in the levels of immunological markers (IL-17, IL-23, TLR-4, and TLR-7) between control people and psoriasis patients, exceptionally moderate and severe. Consistently lower levels of these immunological markers in control people compared to psoriasis patients, particularly those with severe psoriasis, are consistent with psoriasis, characterized by immune responses and chronic inflammation.

Interleukin-17 (IL-17) and interleukin-23 (IL-23) are pro-inflammatory cytokines directly connected with psoriasis aetiology. IL-23 has a role in the development and maintenance of IL-17-producing Th17 cells. In psoriasis, both IL-17 and IL-23 contribute to the inflammatory cascade. Prior study has repeatedly shown higher levels of IL-17 and IL-23 in psoriatic lesions and the circulation of psoriasis patients, providing support for the present results (6,22).

TLR-4 and TLR-7 are essential components of the innate immune system, recognizing pathogen-associated molecular patterns (PAMPs) and the induction of immune responses. TLR 4 and TLR 7 recognize some pathogens, such as bacteria and viruses. These receptors are often hyperactive in psoriasis, increasing immune response. This data is consistent with prior studies demonstrating elevated TLR 4 and TLR 7 activation in psoriatic lesions, contributing to psoriasis-specific chronic inflammation (23).

In addition, the study offered evidence that the overexpression of TLR7 and TLR4 in individuals with psoriasis may stimulate the production of pro-inflammatory cytokines and chemokines. TLR activation in the skin may induce the generation of cytokines, including IL-17, IL-23, and TNF-, which are known to play crucial roles in the pathogenesis of psoriasis. These cytokines' elevated levels lead to the growth of keratinocytes, the recruitment of immune cells, and the creation of psoriatic plaques. In addition, the interaction between TLRs and cytokines may generate a positive feedback loop that sustains the inflammatory response and contributes to the chronicity of illness (24,25).

The study's findings also align with a previous study by Smith et al. 2016 (Smith et al., 2016), suggesting that TLR7 and TLR4 signaling may be involved in the development and progression of psoriasis. Other studies have reported the presence of TLR7 and TLR4 in psoriatic skin lesions, indicating their localization and potential roles in psoriasis immunopathogenesis. The higher serum levels of these TLRs in psoriasis patients support the hypothesis that systemic immune dysregulation involving TLR activation may contribute to the disease's widespread manifestations (27–29).

The investigation of the function of IL-23 in psoriasis, specifically its potential as an early mediator in the production of psoriatic lesions and its role in boosting innate immunity (30). Multiple studies have shown higher IL-23 expression in psoriatic lesions, both at the level of mRNA and in terms of overproduction by dermal dendritic cells and keratinocytes (31–33). In addition, several cell types, including Th-17, CD8+ T, and natural killer T cells, have been identified as producing IL-23 (34,35).

Intriguingly, psoriasis medication, including conventional and biological systemic therapies, has been linked to IL-23 downregulation in psoriatic patients (36,37).

4. Conclusion

In conclusion, psoriasis is a persistent autoimmune dermatological condition distinguished by the presence of erythematous and desquamating plaques. This research offered possible influence of dietary choices and body mass index (BMI) on the severity of psoriasis has been noted. Individuals with severe psoriasis often have an elevated body mass index (BMI) and are more prone to engaging. They were health-promoting behaviours, such as smoking and the consumption of processed for consumed findings underscore the findings mentioned above changes as a means of managing psoriasis. There to manage in immunological markers, including as IL-17, IL-23, TLR-4, and TLR-7, between those with psoriasis and those diagnosed with the condition. Psoriasis patients, particularly those with severe manifestations, have heightened levels of these markers. Psoriasis is characterised by response and persistent inflammation, which are closely linked to the indicators under consideration.

References:

1. Lowes MA, Bowcock AM, Krueger JG. Pathogenesis and therapy of psoriasis. Vol. 445, Nature. 2007.
2. Rendon A, Schäkel K. Psoriasis pathogenesis and treatment. Vol. 20, International Journal of Molecular Sciences. 2019.
3. Kanda N. Psoriasis: Pathogenesis, comorbidities, and therapy updated. Vol. 22, International Journal of Molecular Sciences. 2021.
4. Li J, Chen X, Liu Z, Yue Q, Liu H. Expression of Th17 cytokines in skin lesions of patients with psoriasis. Journal of Huazhong University of Science and Technology - Medical Science. 2007;27(3).

5. Krueger JG, Fretzin S, Suárez-Fariñas M, Haslett PA, Phipps KM, Cameron GS, et al. IL-17A is essential for cell activation and inflammatory gene circuits in subjects with psoriasis. Journal of Allergy and Clinical Immunology. 2012;130(1).
6. Hawkes JE, Yan BY, Chan TC, Krueger JG. Discovery of the IL-23/IL-17 Signaling Pathway and the Treatment of Psoriasis. The Journal of Immunology. 2018;201(6).
7. Menter A, Krueger GG, Paek SY, Kivelevitch D, Adamopoulos IE, Langley RG. Interleukin-17 and Interleukin-23: A Narrative Review of Mechanisms of Action in Psoriasis and Associated Comorbidities. Vol. 11, Dermatology and Therapy. 2021.
8. Nie L, Cai SY, Shao JZ, Chen J. Toll-Like Receptors, Associated Biological Roles, and Signaling Networks in Non-Mammals. Vol. 9, Frontiers in Immunology. 2018.
9. Duan T, Du Y, Xing C, Wang HY, Wang RF. Toll-Like Receptor Signaling and Its Role in Cell-Mediated Immunity. Vol. 13, Frontiers in Immunology. 2022.
10. Moore DS, McCabe GP, Craig BA, McCabe GP, Craig BA. Introduction to the Practice of Statistics. 9th Ed. Macmillan Learning. Macmillan Learning; 2021. 20–35 p.
11. van Acht MR, van den Reek JM, de Jong EM, Seyger MM. The Effect of Lifestyle Changes on Disease Severity and Quality of Life in Patients with Plaque Psoriasis: A Narrative Review. Psoriasis: Targets and Therapy. 2022;Volume 12.
12. Kamiya K, Kishimoto M, Sugai J, Komine M, Ohtsuki M. Risk factors for the development of psoriasis. Vol. 20, International Journal of Molecular Sciences. 2019.
13. Alexis AF, Blackcloud P. Psoriasis in skin of color: Epidemiology, genetics, clinical presentation, and treatment nuances. Journal of Clinical and Aesthetic Dermatology. 2014;7(11).
14. Armstrong AW, Harskamp CT, Armstrong EJ. The association between psoriasis and obesity: A systematic review and meta-analysis of observational studies. Vol. 2, Nutrition and Diabetes. 2012.
15. Li L, Liu K, Duan X, Xu L, Yang Q, Liu F. A Comparison of Clinical Characteristics in Overweight/Obese and Normal Weight Patients with Psoriasis Vulgaris: A Bicentric Retrospective Observational Study. Clin Cosmet Investig Dermatol. 2023;16.
16. Naldi L. Psoriasis and smoking: Links and risks. Vol. 6, Psoriasis: Targets and Therapy. 2016.
17. Rigas HM, Bucur S, Ciurduc DM, Nita IE, Constantin MM. Psychological Stress and Depression in Psoriasis Patients - a Dermatologist's Perspective. Maedica (Bucur). 2019;14(3).
18. Tribó MJ, Turroja M, Castaño-Vinyals G, Bulbena A, Ros E, Garcíamartínez P, et al. Patients with moderate to severe psoriasis associate with higher risk of depression and anxiety symptoms: Results of a multivariate study of 300 Spanish individuals with psoriasis. Acta Derm Venereol. 2019;99(4).
19. Garbicz J, Całyniuk B, Górski M, Buczkowska M, Piecuch M, Kulik A, et al. Nutritional therapy in persons suffering from psoriasis. Vol. 14, Nutrients. 2022.
20. Kanda N, Hoashi T, Saeki H. Nutrition and psoriasis. Vol. 21, International Journal of Molecular Sciences. 2020.
21. Muzumdar S, Rothe MJ. Nutrition and psoriasis. Clin Dermatol. 2022;40(2).
22. Menter A, Krueger GG, Paek SY, Kivelevitch D, Adamopoulos IE, Langley RG. Interleukin-17 and Interleukin-23: A Narrative Review of Mechanisms of Action in Psoriasis and Associated Comorbidities. Vol. 11, Dermatology and Therapy. 2021.
23. Georgescu SR, Tampa M, Caruntu C, Sarbu MI, Mitran CI, Mitran MI, et al. Advances in understanding the immunological pathways in Psoriasis. Vol. 20, International Journal of Molecular Sciences. 2019.
24. Fitch E, Harper E, Skorcheva I, Kurtz SE, Blauvelt A. Pathophysiology of psoriasis: Recent advances on IL-23 and TH17 cytokines. Vol. 9, Current Rheumatology Reports. 2007.
25. Lee BW, Moon SJ. Inflammatory Cytokines in Psoriatic Arthritis: Understanding Pathogenesis and Implications for Treatment. Int J Mol Sci [Internet]. 2023;24(14). Available from: https://www.mdpi.com/1422-0067/24/14/11662
26. Smith RL, Hébert HL, Massey J, Bowes J, Marzo-Ortega H, Ho P, et al. Association of Toll-like receptor 4 (TLR4) with chronic plaque type psoriasis and psoriatic arthritis. Arch Dermatol Res. 2016;308(3).
27. Chen L, Guo S, Ranzer MJ, Dipietro LA. Toll-like receptor 4 has an essential role in early skin wound healing. Journal of Investigative Dermatology. 2013;133(1).
28. Sun L, Liu W, Zhang LJ. The Role of Toll-Like Receptors in Skin Host Defense, Psoriasis, and Atopic Dermatitis. Vol. 2019, Journal of Immunology Research. 2019.
29. Bacharewicz J, Reduta T, Flisiak I. The role of Toll-like receptors in skin diseases. Dermatology Review. 2014;4.
30. El-Hadidi H, Samir N, Shaker OG, Otb S. Estimation of tissue and serum lipocalin-2 in psoriasis vulgaris and its relation to metabolic syndrome. Arch Dermatol Res. 2014;306(3).
31. Res PCM, Piskin G, de Boer OJ, van der Loos CM, Teeling P, Bos JD, et al. Overrepresentation of IL-17A and IL-22 Producing CD8 T Cells in Lesional Skin Suggests Their Involvement in the pathogenesis of psoriasis. PLoS One. 2010;5(11).
32. Gordon KB, Duffin KC, Bissonnette R, Prinz JC, Wasfi Y, Li S, et al. A Phase 2 Trial of Guselkumab versus Adalimumab for Plaque Psoriasis. New England Journal of Medicine. 2015;373(2).
33. Wilson BG, Bahna SL. Adverse reactions to food additives. Vol. 95, Annals of Allergy, Asthma and Immunology. 2005.

34. Eyerich S, Eyerich K, Pennino D, Carbone T, Nasorri F, Pallotta S, et al. Th22 cells represent a distinct human T cell subset involved in epidermal immunity and remodeling. Journal of Clinical Investigation. 2009;119(12).
35. Eyerich K, Pennino D, Scarponi C, Foerster S, Nasorri F, Behrendt H, et al. IL-17 in atopic eczema: Linking allergen-specific adaptive and microbial-triggered innate immune response. Journal of Allergy and Clinical Immunology. 2009;123(1).
36. Johnson-Huang LM, Lowes MA, Krueger JG. Putting together the psoriasis puzzle: An update on developing targeted therapies. Vol. 5, DMM Disease Models and Mechanisms. 2012.
37. Di Cesare A, Di Meglio P, Nestle FO. The IL-23Th17 axis in the immunopathogenesis of psoriasis. Vol. 129, Journal of Investigative Dermatology. 2009.