

# Systemic Immune Inflammatory Index Is Associated with Pustular Psoriasis: A Single Center Retrospective Study

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## Abstract

**Introduction:** Psoriasis is a chronic multi-systemic inflammatory skin disease that presents with erythema, thickness, and scaling of the skin. Genetic and environmental factors are associated with its etiology. Recently systemic immune inflammatory index, has been proposed as a biomarker for prognosis and severity prediction. Although it has been studied in psoriasis in general, no study exists for its association with the individual types of psoriasis. This study thus aimed to determine its association with clinical characteristics of psoriasis subtypes. **Materials and Methods:** Data were retrospectively retrieved from the hospital electronic medical database from January 2020 to August 2022. Only patients with CBC results were included. Clinical data retrieved were: Patients' age, gender, type of psoriasis diagnosed, body mass index, duration of the disease, family history of psoriasis, history of smoking, diabetes, and hypertension records. Laboratory data retrieved were: Complete blood count (CBC), C-reactive protein, Immunoglobulin E (IgE), Total cholesterol, Triglycerides and Low-density lipoprotein cholesterol. Data were analyzed in SPSS and GraphPad prism. **Results:** The study enrolled 85 patients with psoriasis; 56.47% males, and 43.53% females. 7.6% had psoriasis for less than 10 years, while 42.4% had the disease for more than 10 years. Psoriasis vulgaris was the most common diagnosis, 41.2%, followed by p. pustular, 30.6% and then p. erythroderma 28.2%. Mean age  $\pm$  SD of the p. vulgaris, p. pustular and p. erythroderma patients were  $47.3 \pm 15.3$ ;  $45.3 \pm 14.6$ , and  $57.1 \pm 11.7$  respectively. SII was significantly higher in p. pustular than the rest, ( $p < 0.0001$ ). SII was significantly associated with hypertension p. pustular patients. C-reactive protein was significantly upregulated in both psoriasis pustular and erythroderma but not vulgaris (all  $p < 0.001$ ), while leukocytosis was observed in psoriasis pustular. **Conclusion:** In summary, systemic immune inflammatory index (SII) was significantly higher in psoriasis pustular

than other subtypes of psoriasis, and had an association with hypertension in psoriasis pustular patients. These findings suggest a possible association between SII and psoriasis pustular that should be investigated in an independent study.

## Keywords

Systemic, Immune, Inflammatory, Index, Psoriasis, Pustular

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## 1. Introduction

Psoriasis is a chronic multi-systemic inflammatory skin disease affecting approximately 1% - 3% of the world population [1]. The global prevalence of psoriasis is estimated to be between 0.09% and 11.43% [2], varying from 0.23% to 0.47% in Asian countries, and 2.3% to 3.2% in Europe and the United States [3], while prevalence by age varies from 0.02% to 0.21% in children to 0.14% and 2% in adults respectively. Its subtypes include psoriasis vulgaris, psoriasis pustular, psoriasis erythroderma and other relatively rare variants [4]. In China, p. vulgaris accounts for 82.6% - 97.9% of all cases, while p. pustular and p. erythroderma account for 0.69% - 2.17%, and 0% - 8.7% respectively [5]. Psoriasis is strongly mediated by genetic susceptibility, autoimmune disease, and environmental factors including infection, stress, and trauma. Its pathogenesis is closely related to the abnormal interaction among innate immunity, T cells, and keratinocytes [6]. Average age of onset is approximately 33 years, with two peaks of onset; the first at age 20 to 30 years and the second at age 50 to 60 years [7].

Psoriasis manifests as erythema, thickness, and scaling of the skin, with the skin area often appearing red, itchy, scaly, burning, and sore [8] [9]. Associated comorbidities include: autoimmune diseases, cardiovascular diseases, infections, cancers, metabolic diseases, mental diseases, and psoriatic arthritis [10]. Although the genetic predisposition, pathogenesis, and management of psoriasis are better known today, it still remains incurable [11], with treatment primarily focused on reducing symptoms and enhancing quality of life. Although psoriasis is difficult to treat, various attempts are being made to manage the condition. However, prognosis prediction remains poor, making it hard to evaluate disease severity and patients' treatment progress. Recently systemic immune inflammatory index, has been explored as a biomarker for prognosis and severity prediction of psoriasis. Using the neutrophils, platelet, and lymphocyte, an index is calculated, that is then correlated to the severity and prognosis of the disease [8] [12].

Given the existing variations in how the different types of psoriasis present, with overlaps at certain points, it's important to know the key clinical characteristics of each, and how they interact to influence the disease progression and severity. Therefore, in this study, we assessed the association between systemic immune inflammatory index and the clinical characteristics of each of the three types of psoriasis, in order to assess how it can be used to monitor prognosis and

disease severity in each of them individually.

## 2. Materials and Methods

This was a retrospective study conducted at the First Hospital of Jilin University, in Chaoyang District, Changchun, Jilin, China, from January 2020 to August 2022. Patient data was retrospectively retrieved from the electronic medical database. Patient selection was limited to the availability of complete blood count (CBC) records as the key selection criterion. Patients without CBC results or incomplete results were excluded. A total of 85 patients had their records retrieved; these included 35 for psoriasis vulgaris, 26 for psoriasis pustular and 24 for psoriasis erythroderma. The study was conducted in accordance with the Declaration of Helsinki. Study protocol was approved by the First Hospital of Jilin University Research Ethics Committee and patient consent was waived since the data were retrospectively collected. Clinical data retrieved were: Patients' age, gender, type of psoriasis diagnosed, body mass index, duration of the disease, family history of psoriasis, history of smoking, diabetes, and hypertension records. Laboratory data retrieved were: Complete blood count (CBC), C-reactive protein, Immunoglobulin E (IgE), Total cholesterol, Triglycerides and Low-density lipoprotein cholesterol.

### 2.1. Systemic Inflammatory Indices

Neutrophil-lymphocyte ratios (NLR) were calculated from the CBC results as absolute neutrophil count divided by absolute lymphocyte count ( $\#N/\#L$ ), while systemic inflammatory indices, (SII) were calculated from the platelet count and the neutrophil-lymphocyte ratios as  $P*NLR$ .

### 2.2. Data Analysis

Data analysis was conducted using Microsoft excel software version 2013, (Microsoft Inc. USA), GraphPad prism version 8.0.2 (GraphPad software Inc. USA), and Statistical Package for the Social Sciences (SPSS) version 22. (IBM Inc. USA). Continuous variables were summarized as mean  $\pm$  standard deviation, while categorical variables were summarized as numbers and percentages. The student's independent T-test and one-way ANOVA were used to evaluate difference among group means for continuous data, while Pearson's Chi-square test or Fischer's exact test was used to determine the differences between categorical variables. Statistical significance was set at a two-sided  $p < 0.05$ .

## 3. Results

### 3.1. Patient Characteristics

The study enrolled 85 patients with psoriasis; 48 (56.47%) males, and 37 (43.53%) females. 49 (57.6%) of the patients had Psoriasis for less than 10 years, while 36 (42.4%) had the disease for more than 10 years. Psoriasis vulgaris was the most common diagnosis, 35 (41.2%), followed by Psoriasis pustular, 26 (30.6%) and

then Psoriasis erythroderma (28.2%). The mean age  $\pm$  SD of the Psoriasis vulgaris, Psoriasis pustular and Psoriasis erythroderma patients were  $47.3 \pm 15.3$ ;  $45.3 \pm 14.6$ , and  $57.1 \pm 11.7$  respectively. Full patient information is presented in **Table 1**.

### 3.2. Laboratory Findings and the Systemic Immune Inflammatory Index (SII)

All patients included in the study had complete blood count (CBC) records in addition to other laboratory findings. White blood cell (WBC) counts, neutrophil counts and platelet counts were all higher in Psoriasis pustular than vulgaris and erythroderma, ( $p < 0.0001$ ,  $p < 0.0010$ , and  $p = 0.01$  respectively) (**Figure 1**). Meanwhile lymphocyte count was higher in Psoriasis vulgaris ( $p = 0.0467$ ). C-reactive protein (CRP) was significantly higher in Psoriasis erythroderma than the others ( $p < 0.0001$ ), while IgE was also higher in Psoriasis erythroderma but not statistically significant, ( $p > 0.05$ ). Details of the laboratory findings are presented in **Table 2**.

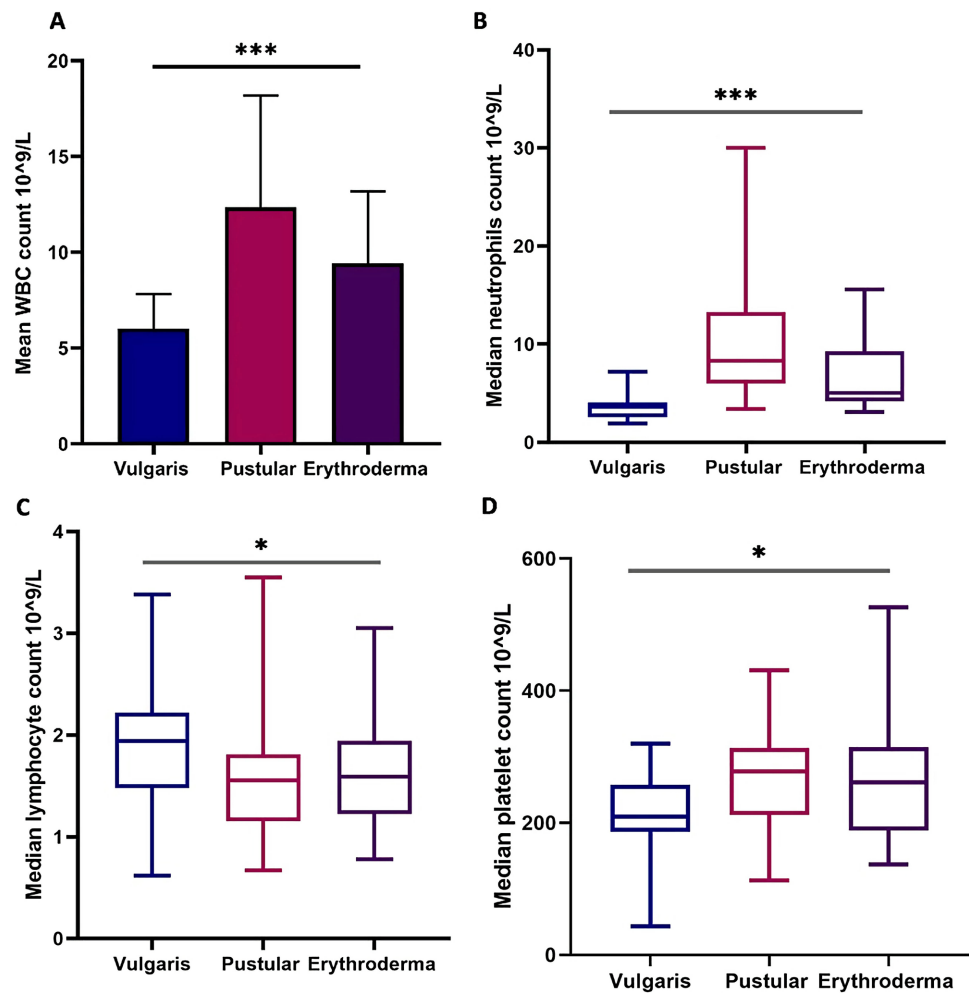
### 3.3. Lipid Profile and C-Reactive Protein

Lipid abnormality is a common occurrence in psoriasis patients. It is often associated with increased mortality owing to increased risks of myocardial infarction

**Table 1.** Clinical characteristics of study participants.

Characteristics	Categories	Psoriasis vulgaris (n = 35)	Psoriasis pustular (n = 26)	Psoriasis erythroderma (n = 24)	P-value
Age (years)		$47.3 \pm 15.3$	$45.3 \pm 14.6$	$57.1 \pm 11.7$	0.009 <sup>#</sup>
Gender	Male	22 (62.9)	11 (42.3)	15 (62.5)	0.217
	Female	13 (37.1)	15 (57.7)	9 (37.5)	
BMI	<18.5	0 (0)	3 (11.5)	0 (0.0)	0.086
	18.5 - 24.9	20 (57.1)	16 (61.5)	18 (75)	
	25 - 29.9	11 (31.4)	5 (19.3)	6 (25)	
	>30.0	4 (11.4)	2 (7.7)	0 (0.0)	
Duration (months)		10 (4.5, 20)*	8 (3.25, 10.75)*	10.25 (3.75, 22.5)*	0.388
Smoking history	Yes	4 (11.4)	3 (11.5)	3 (12.5)	0.991
	No	31 (88.6)	23 (88.5)	21 (87.5)	
Family history	Yes	0 (0.0)	2 (7.7)	1 (4.2)	0.268
	No	35 (100)	24 (92.3)	23 (95.8)	
Diabetes	Yes	7 (20)	3 (11.5)	3 (12.5)	0.599
	No	28 (80)	23 (88.5)	21 (87.5)	
Hypertension	Yes	6 (17.1)	3 (11.5)	4 (16.7)	0.815
	No	29 (82.9)	23 (88.5)	20 (83.3)	

BMI: Body mass index. \*Median (IQR). <sup>#</sup>significant p-value.



**Figure 1.** Full blood count indices among the three psoriasis types. (A) Mean WBC count  $***p < 0.0001$ . (B) Median neutrophils count  $***p < 0.0001$ . (C) Median platelet count.  $*p < 0.05$ . (D) Median Lymphocyte count.  $*p < 0.05$ .

**Table 2.** Comparison of routine blood test levels between psoriasis vulgaris, psoriasis pustular and psoriasis erythroderma.

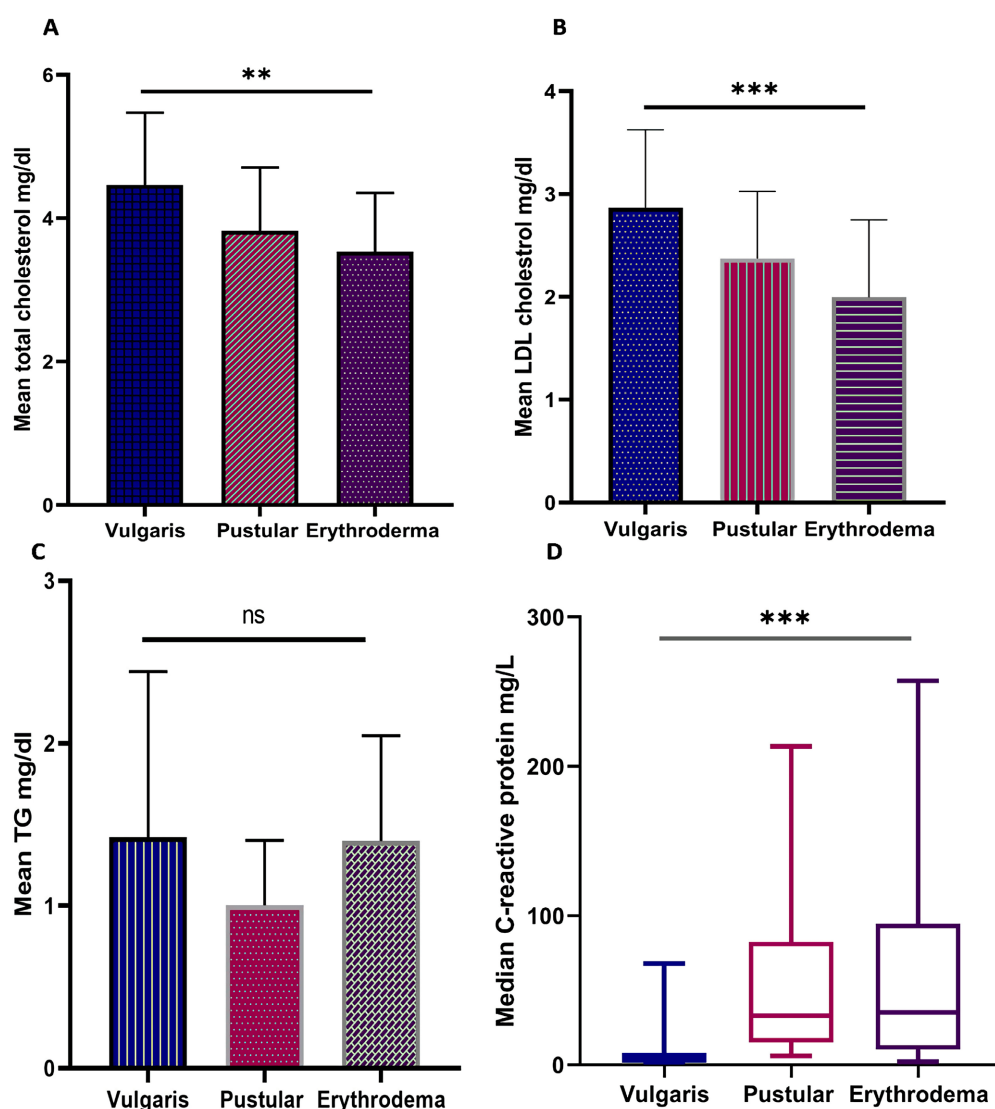
Routine blood test	Psoriasis vulgaris (n = 35)	Psoriasis pustular (n = 26)	Psoriasis erythroderma (n = 24)	P-Value
WBC count ( $10^9/L$ )*	7.41 (3.78)	12.34 (5.83)	9.41 (3.76)	$<0.0001^{\#}$
Neutrophil count ( $10^9/L$ )**	3.765(2.747, 5.187)	8.305 (6.05, 12.88)	5.025 (4.26, 8.93)	$<0.0001^{\#}$
Lymphocyte count ( $10^9/L$ )*	1.866 (0.631)	1.59 (0.58)	1.59 (0.54)	0.0467 <sup>#</sup>
Platelet count ( $10^9/L$ )**	220 (194.25, 274.25)	277.5 (214.75, 312.25)	261 (200.75, 313.5)	0.010 <sup>#</sup>
CRP (mg/L)**	4.93 (2.33, 21.16)	32.84 (16.3, 77.68)	35.12 (16.78, 88.18)	$<0.0001^{\#}$
IgE (mg/L)**	72.95 (18.8, 152.5)	68.25 (18.77, 263.5)	334 (79.65, 857.75)	0.427
Total cholesterol (mg/dl)*	4.22 (1.05)	3.82 (0.88)	3.53 (0.81)	0.0007 <sup>#</sup>
LDL-C (mg/dl)*	2.7 (0.76)	2.37 (0.65)	1.99 (0.75)	$<0.0001^{\#}$
TG (mg/dl)*	1.31 (0.92)	1.00 (0.4)	1.39 (0.64)	0.0781
NLR**	1.98 (1.6, 2.8)	5.98 (3.58, 7.35)	3.94 (2.23, 6.78)	$<0.0001^{\#}$
SII**	384.68 (282.92, 482.75)	1370.9 (1035.24,2306.47)	879.89 (243.1, 1886.8)	$<0.0001^{\#}$

CPR: C-reactive protein, IgE: Immunoglobulin E, TG: Triglycerides, NLR: Neutrophil-Lymphocyte ratio, SII: systemic immune inflammation index. <sup>#</sup>significant p-value.

and stroke. On the other hand, elevated C-reactive protein is a predictor of cardiovascular disease (CVD). So we assessed the lipid profiles and plasma levels of C-reactive proteins among the different types of psoriasis. The mean total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were significantly higher in psoriasis vulgaris ( $p < 0.01$ , and  $p < 0.001$ ) than pustular and erythroderma. However, despite the significant difference, the mean TC and LDL-C were all within the normal ranges for the variables. C-reactive protein on the other hand was 2 - 3 times above the upper limit of the reference range in psoriasis pustular and psoriasis erythroderma, and was significantly higher in psoriasis erythroderma ( $p < 0.001$ ) compared to the others, **Figure 2**.

### 3.4. SII Was Significantly Increased in Psoriasis Pustular

From the CBC results, the following parameters were extracted to calculate the



**Figure 2.** Lipid profile and C-reactive protein. (A) Mean TC, (B) Mean LDL-C. (C) Mean TG. (D) median C-reactive protein.

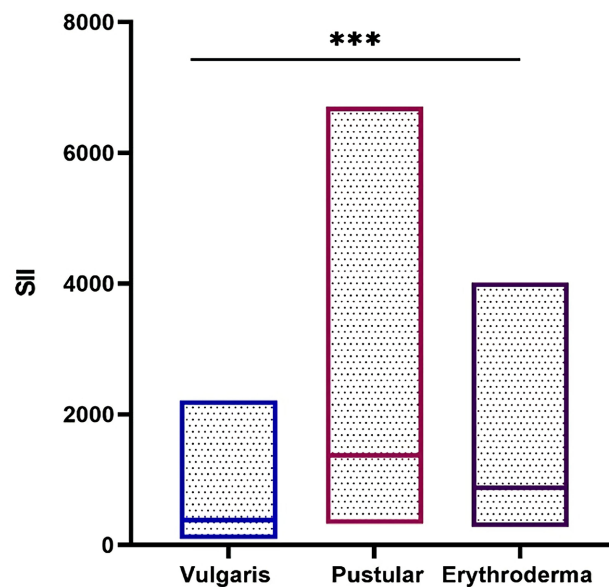
systemic immune inflammatory indices for each patient (SII): Absolute neutrophil counts, absolute lymphocyte counts, and platelet counts. Neutrophil-lymphocyte ratio was determined and then SII calculated as: neutrophil (N)  $\times$  platelet (P)/lymphocyte (L), (SII =  $N \times P/L$  ratio). The median SII (IQR) were 384.68 (282.92, 482.75) for vulgaris, 1370.9 (1035.24, 2306.47) for pustular and 879.89 (243.1, 1886.8) for erythroderma. Median SII was thus significantly higher in Psoriasis pustular than the rest, ( $p < 0.0001$ ), **Figure 3**.

### 3.5. SII Was Not Associated with Duration of Psoriasis

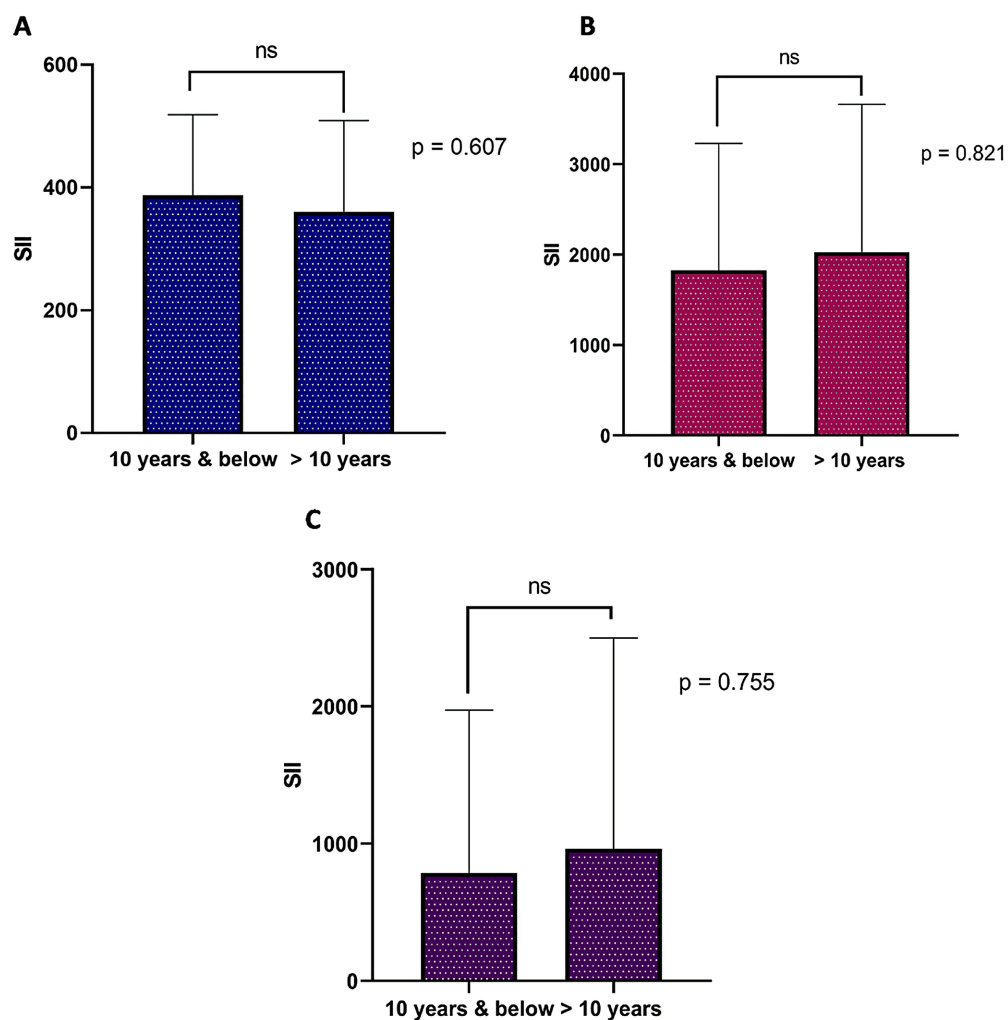
The median (IQR) duration of symptoms was slightly higher in Psoriasis erythroderma; 10.25 (3.75, 22.5), than vulgaris 10 (4.5, 20), and pustular 8 (3.25, 10.75), however, no statistically significant difference was noticed in the duration of symptoms among the three disease subtypes, (all  $p$  values  $> 0.05$ ). We divided the psoriasis patients into two categories according to the duration of disease; 10 years, and  $>10$  years. Those with the disease for more than ten years were considered to have a more severe disease than those who had it for less than 10 years. We then determined the relationship between SII and the duration of disease in the different subtype of Psoriasis. There was no statistically significant relationship between duration of psoriasis and SII among all the three types, **Figure 4**.

### 3.6. SII Was Associated with Hypertension in P. Pustular

The non-parametric T test (Mann-Whitney test) was conducted to determine if any relationship existed between SII and smoking, diabetes, hypertension and patients having family history of psoriasis. The results showed a significant relationship between SII and hypertension in psoriasis pustular ( $p < 0.05$ ) (**Table 3**).



**Figure 3.** Systemic immune inflammatory index (SII). Comparison of SII values in the three Psoriasis subtypes (\*\*\*) ( $p < 0.0001$ ).



**Figure 4.** Relationship between SII and duration of symptoms. (A) SII vs Symptoms in psoriasis vulgaris. (B) SII vs symptoms in psoriasis pustular. (C) SII vs symptoms in psoriasis erythroderma. All  $P > 0.05$ .

**Table 3.** Relationship between SII and important clinical characteristics of psoriasis.

Characteristics	Category	Vulgaris	p-value	Pustular	p-value	Erythroderma	p-value
History of smoking	Yes	281.2 (235.2 - 472.9)	0.318	792.2 (686.8 - 897.6)	0.073	1041.93 (693.15 - 2636.79)	0.145
	No	372.9 (282.1 - 488.6)		1419 (1077 - 2739)		879.89 (540.32 - 1886.85)	
Diabetes	Yes	440.1 (335.8 - 523.1)	0.500	1349 (560.8 - 1854)	0.648	957.17 (599.92 - 2264.162)	0.619
	No	360.8 (274.9 - 488.6)		1393 (1022 - 2833)		879.89 (540.32 - 1886.85)	
Hypertension	Yes	430.3 (360.6 - 611.8)	0.250	897.6 (323.2 - 1076)	0.031 <sup>#</sup>	787.99 (482.31 - 1504.50)	0.794
	No	360.5 (270.3 - 482.8)		1446 (1081 - 2833)		879.89 (540.32 - 1886.85)	

**Continued**

Family history of psoriasis	Yes	Na	Na	792.2 (686.8 - 897.6)	0.073	Na	Na
	No	384.7 (277.6 - 494.4)	Na	1419 (1077 - 2739)		880.5 (484.3 - 2099)	Na

Na: Not enough data to conduct statistical analysis.

The other variables did not have any significant relationship with SII across all types of psoriasis.

#### 4. Discussion

Dysfunction of the immune system is the hallmark of psoriasis [13]. It is manifested as chronic inflammation that involves over proliferation of keratinocytes. In recent years, studies have shown that psoriatic plaques are infiltrated with immune cells and have increased vascularity of the dermis [14]. Whether its keratinocytes or immune cells that trigger the pathological inflammation associated with psoriasis is still unproven. However, psoriasis is generally known as a multisystem inflammatory disease, involving keratinocytes, cells of the immune system and other cells of the body [15] [16] [17] [18]. In the immune system neutrophils, lymphocytes and monocytes are known as the cellular makers of the immune system. To aid prognostic assessment of inflammatory conditions, studies have shown that these immune cells can be useful in clinical practice. As a result, various indices such as neutrophil-lymphocyte ratios (NLR), and platelet-lymphocyte ratios (PLR) have been developed. In psoriasis, NLR is an inexpensive and easily to obtain index that is used in combination with platelet count as systemic immune inflammation index (SII) to predict prognosis and asses severity of the disease [9]. In this study, we assessed the association between SII and the different subtypes of psoriasis in 85 psoriasis patients. We determined whether SII was associated with severity and duration of disease, and other important clinical characteristics of patients with psoriasis, in the different sub types of the diseases.

By demographics, majority of our study population were males, 48 (56.47%), compared to 37 (43.53%) females, however psoriasis in general affects both men and women equally [7]. On average, patients with psoriasis erythroderma were much older than those with p. pustular and p. vulgaris. While there is no empirical evidence to show that onset of the different types of psoriasis are associated with age, studies show that psoriasis has 2 peaks of onset, the first at age 20 to 30 years and the second at age 50 to 60 years [7]. The mean age of affected patients were  $47.3 \pm 15.3$  years for p. vulgaris,  $45.3 \pm 14.6$  for p. pustular and  $57.1 \pm 11.7$  years for p. erythroderma. A 2012 study in China revealed that the two peak onset ages of psoriasis among Chinese was at 20 - 29 years, and at 40 - 49 years, with approximately 68% of patients developing the disease before age 40 years [19].

In our study, 49 (57.6%) of the patients had Psoriasis for less than 10 years, while 36 (42.4%) had the disease for more than 10 years, and psoriasis vulgaris was the most common diagnosis, 35 (41.2%), followed by Psoriasis pustular, 26 (30.6%) and then Psoriasis erythroderma (28.2%). This is consistent with a recent epidemiological study which revealed that p. vulgaris accounts for 82.6% - 97.9% of all psoriasis in China, with p. pustular and p. erythroderma accounting for 0.69% - 2.17%, and 0% - 8.7% respectively [5]. In terms of total white blood cells count, and other white cell indices (neutrophils, lymphocytes, and monocytes), p. pustular had consistently higher counts than all the other types. Even platelet count was higher in p. pustular than in the other sub types. This is consistent with a study by Liu *et al.* [20] who also noticed marked leukocytosis in p. pustular than the rest. The leukocytosis seen in p. pustular is sometimes associated with taking drugs for skin disease such as terbinafine [21], or the anti-cancer drug pembrolizumab [22]. However, our patients were not on any of these drugs, and so the cause of the mild leukocytosis remained unknown.

Considering the other blood biomarkers, mean total cholesterol (TC) and low-density lipoprotein cholesterol (LDL-C) were significantly higher in psoriasis vulgaris ( $p < 0.01$ , and  $p < 0.001$ ) than pustular and erythroderma, despite all of them being within the normal ranges. C-reactive protein on the other hand was 2 - 3 times above the upper limit of the reference range in psoriasis pustular and psoriasis erythroderma, and was significantly higher in psoriasis erythroderma ( $p < 0.001$ ), than the rest. Strong associations have already been reported between psoriasis and cardiovascular diseases, and so increase in cholesterol is constantly seen among psoriasis patients [23]. C-reactive protein meanwhile is a predictor of cardiovascular disease in psoriasis [24], and an indicator of SII [9]. According to our results, p. pustular and p. erythroderma had dramatic rise in C-reactive protein, which would indicate increased risk for CVD in these patients. However, whether C-reactive protein is a good predictor of SII is still controversial; according to Sokolova *et al.* [25], C-reactive protein was not elevated in 105 patients with psoriasis assessed, neither was it elevated among the subgroups of psoriasis. Therefore, further large-scale studies are needed to confirm the role of C-reactive protein in predicting SII.

Previous studies have already demonstrated that SII is higher in psoriasis patients compared to normal individuals [9] [25]. However, this is the first study to determine the association between SII and the different types of psoriasis. In our findings, SII was significantly higher in p. pustular ( $p < 0.01$ ), than the other subtypes of psoriasis. There was no association between SII and duration of psoriasis in any of the subtypes. When determined by other comorbidities, a significant relationship was noted between SII and hypertension in p. pustular patients ( $p < 0.05$ ), while smoking, diabetes and others were non-significant. This result is consistent with previous studies that demonstrated association between psoriasis and cardiovascular diseases [26] [27], however, it is the first study to show an association between SII and a cardiovascular disease in p. pustular as a

subtype of psoriasis. Looking at our study as a whole, there appears to be a relationship between SII and p. pustular whereas no relationship exists with p. vulgaris and p. erythroderma.

## 5. Conclusion

In summary, this study demonstrated that systemic immune inflammatory index (SII) is significantly higher in psoriasis pustular than other subtypes of psoriasis. It further demonstrated that an association existed between hypertension and SII in psoriasis pustular patients. However, there was no relationship between SII and duration of psoriasis or other clinical characteristics such as diabetes, family history and history of smoking. C-reactive protein was significantly upregulated in both psoriasis pustular and erythroderma but not vulgaris, while leukocytosis was observed in psoriasis pustular. These findings suggest a possible association between SII and p. pustular that should be investigated in an independent study.

## Author Contribution

Salah Hassan Ibrahim conducted data analysis and manuscript drafting. Guan mengqi conducted data collection. Li Shanshan conceptualized the study and supervised the entire process. All authors read and approved the final manuscript.

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## Conflicts of Interest

All authors declare that there was no conflict of interest.

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