


# Comorbidity Pattern in Patients with Moderate-to-Severe Plaque Psoriasis: Network Analysis of a Hospitalized Database in China

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**Introduction:** Psoriasis is a chronic systemic inflammatory disorder characterized by a high prevalence of comorbid conditions, profoundly affecting patient quality of life and complicating treatment strategies. This study aims to analyze demographic characteristics, prevalence, age distribution, and gender differences of psoriatic comorbidities in hospitalized patients with moderate-to-severe psoriasis at a single center. Additionally, we explore the correlation between comorbidities and psoriasis through network analysis.

**Methods:** A retrospective cross-sectional study was conducted using electronic medical records from the Shanghai Skin Disease Hospital, spanning 2021 to 2023. After removing duplicates, 506 patients diagnosed with plaque psoriasis were included. Comprehensive data on demographics, medical histories, laboratory indices, and comorbid conditions were collected. The Phenotypic Comorbidity Network (PCN) method was employed to examine coexistence patterns of psoriasis with various diseases.

**Results:** 79.64% of patients had at least one comorbidity, with Non-alcoholic Fatty Liver Disease (NAFLD), hypertension, hyperlipidemia, overweight/obesity, and hyperuricemia being the top five common comorbidities. The prevalence of these comorbidities increased substantially in the 30–40 and 50–70 age cohorts, notably in hepatic dysfunction and metabolic syndrome. Male patients showed a slightly higher propensity for comorbidities compared to females. Early-onset psoriasis (EOP) patients showed a higher risk for specific conditions than late-onset psoriasis (LOP) patients. PCN analysis identified hepatic dysfunction, hypertension, metabolic syndrome, NAFLD, obesity, hyperlipidemia, and diabetes as strongly associated with psoriasis.

**Conclusion:** This study underscores the systemic nature of psoriasis and its association with diverse comorbidities, emphasizing the necessity of a holistic management approach that addresses both dermatological and comorbid conditions. Identifying key comorbidities guides clinicians in implementing targeted screening and preventive strategies, enhancing patient care and potentially alleviating the overall disease burden.

**Keywords:** plaque psoriasis, comorbidity, age distribution, phenotypic comorbidity network, PCN

## Introduction

Psoriasis is a chronic, systemic inflammatory disease with a global prevalence of approximately 2–3%,<sup>1</sup> with chronic plaque psoriasis being the most prevalent form. Psoriasis is intricately linked to multiple disease and health conditions. Numerous studies have demonstrated a high prevalence of metabolic diseases, cardiovascular diseases,<sup>2</sup> mental and psychological disorders, as well as various other autoinflammatory and metabolic diseases, which are recognized as comorbidities of psoriasis.<sup>3,4</sup> Concerning the broad spectrum of comorbidities associated with psoriasis and the underestimation and underreporting of many comorbidities, the overall disease burden of psoriasis is often significantly underestimated.

Comorbidities can significantly increase the overall disease burden, economic impact, and complexity of treatment for patients with psoriasis. Therefore, comprehensive assessment and management of psoriasis, alongside early identification and intervention of comorbidities, are crucial for enhancing patients' quality of life and prognosis. Additionally, a higher comorbidity burden in psoriasis is associated with a reduced clearance rate of skin lesions.<sup>5</sup> Understanding the interactions between psoriasis and its comorbidities is essential for holistic management and treatment selection. Previous studies have predominantly focused on the correlation between psoriasis and individual diseases,<sup>2,6</sup> yet it is common for patients with psoriasis to simultaneously have multiple comorbid conditions. Thus, elucidating the pattern of multiple comorbidities in psoriasis is imperative.

The Phenotypic Comorbidity Network (PCN) is a method used to study and visualize the interrelationships between different diseases or symptoms.<sup>7</sup> PCN allows for the visualization and analysis of multi-comorbidities interactions within a holistic network framework, highlighting potential indirect relationships and central nodes of comorbidity. It has been widely employed to explore the comorbidity patterns of various chronic diseases, such as ischemic heart disease,<sup>8</sup> cancer,<sup>9</sup> and depression.<sup>10</sup> In a PCN, nodes represent coexisting diseases, while edges are assigned weights that indicate the strength of their connections and the frequency of their coexistence. This approach can uncover previously unknown disease patterns and help predict the risk of future comorbidities.

Although some studies have characterized psoriasis and its comorbidities from various perspectives, analyses using PCN are relatively rare.<sup>11–13</sup> In this study, we aim to employ a network-based method to summarize the comorbidity patterns using data from a hospital database in Shanghai, China. Specifically, this study aims to describe the demographic characteristics, prevalence of comorbidities, and the relationship between gender disparity or age of onset and psoriatic comorbidities.

## Methods

### Study Populations

We conducted a single-center, retrospective cross-sectional study utilizing electronic medical records from the hospitalized database of the Shanghai Skin Disease Hospital. The inpatient electronic medical record system was thoroughly reviewed, covering data collected from January 1, 2021, to December 30, 2023. Diagnoses were identified by querying International Classification of Diseases, 10th Edition (ICD-10-CM) codes specific to psoriasis vulgaris or plaque psoriasis. After removing duplicate records, we identified 621 hospitalizations related to plaque psoriasis and retained the most recent hospitalization data for analysis. Consequently, 506 unique patients were included in this study. This study received approval from the Ethics Committee of the Shanghai Skin Disease Hospital, Tongji University School of Medicine (approval number 2021–37), and adhered to the ethical principles outlined in the Declaration of Helsinki. This is a retrospective study and all patient data are anonymous, the requirement for informed consent was therefore waived.

### Data Collection

A comprehensive dataset was compiled, encompassing demographics, medical history, laboratory indices, personal medical history, and comorbidities. The comorbidity assessment included a detailed examination of the presence or history of type 2 diabetes, obesity, arterial hypertension, cardio-cerebrovascular disease (CCVD), dyslipidemia, and hyperuricemia. Additionally, data were collected on the history of malignancy, thyroid diseases, and schizophrenia. However, due to the limited number of cases with these specific comorbidities, we excluded them from subgroup analysis and heatmap visualization. Patients with psoriatic arthritis were also excluded, as this condition is typically categorized as a subtype of arthropathic psoriasis at department of dermatology in China, a distinct form of psoriasis.

### Temporal Relationships

The study further investigated the temporal interval between the onset of comorbidities, such as hypertension and type 2 diabetes, and the timing of the psoriasis diagnosis. Co-occurrence of psoriatic lesions and comorbidities was defined as occurring when the interval between the two was less than one year. The onset date of a disease was determined as the day when the first symptom was observed.

## Phenotypic Comorbidity Network Construction

The coexistence patterns of psoriasis with multiple diseases were analyzed using the Phenotypic Comorbidity Network (PCN) method. In the PCN, disease codes are represented by nodes, and these nodes are connected by edges to illustrate their co-occurrence. Node sizes were assigned in proportion to the corresponding disease prevalence rates, and the weights of the edges were determined using the Jaccard similarity coefficient, as defined in Equation (1). This coefficient was utilized to plot the comorbidity network in R Studio, allowing for the identification of key nodes and connection patterns within the network.

$$J(A, B) = \frac{|A \cup B|}{|A \cap B|} \quad (1)$$

## Statistical Analysis

Quantitative variables were presented as mean and standard deviation (SD) or median and interquartile range (p25–p75), depending on the normality assessed by the Shapiro–Wilk test. Categorical variables were expressed as percentages. Prevalence was reported in percentage terms. Prevalence ratios for comorbidities were calculated based on the incidence ratio of a specific comorbidity among the total population of patients with psoriasis included in the study. Subgroup analyses utilized the Mann–Whitney *U*-Test for continuous variables and the chi-square test for categorical variables. All statistical tests were two-sided, with significance set at *p*-values < 0.05. Data analysis was conducted using SPSS software (version 25), while R (version 4.3.1) was used for data plotting and additional analyses. Visualizations were performed in R using the ggplot2 package for plotting heatmaps and the igraph and ggraph libraries for network visualization.

## Results

### Overall Characteristics of Patients With Plaque Psoriasis

In this study, we enrolled a total of 506 patients, comprising 398 males and 108 females, resulting in a male-to-female ratio of 3.69:1. The mean age of all patients was 52.21 years (SD = 17.48), and the mean age at onset of skin lesions was 39.65 years (SD = 18.10). The average duration of psoriasis among the patients was 12.50 years (SD = 10.85). Although male patients tended to develop the condition at a slightly later age than females, this difference was not statistically significant (median age of onset: 40.00 years [IQR: 27.98–52.00] vs 33.48 years [IQR: 19.00–54.00], *P* = 0.0532). However, the duration of the disease was significantly longer in males than in females (median duration: 10.00 years [IQR: 5.00–20.00] vs 8.00 years [IQR: 2.00–18.00], *P* = 0.0345).

Recognizing psoriasis as a systemic disease, we assessed the prevalence of comorbidities among our cohort. As shown in Table 1, the distribution of patients with 1 to 6 or more comorbidities was 24.70%, 24.11%, 15.22%, 8.50%, 4.55%, and 2.57%, respectively. Notably, only 20.36% of the patients had plaque psoriasis without any comorbid conditions. Overall, 79.64% of the patients with plaque psoriasis presented with at least one comorbidity. The five most prevalent comorbid conditions identified were Non-alcoholic Fatty Liver Disease (NAFLD) (42.69%), hypertension (30.33%), hyperlipidemia (27.67%), overweight/obesity (24.31%), and hyperuricemia (15.81%) (Table 2).

### Age Distribution of Comorbidities in Plaque Psoriasis

To illustrate the age distribution of comorbidities associated with psoriasis, we created a heatmap based on age stratification factors (Figure 1). The figure reveals notable differences across various age groups. Most patients presented with 1–2 comorbidities. However, a significant increase in the prevalence of comorbidities (ranging from 1 to 6 or more) was observed particularly in the age groups of 30–40, 50–60, and 60–70 years.

The age distribution patterns for each comorbidity were also analyzed and are illustrated in Figure 2. The prevalence rates were determined by calculating the proportion of psoriasis patients with specific comorbidities relative to the total number of patients enrolled in the study. The heatmap effectively visualizes the comorbidity burden across different age groups.

**Table 1** Demographic and Clinical Data of Hospitalized Plaque Psoriasis

Variable	N=506
Demographic information	
Sex, Male: Female ratio	3.69:1 (398:108)
Age, years (mean $\pm$ SD)	52.21 $\pm$ 17.48
Onset of skin lesions, years (mean $\pm$ SD)	39.65 $\pm$ 18.10
Disease duration of psoriasis, years (mean $\pm$ SD)	12.50 $\pm$ 10.85
Morbidity of comorbidities (classes)	103 (20.36%)
0 n (%)	
1 n (%)	125 (24.70%)
2 n (%)	122 (24.11%)
3 n (%)	77 (15.22%)
4 n (%)	43 (8.50%)
5 n (%)	23 (4.55%)
6+ n (%)	13 (2.57%)

**Abbreviation:** SD, standard deviation.

**Table 2** Prevalence Rates of Comorbidities in Subjects with Plaque Psoriasis

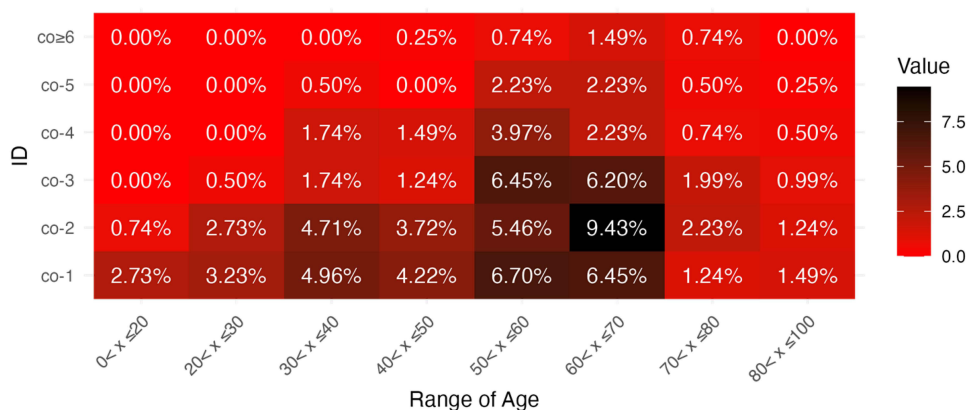
Comorbid conditions	n (%)
Total prevalence	403 (79.64%)
NAFLD, n (%)	216 (42.69%)
Hypertension, n (%)	155 (30.33%)
Hyperlipidaemia, n (%)	140 (27.67%)
Overweight and obese, n (%)	123 (24.31%)
Hyperuricemia, n (%)	80 (15.81%)
Type 2 diabetes, n (%)	67 (13.11%)
CCVD, n (%)	62 (12.25%)
History of malignancy	15 (2.96%)
Thyroid diseases, n (%)	7 (1.38%)
Schizophrenia, n (%)	3 (0.59%)

**Abbreviations:** NAFLD, Non-alcoholic Fatty liver disease; CCVD, Cardio-cerebrovascular disease.

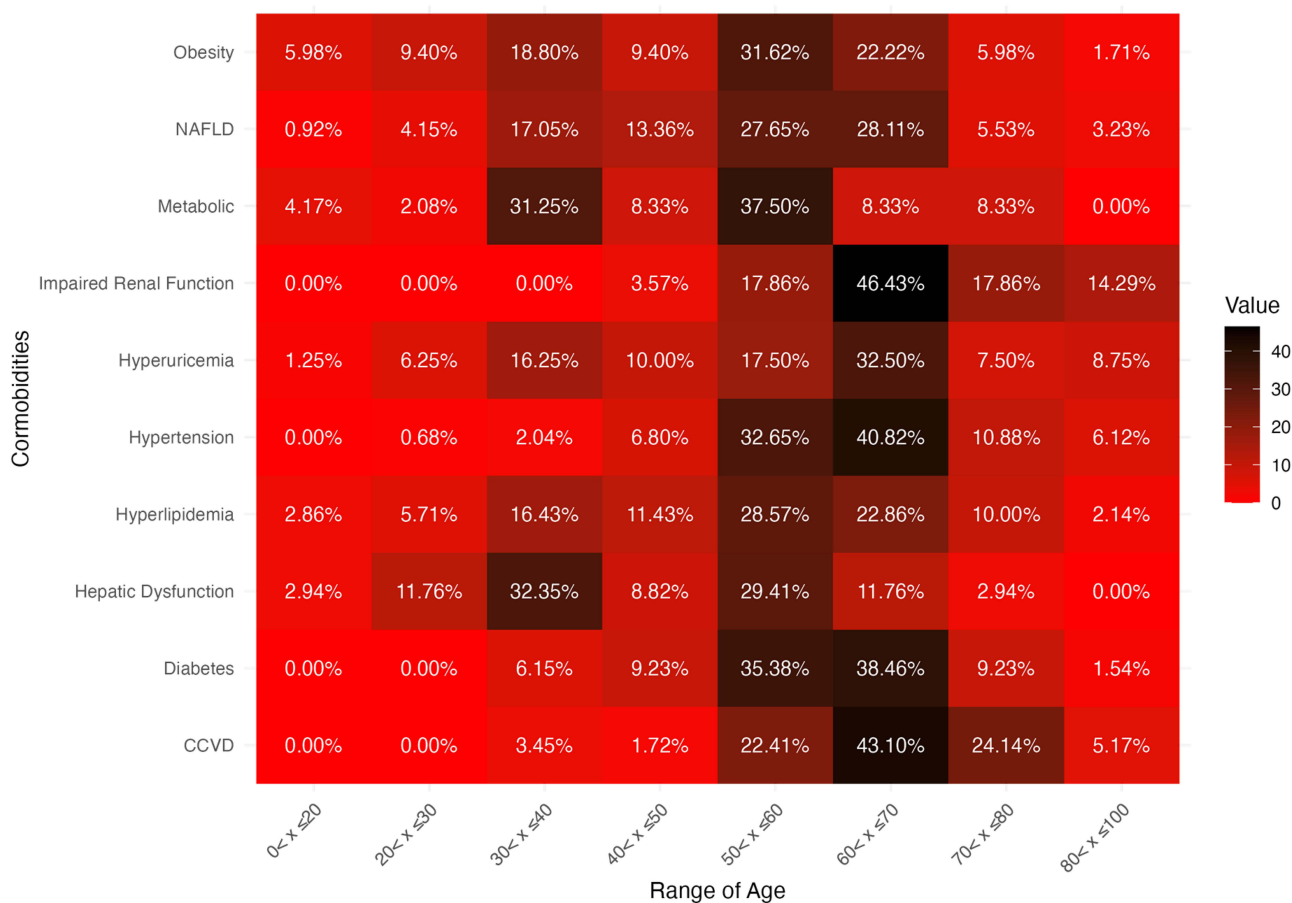
Obesity was found to have the highest prevalence in the 50–60 age group, with a rate of 31.62%, followed by the 60–70 age group at 22.22%. Non-alcoholic Fatty Liver Disease (NAFLD) shows an increasing trend with age, peaking in the 60–70 age group at 28.11%, highlighting a significant comorbidity burden in older psoriasis patients. Metabolic comorbidities were notably prevalent in the 30–40 and 50–60 age groups, with prevalence rates of 37.50% and 31.25%, respectively, suggesting a critical intersection between metabolic disorders and psoriasis in younger and middle-aged individuals.

Impaired renal function was particularly prevalent in the 60–70 age group. Both hyperuricemia and hyperlipidemia demonstrated a consistent increase in prevalence with age, with noticeable rises in the 30–40 age group and significant increases in the 50–60 and 60–70 age groups. This indicates a potential link between uric acid, lipid metabolism disorders, and psoriasis.

Hepatic dysfunction was notably prevalent in the 40–50 and 50–60 age groups, with prevalence rates of 32.35% and 29.41%, respectively. Hypertension and diabetes exhibited similar trends, with high prevalence rates in the 50–70 age group. Cardiovascular and cerebrovascular diseases (CCVD) showed the highest prevalence in the 60–80 age group. These findings underscore the cardiovascular risks associated with psoriasis, particularly in older populations.



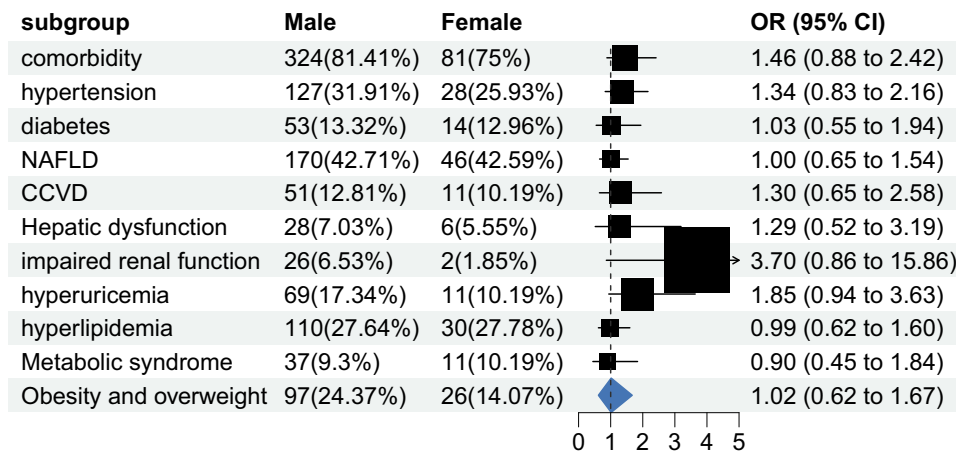
**Figure 1** Age Distribution of the prevalence about comorbidity in Plaque Psoriasis. The distribution of patients with plaque psoriasis who have 1 to 6 or more comorbidities across different age groups. Each cell represents the prevalence of a specific factor within a particular age group, with the color gradient indicating the relative prevalence. **Notes:** Co-n: comorbid with n disease, number in the column of heatmap represent the prevalence percent of comorbidity in different age group.



**Figure 2** Distribution of each comorbidity based on age in Plaque Psoriasis. The trends in various comorbidities across different age groups, with color ranging from light to dark representing low to high prevalence. **Notes:** Number in the column of heatmap represent the prevalence percent of comorbidity in different age group.

### Gender Disparity of Psoriatic Comorbidity

As depicted in Figure 3, a higher percentage of males (81.41%, n=324) present with comorbidities compared to females (75%, n=81), with an odds ratio of 1.46 (95% CI: 0.88 to 2.42). This suggests a slightly increased likelihood of comorbidities in males. Specifically, males exhibited a higher prevalence of hypertension [OR 1.339; 95% CI



**Figure 3** Forest plot of gender factors of comorbidities in Chinese plaque psoriasis. The prevalence of various comorbidities in male and female of plaque psoriasis patients, along with the odds ratios (OR) and 95% confidence intervals (CI) for each subgroup.

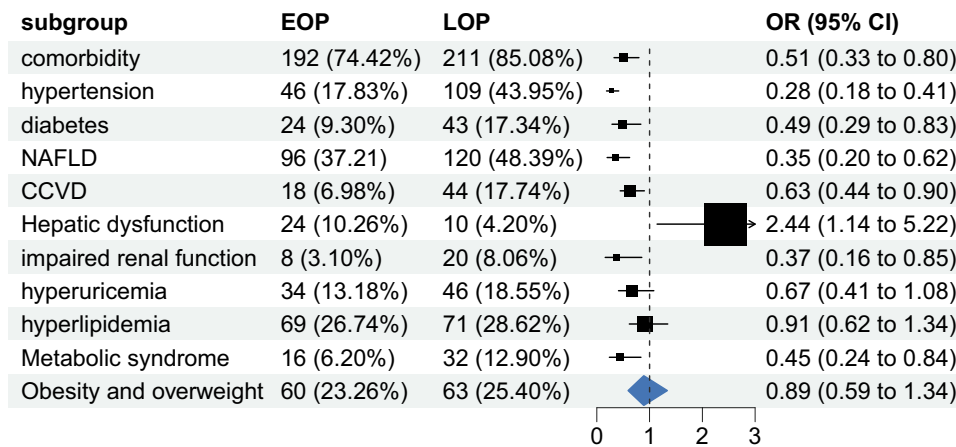
(0.83–2.16),  $P = 0.232$ ], cardiovascular and cerebrovascular diseases (CCVD) [OR 1.296; 95% CI (0.65–2.58),  $P = 0.46$ ], hepatic dysfunction [OR 1.286; 95% CI (0.52–3.19),  $P = 0.586$ ], impaired renal function [OR 3.704; 95% CI (0.87–15.86),  $P = 0.059$ ], and hyperuricemia [OR 1.849; 95% CI (0.94–3.63),  $P = 0.071$ ].

While the prevalence of diabetes [OR 1.031; 95% CI (0.55–1.94),  $P = 0.923$ ], non-alcoholic fatty liver disease (NAFLD) [OR 1.005; 95% CI (0.65–1.55),  $P = 0.982$ ], and obesity/overweight [OR 1.016; 95% CI (0.62–1.67),  $P = 0.949$ ] was similar between the genders. In contrast, hyperlipidemia and metabolic syndrome had slightly higher incidence rates in female patients than in male patients.

### Association of Psoriatic Onset Age With Comorbidities

Patients were categorized into early-onset psoriasis (EOP, <40 years) and late-onset psoriasis (LOP, ≥40 years) based on prior research.<sup>14</sup> Figure 4 illustrates the differences in the prevalence of various comorbidities between EOP and LOP patients. There is a significant difference in comorbidity prevalence between EOP (74.81%) and LOP (85.48%) patients, with an odds ratio of 0.51 (95% CI: 0.33 to 0.80), indicating a higher likelihood of comorbidities in LOP patients.

Significant differences between the groups were observed for several conditions, including hypertension ( $P < 0.001$ ), diabetes ( $P = 0.008$ ), non-alcoholic fatty liver disease (NAFLD) ( $P = 0.011$ ), cardio-cerebrovascular disease ( $P < 0.001$ ), hepatic dysfunction ( $P = 0.018$ ), impaired renal function ( $p = 0.016$ ), and metabolic syndrome ( $P = 0.01$ ). However, there



**Figure 4** Forest plot of Onset Age factors of comorbidities in Chinese plaque psoriasis. Subgroup analysis by onset age for the association between comorbidities and plaque psoriasis patients.

were no statistically significant differences between the subgroups for hyperlipidemia ( $P = 0.636$ ), hyperuricemia ( $P = 0.098$ ), and obesity/overweight ( $P = 0.537$ ).

## Association of Hypertension, Diabetes, CCVD With Psoriasis

Previous studies have established a definitive causal relationship between psoriasis and various comorbidities, which may manifest either before or after the onset of psoriasis. In this section, we explore the associations between psoriasis and hypertension, diabetes, and cardiovascular and cerebrovascular diseases (CCVD).

As illustrated in [Figure 5A](#), the average time interval from the onset of hypertension to the diagnosis of psoriasis was 6 years [2.94–10], which is significantly shorter than the interval from psoriasis to hypertension, measured at 10 years [5.00–19.38] ( $P < 0.05$ ). Specifically, 76 patients (51.70%) with psoriasis were subsequently diagnosed with hypertension, whereas 56 patients (38.10%) were diagnosed with psoriasis following an initial diagnosis of hypertension. Additionally, 10.20% of patients received diagnoses for both conditions almost simultaneously.

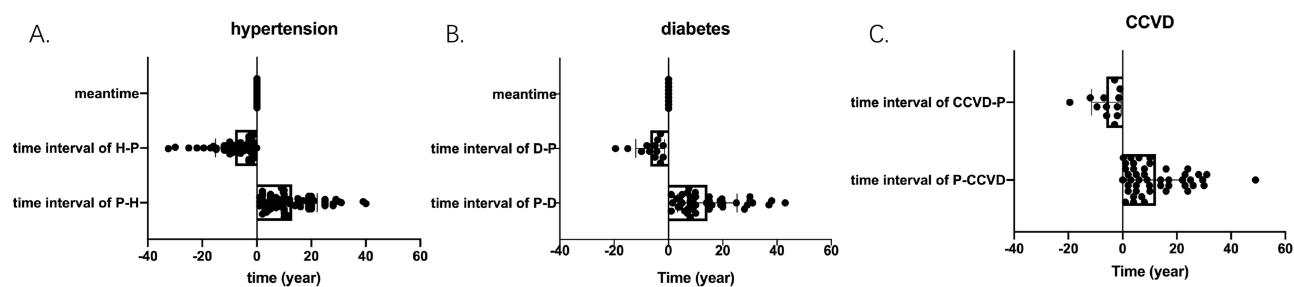
A similar pattern was observed for diabetes ([Figure 5B](#)). The average time interval from the onset of diabetes to the diagnosis of psoriasis was 5.0 years [3.00–8.96], which is significantly shorter than the interval from psoriasis to diabetes, measured at 10 years [7.00–20.00] ( $P < 0.01$ ). Among the patients, 43 (66.15%) with psoriasis were subsequently diagnosed with diabetes. Conversely, 13 patients (20%) were diagnosed with psoriasis following an initial diagnosis of diabetes, and 9 patients (13.85%) received diagnoses for both conditions nearly simultaneously.

Regarding cardiovascular and cerebrovascular diseases (CCVD) ([Figure 5C](#)), the average time interval from the onset of CCVD to the diagnosis of psoriasis was 4.45 years [2.00–8.85], which is significantly shorter than the interval from psoriasis to CCVD, measured at 8.50 years [4.00–22.25] ( $P < 0.01$ ). These findings suggest a notable association between the onset of these comorbidities and psoriasis.

## Phenotypic Comorbidity Network in Patients With Plaque Psoriasis

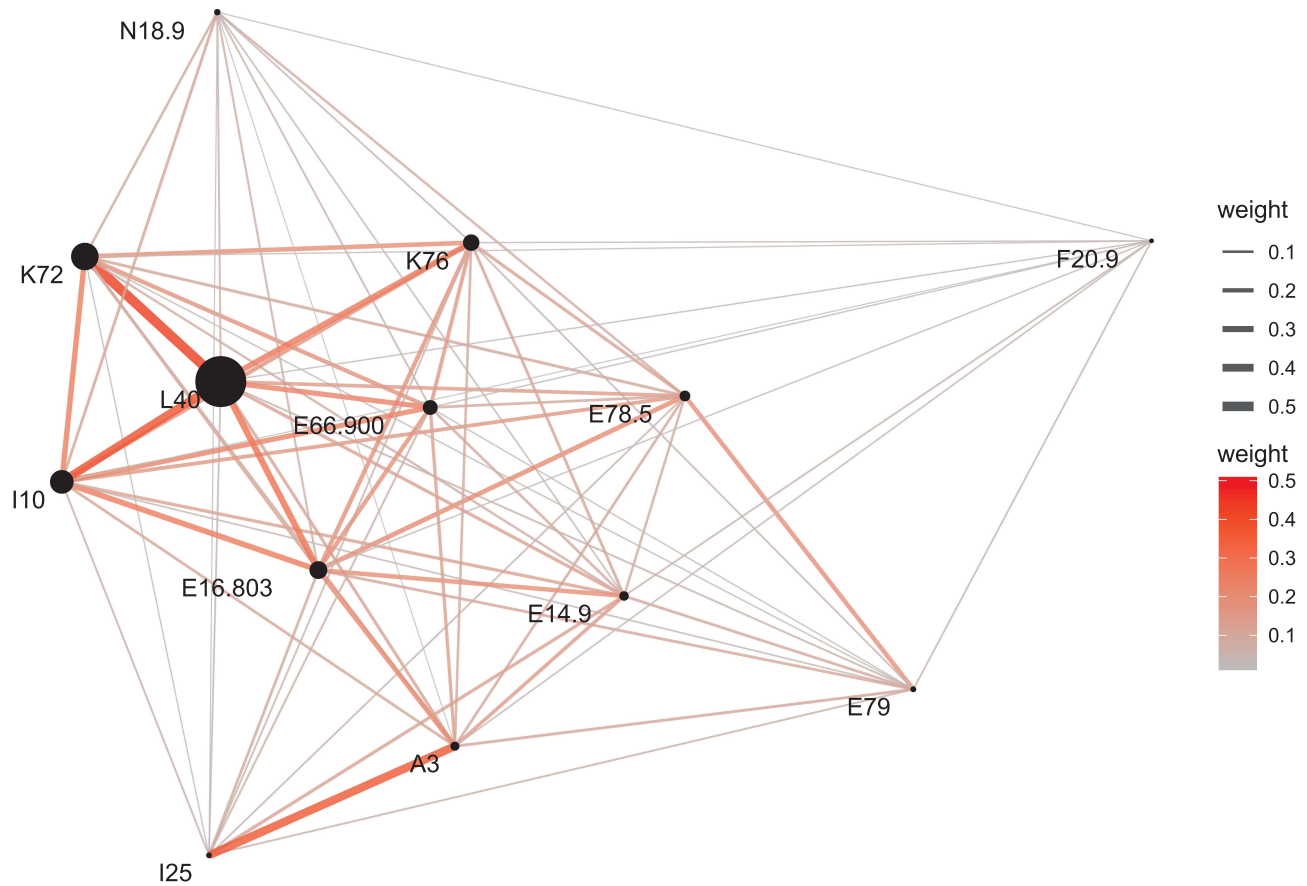
The Phenotypic Comorbidity Network (PCN) diagram illustrates the complex interrelationships among various diseases. In this network, each node represents a distinct disease, while the edges connecting these nodes indicate the presence of comorbidity between them. The thickness of the edges reflects the strength of the association, quantified by weight values ranging from 0.1 to 0.5, with higher values indicating a stronger comorbidity link. The results of the PCN analysis demonstrate that the strongest comorbidity associated with psoriasis is hepatic dysfunction, followed by hypertension, metabolic syndrome, non-alcoholic fatty liver disease (NAFLD), obesity, hyperlipidemia, and diabetes. The Jaccard similarity coefficient for the remaining included comorbidities is less than 0.1, indicating weaker associations.

The nodes, representing various ICD codes, were analyzed based on their degree and strength, as illustrated in [Figure 6](#) and [Table 3](#). L40 (psoriasis) demonstrated the highest degree with 12 connections and a strength of 2.38, highlighting its pivotal role within the network and its significant impact on the overall structure. Both I10 (hypertension) and E16.803 (metabolic syndrome) also had a degree of 12, with strengths of 2.02 and 2.05, respectively, emphasizing their critical roles and extensive connections. K72 (hepatic dysfunction) and K76 (NAFLD) showed strengths of 1.72 and 1.56, indicating a substantial presence and influence within the network. E66.900 (obesity), E14.9 (diabetes), and A3



**Figure 5** (A) The mean time interval of the diagnose from hypertension to psoriasis and reverse. (B) The mean time interval of the diagnose from diabetes to psoriasis and reverse. (C) The mean time interval of the diagnose from CCVD to psoriasis and reverse.

Multimorbidity network



**Figure 6** Phenotypic comorbidity network (PCN) in patients with Plaque Psoriasis PCN diagram illustrate the complex interrelationships among various diseases. Each node in the network represents a distinct disease, and the edges connecting these nodes indicate the presence of comorbidity between them. L40: Psoriasis vulgaris, K72: Hepatic dysfunction, N18.9: Impaired renal function, E79: Hyperuricemia, E78.5: Hyperlipidemia, K76: NAFLD, I10: Hypertension, E16.803: Metabolic syndrome, E66.900: Obesity/overweight, E14.9: Diabetes, I25: CCVD, A3: Thyroid disease, F20.9: Psychological and psychiatric disorders.

(thyroid disease) each exhibited a degree of 12 but had lower strengths of 1.54, 1.33, and 1.59, respectively, suggesting a broad yet less intense involvement in the network. I25 had a degree of 11 and a strength of 1.03, indicating a moderate level of comorbidity. N18.9 (impaired renal function), E79 (hyperuricemia), and E78.5 (hyperlipidemia) each showed a degree of 11, with strengths of 0.61, 0.84, and 1.41, respectively, reflecting their interconnectedness with other

**Table 3** Jaccard Similarity Coefficient, Nodes Degree and Nodes Strength of Each Comorbidity With Psoriasis

Comorbidity	ICD Code	Jaccard Similarity Coefficient	Nodes Degree	Nodes Strength
Psoriasis vulgaris	L40	/	12	2.38
Hepatic dysfunction	K72	0.507905	12	1.72
Hypertension	I10	0.426877	12	2.02
Metabolic syndrome	E16.803	0.306324	12	2.05
NAFLD	K76	0.27668	12	1.56
Obesity/overweight	E66.900	0.243083	12	1.54
Hyperlipidemia	E78.5	0.158103	11	1.41
Diabetes	E14.9	0.132411	12	1.33
Thyroid disease	A3	0.12253	12	1.59
Impaired renal function	N18.9	0.067194	11	0.61
Hyperuricemia	E79	0.055336	11	0.84
CCVD	I25	0.051383	11	1.03
Psychological and psychiatric disorders	F20.9	0.029644	10	0.32

conditions in the network. F20.9 (psychological and psychiatric disorders) had the lowest degree of 10 and the weakest strength of 0.32, indicating its limited connections and influence in the multimorbidity network.

## Discussion

Psoriatic disease is recognized as a systemic condition, commonly associated with a higher prevalence of various comorbidities. Psoriasis comorbidities can increase the disease burden and affect the quality of life of patients. Some studies also suggest that having certain comorbidities may influence the efficacy of medications or lead to a recurrence of psoriasis. Osman et al<sup>15</sup> conducted a qualitative systematic review and found cardiovascular risk factors are associated with a lower PASI response rate of biologic treatment. Therefore, systematically studying the patterns of comorbidities in psoriasis is essential for its management and treatment selection. This study provides a comprehensive exploration of plaque psoriasis characteristics, focusing on its comorbidities. A significant finding is that the majority of psoriatic patients are multimorbid, with only 20.36% having no comorbidities. In contrast, a study conducted in Germany found that 57.9% of psoriasis patients were diagnosed with at least one comorbidity,<sup>13</sup> whereas our study identifies a prevalence of 79.64%. Most patients (64.03%) have 1–3 comorbidities, while only 15.62% present with 4–7 related diseases. This is consistent with findings from previous studies on Finnish and Canadian psoriasis patients, which underscore the prevalence of hypertension, type 2 diabetes, and other comorbidities. In Finland, the prevalence of hypertension and type 2 diabetes mellitus was 32.2% and 17.9%, respectively. The Canadian PSOLAR cohort reported prevalence of psoriatic arthritis (31.5%), hypertension (34.6%), hyperlipidemia (24.3%), mental illness (24.1%), and inflammatory bowel disease (1.6%).<sup>16</sup> Our results further underscore an increase in psoriasis comorbidities in the 50–70 age group, with particular emphasis on hepatic dysfunction and metabolic syndrome in the 31–40 and 51–60 age groups. Screening for comorbidity risks is necessary, especially in patients aged 51 to 70.

Based on the analysis results, we constructed a Phenotypic Comorbidity Network plot, which offers a detailed visualization of the intricate relationships among various diseases associated with psoriasis. The network, illustrated in Figure 6, provides valuable insights into the co-occurrence of diseases and their potential shared pathophysiological mechanisms. Nodes with high degree and strength, such as K72 and I10, demonstrate their central role within this comorbidity network, suggesting they may act as hubs that influence the severity and management of psoriasis. The elevated strength values indicate not only a frequent co-occurrence with psoriasis but also a significant impact on patient outcomes. This finding is consistent with previous studies that have identified these diseases as common comorbidities in patients with psoriasis. The prominence of hepatic dysfunction as a key comorbidity corresponds with recent research linking liver disease to psoriasis, possibly due to shared inflammatory pathways.<sup>17</sup>

The complex relationship between psoriasis and its associated comorbidities, as well as the direction of causality, continues to be a subject of investigation. Rosenø's study<sup>18</sup> on disease trajectories highlights the time-sensitive associations between psoriasis and various comorbidities. While certain conditions, such as rheumatoid arthritis and post-infective arthropathies, increase the risk of developing psoriasis, psoriasis itself serves as a risk factor for conditions like alcoholic liver disease, liver disease, osteoporosis, diabetes mellitus, and essential primary hypertension. Our analysis of the temporal relationship between the onset of psoriasis and metabolic diseases supports the hypothesis that psoriasis may predispose individuals to metabolic and cardiovascular diseases. The increased incidence of hypertension, diabetes, and cardiovascular disease following the onset of psoriasis suggests a potential causal link. This aligns with a previous nationwide cohort study indicating that patients with psoriasis have a higher risk of developing new-onset diabetes mellitus compared to the general population.<sup>19</sup> In our study, 65% developed psoriasis skin manifestations before developing diabetes among patients comorbid with diabetes. A study from Taiwan further corroborates these findings, demonstrating that patients with psoriasis are more likely to develop metabolic disorders and severe vascular disease.<sup>20</sup>

Gender differences in comorbidities are apparent, with men exhibiting a higher risk for conditions such as hyperuricemia, hypertension, cardiovascular disease, hepatic dysfunction, and impaired renal function, even though these differences do not reach statistical significance. Consistent with previous research, male patients with psoriasis tend to have a higher prevalence of cardiovascular disease compared to their female counterparts (66.9% vs 33.1%).<sup>21</sup>

The age of onset, whether early-onset psoriasis (EOP) or late-onset psoriasis (LOP), reveals differences in the prevalence of comorbidities. Patients with EOP are at a higher risk of developing certain conditions. EOP is associated

with a more pronounced inflammatory response or a more severe clinical course compared to LOP. A retrospective study comparing comorbidities in geriatric psoriasis patients found that the prevalence of overweight, coronary heart disease, and diabetes was higher in the EOP group than in the LOP group, with the opposite trend observed for hypertension.<sup>14</sup> This contrasts with findings from a study on Thai patients, which showed that the prevalence of comorbidities was significantly higher in the LOP group compared to the EOP group.<sup>22</sup> Generally, elderly patients tend to have higher incidence rates of comorbidities compared to younger patients.

This study has certain limitations, including its reliance on inpatient data, which may predominantly represent patients with moderate to severe psoriasis. Besides, many other psoriasis-related comorbidities were not included in this study (such as uveitis, COPD and so on). Psoriasis is a systemic disease that can present with nail changes, arthritic changes, and manifestations in difficult-to-treat areas, all of which may be associated with an increased risk of comorbidities. Despite these constraints, the study offers valuable insights into the complex interplay between psoriasis and its comorbidities.

In conclusion, this study highlights the systemic nature of psoriasis and its association with a wide range of comorbidities. Understanding these relationships is crucial for enhancing patient management and emphasizes the need for interdisciplinary care for individuals with psoriasis. The network analysis reinforces the importance of adopting a holistic approach to psoriasis management, where treatment plans address both the skin condition and its associated comorbidities. Identifying key comorbidities can guide clinicians in implementing targeted screening and preventive measures, thereby improving patient care and potentially reducing the overall disease burden.

## Abbreviations

NAFLD, Non-alcoholic Fatty liver disease; CCVD, Cardio-cerebrovascular disease.

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## Disclosure

The authors report no conflicts of interest in this work.

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