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A Retrospective Study of Medical Comorbidities among Adult Psoriasis Patients in Tianjin

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Abstract

Objectives:

This study aims to examine the prevalence of comorbidities in adult patients with psoriasis and compare them with those in control subjects without psoriasis in the Tianjin, China.

Design:

This study utilized data from the Inspur Health Database in Tianjin to examine the prevalence of comorbidities in adult patients with psoriasis compared to a control group.

Participants:

The participants were established by identifying all patients (age ≥ 18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019.

Setting:

The study group consisted of 20,678 adult patients with psoriasis, and a comparison group was created after 1:1 propensity score matching. Logistic regression analyses were conducted to examine the risk of 22 comorbidities for these two groups.

Outcome measures:

We focused on several health outcomes of interest, including hypertension, dyslipidemia, diabetes, hyperuricemia, obesity, metabolic syndrome, myocardial infarction, coronary atherosclerotic heart disease, cerebrovascular disease, peripheral vascular disease, inflammatory bowel diseases, non-alcoholic fatty liver disease, chronic kidney disease, infection, thyroid disease , psychiatric diseases, rheumatoid arthritis, arthritis, acquired immune deficiency syndrome (AIDS), lymphoma, and malignancy.

Results:

Patients with psoriasis had a significantly higher prevalence of 11 comorbidities and a lower

prevalence of 2 comorbidities within 12 months of follow-up. Our results also showed that the proportion of psoriatic arthritis might account for approximately 2% of all psoriasis patients. And this psoriatic arthritis group had a higher average age and CCI index score (2.27 > 1.62, P < 0.001) than the non-arthritis group.

Conclusions:

This study showed that psoriasis in the Tianjin area is associated with various comorbidities. And it also emphasizes the importance of clinical treatment in improving therapeutic effects and reducing the burden of psoriasis in China.

Key words: psoriasis, adult dermatology, dermatological epidemiology

Introduction

Psoriasis is a chronic autoimmune inflammatory condition that affects not only the skin but also extracutaneous systems. The disease burden is likely greater than reported due to the associated comorbidities,[1] including cardiometabolic, gastrointestinal, renal, malignancy, infection, mental, and ocular diseases, and psoriatic arthritis (PsA).[2 3] The abnormal immune response that causes psoriasis leads to systemic inflammation and a higher prevalence of comorbidities compared to the general population.[4] Understanding these comorbidities is crucial for better disease management and reducing the burden on individuals and society.[5]

According to the "Global Burden of Disease study" in 2019, the prevalence of psoriasis in China is estimated to be 0.56%,[6] suggesting based on the estimated population of China in 2023, which is approximately 1.4 billion people, a prevalence rate of 0.56% would correspond to over 7 million individuals with psoriasis in the country. Despite China having the largest population and the most prevalent cases of psoriasis,[7] epidemiological studies on psoriasis prevalence and

comorbidity risk are rare. Available data mostly come from the USA and Europe,[1] but baseline disease characteristics and comorbidity frequencies may differ between geographic regions,[8] including China. The World Health Organization (WHO) has recently released a report to bring attention to the public health impact of psoriasis. The report emphasizes that obtaining quality data on the epidemiology of psoriasis is a key area of research globally to better understand the size and distribution of the problem. Such data are essential for disease control and appropriate healthcare planning.

Hence, to address the gap in epidemiological data on the prevalence of psoriasis comorbidities in China, we conducted a retrospective study to determine the prevalence of a variety of comorbidities in adult patients with psoriasis. Our study also compared these prevalences with those of control subjects without psoriasis in the Tianjin area.

Methods

Study Design

This study utilized data from the Inspur Health Database in Tianjin to examine the prevalence of comorbidities in adult patients with psoriasis compared to a control group. The study and control groups were established by identifying all patients (age≥18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019. Patients with two or more psoriasis-related diagnoses were selected as the study group, while those who had never received a psoriasis diagnosis were classified as the control group. The incidence date for the psoriasis cohort was defined as the date of the first psoriasis diagnosis, while the index date for the control group was defined as the first hospital visit during the recognition period. After excluding individuals with abnormal age, visiting frequency, or missing data, 20,678 subjects were included in each group following 1:1 propensity score matching. Follow-up continued until the end of the study period on 31 October 2020. The baseline period included data within

a range≥12 months before the incidence or index date, while the follow-up period included data within a range≥12 months after the incidence or index date. The flow of participants through the study is illustrated in a consort diagram in figure 1.

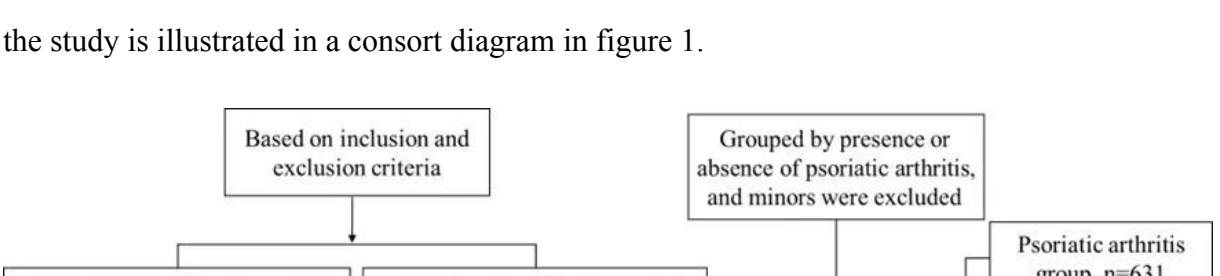

Figure 1 A consort diagram to show study process.

Outcome

In this study, we focused on several health outcomes of interest, including hypertension, dyslipidemia, diabetes, hyperuricemia, obesity, metabolic syndrome, myocardial infarction, coronary atherosclerotic heart disease, cerebrovascular disease, peripheral vascular disease, inflammatory bowel diseases, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), infection, thyroid disease (including autoimmune thyroid disease, hypothyroidism, hyperthyroidism, thyroiditis, and thyroid cancer), psychiatric diseases, rheumatoid arthritis, arthritis, acquired immune deficiency syndrome (AIDS), lymphoma, and malignancy. The ICD-10 diagnostic codes chosen for each outcome were based on medical judgment.

Statistical Analysis

Categorical variables were reported as frequency and percentage, while continuous variables were summarized using the maximum, minimum, mean, standard deviation, median, and interquartile range. Due to the non-normal distribution of continuous data, the Wilcoxon rank sum test or Kruskal-Wallis rank sum test was used to compare group differences, as appropriate. The $\chi 2$ or Fisher's exact test was used to compare categorical variables between groups. A P-value of less than 0.05 was considered statistically significant.

To address potential confounding factors, a propensity score matching analysis was conducted. A logistic regression model was developed, including age, sex, hospital visited, and type of medical insurance as covariates to generate scores, with age as the primary matching variable. One-to-one nearest-neighbor matching was performed using a caliper width of 0.05. A standardized mean difference (SMD) value of less than 0.2 was considered a good match.

Sensitivity analysis

To assess the robustness of our results, we constructed a logistic regression model and a corresponding forest plot to investigate any differences in the prevalence of the comorbidities of interest between the study and control groups over the follow-up period. The dependent variable was whether individuals developed the relevant outcomes during this period, while the independent variable was the group (psoriasis group vs. control group), as well as the presence of the target comorbidities at baseline. We obtained the odds ratio (OR) and its 95% confidence interval (CI), with statistical significance defined as a two-sided P-value of less than 0.05.

Results

The distribution of baseline characteristics between psoriasis and non-psoriasis groups before and after propensity score matching (PSM) is presented in table 1. Among the 41,296 sampled patients, the mean ± SD age was 45.37 ± 16.4 years, with 47% and 44.7% were female in the

control and psoriasis groups, respectively. No significant differences were observed between these two groups based on gender, age, type of health insurance, and hospital grade.

Table 1 Differences in Baseline Characteristics between Psoriasis Patients and Controls before and after PSM.

	Before PSM				After PSM			
	Control group, n=82430[1]	Psoriasis group, n=29949[1]	P[2]	SMD	Control group, n=21138[1]	Psoriasis group, n=21138[1]	P[2]	SMD
Sex Female Male	37616 (45.6) 44814(54.4)	12677 (42.3) 17272(57.7)	<0.001	0.067	9938 (47.0) 11200(53)	9449 (44.7) 11689(55.3)	<0.001	0.046
Age (mean (SD))	46.86 (16.81)	43.54 (16.55)	<0.001	0.199	45.37 (16.40)	45.37 (16.40)	1	<0.001
Type of payouts			<0.001	0.255			0.029	0.026
medical insurance payouts	68095 (82.6)	27295 (91.1)			18601 (88.0)	18504 (87.5)		
off-site medical insurance payouts	987 (1.2)	159 (0.5)			116 (0.5)	157 (0.7)		
self-paying	13348 (16.2)	2495 (8.3)			2421 (11.5)	2477 (11.7)		
Hospital grade = tertiary hospital （%）	65452 (79.4)	26104 (87.2)	<0.001	0.209	17436 (82.5)	17303 (81.9)	0.093	0.016

[1]n (%)
[2]Wilcoxon Rank-Sum Test; The χ^2 test of independence.

The prevalence of comorbidities in patients with and without psoriasis is shown in table 2 with the main analysis methods of Pearson χ2 independence test and Fisher's exact test. The results indicate that patients with psoriasis had a significantly higher prevalence of 11 comorbidities,

including hypertension, dyslipidemia, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, inflammatory bowel disease, nonalcoholic fatty liver disease (NAFLD), infection, psychiatric disorders, rheumatoid arthritis, and arthritis. On the other hand, patients with psoriasis had a considerably lower prevalence of 2 comorbidities, including hyperthyroidism and malignant tumor, within 12 months of the follow-up period. The sensitivity analysis showed that psoriasis patients had significantly higher probability of developing dyslipidemia (OR [CI 95%] 1.11 [1.04 – 1.19], P = 0.003), hyperuricemia (OR [CI 95%] 1.50 [1.34 – 1.81], P < 0.001), peripheral vascular disease (OR [CI 95%] 1.17 [1.02 – 1.34], P = 0.024), infection (OR [CI 95%] 1.54 [1.48 – 1.60], P < 0.001), psychiatric disorders (OR [CI 95%] 1.14 [1.05 – 1.74], P < 0.001), and rheumatoid arthritis (OR [CI 95%] 3.09 [2.44 – 3.95], P < 0.001), arthritis (OR [CI 95%] 1.61 [1.48 – 1.74], P < 0.001), while they had significantly lower probability of developing malignancy (OR [CI 95%] 0.71 [0.61-0.84], P < 0.001), cerebrovascular disease (OR [CI 95%] 0.92 [0.85-1.00], P = 0.04), and chronic kidney disease (OR [CI 95%] 0.89 [0.81-0.98], P = 0.017), compared to the control group during the 12-month follow-up period. These results are presented in figure 2.

Table 2 Prevalence of medical comorbidities in patients with psoriasis vs. comparison two groups in baseline and 12 mouths follow-up period.

	Baseline			12 mouths follow-up period		
Variable	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[3]	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[3]
Hypertension	2,773 (13%)	3,408 (16%)	<0.001	3,256 (16%)	3,613 (17%)	<0.001
Dyslipidemia	1,518 (7.3%)	2,020 (9.8%)	<0.001	1,957 (9.5%)	2,316 (11%)	<0.001
Hyperuricemia	126 (0.6%)	201 (1.0%)	<0.001	187 (0.9%)	296 (1.4%)	<0.001
Peripheral Vascular Disease	350 (1.7%)	474 (2.3%)	<0.001	423 (2.0%)	530 (2.6%)	<0.001
Infection	7,813 (38%)	9,538 (46%)	<0.001	8,258 (40%)	10,733 (52%)	<0.001
Psychiatric Diseases	958 (4.6%)	1,346 (6.5%)	<0.001	1,356 (6.6%)	1,687 (8.2%)	<0.001

Rheumatoid Arthritis	58 (0.3%)	213 (1.0%)	<0.001	93 (0.4%)	353 (1.7%)	<0.001
Arthritis	926 (4.5%)	1,816 (8.8%)	<0.001	1,092 (5.3%)	2,004 (9.7%)	<0.001
Coronary Atherosclerotic Heart Disease	2,188 (11%)	2,571 (12%)	<0.001	2,567 (12%)	2,727 (13%)	0.019
Non-alcoholic Fatty Liver Disease (NAFLD)	291 (1.4%)	408 (2.0%)	<0.001	341 (1.6%)	404 (2.0%)	0.02
inflammatory bowel diseases	34 (0.2%)	54 (0.3%)	0.033	36 (0.2%)	55 (0.3%)	0.046
Hyperthyroidism	154 (0.7%)	121 (0.6%)	0.046	196 (0.9%)	150 (0.7%)	0.013
Malignancy	269 (1.3%)	306 (1.5%)	0.12	468 (2.3%)	393 (1.9%)	0.01
Hypothyroidism	224 (1.1%)	292 (1.4%)	0.003	314 (1.5%)	327 (1.6%)	0.6
Thyroid Cancer	11 (<0.1%)	23 (0.1%)	0.04	22 (0.1%)	29 (0.1%)	0.3
Cerebrovascular Disease	1,276 (6.2%)	1,383 (6.7%)	0.032	1,551 (7.5%)	1,489 (7.2%)	0.2
Chronic Kidney Disease (CKD)	773 (3.7%)	852 (4.1%)	0.046	1,035 (5.0%)	966 (4.7%)	0.11
AIDS	19 (<0.1%)	12 (<0.1%)	0.2	27 (0.1%)	16 (<0.1%)	0.093
Myocardial Infarction	131 (0.6%)	151 (0.7%)	0.2	123 (0.6%)	147 (0.7%)	0.14
Diabetes	1,379 (6.7%)	1,472 (7.1%)	0.071	1,560 (7.5%)	1,629 (7.9%)	0.2
Autoimmune Thyroid Disease	14 (<0.1%)	24 (0.1%)	0.1	29 (0.1%)	41 (0.2%)	0.2
Lymphoma	14 (<0.1%)	12 (<0.1%)	0.7	24 (0.1%)	17 (<0.1%)	0.3
Obesity	16 (<0.1%)	23 (0.1%)	0.3	41 (0.2%)	33 (0.2%)	0.4
Metabolic Syndrome	5 (<0.1%)	2 (<0.1%)	0.5	2 (<0.1%)	0 (0%)	0.5
Thyroiditis	59 (0.3%)	82 (0.4%)	0.052	98 (0.5%)	104 (0.5%)	0.7
Thyroid Disease	740 (3.6%)	774 (3.7%)	0.4	902 (4.4%)	892 (4.3%)	0.8
Nonalcoholic Steatohepatitis (NASH)	0 (0%)	4 (<0.1%)	0.12	1 (<0.1%)	0 (0%)	>0.9

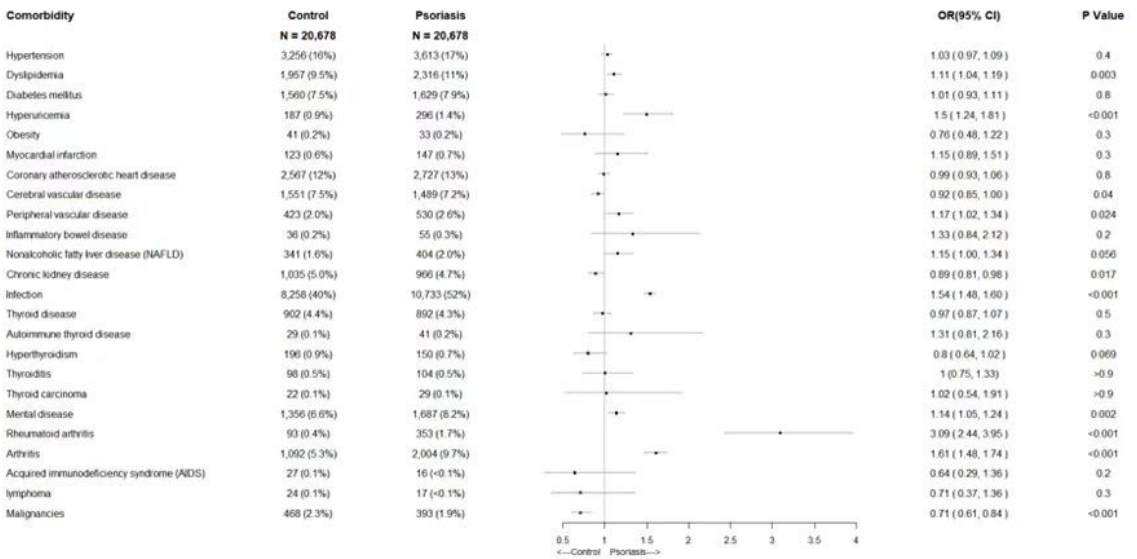

Figure 2. Adjusted odds ratios (ORs) of medical comorbidities in patients with psoriasis vs. comparison group by sensitivity analysis (OR>1 indicates that patients with psoriasis have greater incidence).

We conducted further analysis by dividing psoriasis patients into those with or without psoriatic arthritis. There were 2% psoriatic arthritis in all of psoriasis patients. Meanwhile, average age was higher in psoriatic arthritis group than the non-arthritis group ($P < 0.001$). No gender difference was observed ($P = 0.4$). Moreover, patients with psoriatic arthritis were more likely to have comorbidities such as hypertension, dyslipidemia, diabetes, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, NAFLD, chronic kidney disease, and rheumatoid arthritis. These results are shown in table 3. Additionally, we compared the CCI index in two groups during the 12-month follow-up period using the Wilcoxon rank sum test. We found that the psoriatic arthritis group had a distinct higher CCI index score ($2.27 > 1.62$, $P < 0.001$).

Table 3 Comorbidities in patients with psoriatic arthritis vs. without psoriatic arthritis group.

	12 mouths follow-up period

Variable	Psoriasis without arthritis, n = 28,240[1]	Psoriatic arthritis, n = 631[1]	*P*-value[3]
Arthritis	1,678 (5.9%)	560 (89%)	<0.001
Infection	14,287 (51%)	251 (40%)	<0.001
Rheumatoid Arthritis	232 (0.8%)	147 (23%)	<0.001
Hypertension	3,984 (14%)	120 (19%)	<0.001
Coronary Atherosclerotic Heart Disease	2,965 (10%)	86 (14%)	0.011
Dyslipidemia	2,540 (9.0%)	83 (13%)	<0.001
Diabetes	1,747 (6.2%)	68 (11%)	<0.001
Chronic Kidney Disease (CKD)	1,094 (3.9%)	46 (7.3%)	<0.001
Hyperuricemia	324 (1.1%)	29 (4.6%)	<0.001
Non-alcoholic Aatty Liver Disease (NAFLD)	447 (1.6%)	23 (3.6%)	<0.001
Peripheral Vascular Disease	569 (2.0%)	22 (3.5%)	0.01
Hyperthyroidism	170 (0.6%)	8 (1.3%)	0.062
Thyroid Disease	990 (3.5%)	30 (4.8%)	0.093
Psychiatric Diseases	1,885 (6.7%)	52 (8.2%)	0.12
Autoimmune Thyroid Disease	40 (0.1%)	2 (0.3%)	0.2
Hypothyroidism	351 (1.2%)	5 (0.8%)	0.3
Acquired Immune Deficiency Syndrome (AIDS)	18 (<0.1%)	1 (0.2%)	0.3
Thyroid Cancer	30 (0.1%)	1 (0.2%)	0.5
Malignancy	428 (1.5%)	8 (1.3%)	0.6
Myocardial Infarction	152 (0.5%)	4 (0.6%)	0.6
Thyroiditis	108 (0.4%)	3 (0.5%)	0.7
Cerebrovascular Disease	1,649 (5.8%)	37 (5.9%)	>0.9
Lymphoma	20 (<0.1%)	0 (0%)	>0.9
Inflammatory Bowel Diseases	60 (0.2%)	1 (0.2%)	>0.9
Obesity	36 (0.1%)	0 (0%)	>0.9
Nonalcoholic Steatohepatitis (NASH)	0 (0%)	0 (0%)	
Metabolic Syndrome	0 (0%)	0 (0%)	

Discussion

It is widely recognized that psoriasis patients usually suffer a heavy economic and mental burden. It affects not only at the skin level but also multiple systems and organs. Numerous epidemiological data on psoriasis have been collected from European countries, the U.K., and the U.S.A[1] that addressed comorbidities are quite common in psoriasis

patients, however, there are few information on Asian populations. This study aimed to proceed a large retrospective study based on the Inspur Tianjin Health Database to assess the comorbidities in psoriasis patients in Tianjin and provide more insights on psoriasis in the Han nationality. Due to the COVID-19 outbreak, the time for us to supplement and optimize data and analysis results has been extended, and it was not until recently that all of it was completed. Our current study found that the comorbidity with the highest prevalence among psoriasis patients was infection, with a significantly higher prevalence than that of the control group (52% > 40%, P < 0.001). Psoriasis patients are at an increased risk of infection, which may be due to treatment with immunomodulatory or immunosuppressive drugs[9]. Vaccinations may prevent specific infections, but they can also trigger and exacerbate psoriasis, as studies have shown in relation to flu vaccination[10]. There have also been reports of psoriatic disease exacerbation triggered by COVID-19 mRNA vaccination, with the mechanism similar to that of other vaccines in that vaccination induces IL-6, which stimulates Th17 cells to produce IL-22, a significant contributor to keratinocyte proliferation in psoriasis[11]. Recently, increasing epidemiological studies have shown a close correlation between psoriasis and metabolic syndrome and cardiovascular factors. Our findings are consistent with these results, with the most prevalent comorbidities being hypertension (17%), hyperlipidemia (11%), diabetes mellitus (7.9%), and coronary heart disease (13%). Compared to the prevalence of metabolic diseases in Western countries, such as the United States, France, and Chile,[12-14] our results revealed a much lower prevalence of metabolic diseases but an increased prevalence of cardiovascular diseases. This may be due to a large population unable to obtain adequate medical resources[15]. However, the cross-sectional design of this study did not allow us to establish a temporal relationship between metabolic comorbidities and cardiovascular disease. Further prospective longitudinal cohort studies are needed to confirm this. Although there was

no significant difference between the two groups, the prevalence of diabetes mellitus was slightly higher in the psoriasis group than in the control group. A nationally representative Chinese cross-sectional survey in 2018 showed that the prevalence of diabetes had significantly risen from 10.9% (95%CI, 10.4%-11.5%) in 2013 to 12.4% (95%CI, 11.8%-13.0%) in 2018.[16] Therefore, one possible reason for the lack of a significant difference between the two groups is that other independent risk factors for diabetes may have attenuated the role of psoriasis as a risk factor. On the other hand, the comparison subjects selected were non-psoriatic patients who came to the hospital, and they may have had comorbidities of concern, such as diabetes, hypertension, CVD, and other chronic diseases, or have had high-risk factors for these diseases. This may explain why some of the differences in the diseases reported between the two groups were not significant. Psoriasis is associated with various negative impacts on mental health, including increased risks of anxiety, depression, low self-esteem, alexithymia, stress, self-harm, and suicidality.[17] Patients with psoriasis experience greater mental health comorbidity burdens, [18] [19] a recent large case-control study from Denmark evaluated the occurrence of mental health disorders by reviewing patient records and found that mental health disorders were observed in 3.1% of patients with psoriasis compared to 2.2% of controls.[20] This finding is consistent with our results showing that the prevalence of psychiatric disorders was significantly higher in psoriasis patients (8.2% vs. 6.6%, $P < 0.05$). Currently, some research focuses on the impact of psychiatric complications during psoriasis treatment.[21] Dermatologists need to screen patients with psoriasis for psychiatric comorbidities and provide appropriate mental health support. Inflammatory bowel disease (IBD) has been caused attention among comorbidities of psoriasis, with a prevalence about 0.3%.[22] There is growing evidence that they could be interacted on each other. Our results confirm that the prevalence of psoriasis in our study group is significantly higher than that of the control group (0.3% > 0.2%, P=0.046), which

is consistent with other studies. There are many overlaps in pathophysiological mechanisms between the two conditions, consequently, drugs targeting these common pathways have become a hot topic in the treatment of these two comorbidities.[23 24] Non-alcoholic fatty liver disease (NAFLD), is now regarded as the hepatic manifestation of metabolic syndrome. The relationship between psoriasis and NAFLD was independent of other hepatic risk factors, such as potentially hepatotoxic anti-psoriatic therapy and alcohol consumption.[25] Our results confirm that the prevalence of NAFLD in psoriasis patients is significantly higher than in controls (2.0% > 1.6%, P=0.02). NAFLD might actively contribute to the severity of psoriasis through the release of pathogenic mediators from the inflamed liver,[26] the systemic release of pro-inflammatory/pro-atherogenic mediators from the steatotic liver is also one of the underlying mechanisms by which NAFLD may contribute to accelerated atherogenesis.[27] It is worthy to note that the presence of NAFLD should be taken into consideration when choosing therapy, as some anti-psoriatic drugs are potentially hepatotoxic.[28]

In our study, we found a lower incidence of malignant tumors compared to the control group (1.9%＜2.3%, P=0.01), which contrasts with some other studies. Chronic inflammation and impaired immune surveillance have been suggested to be linked to an increased risk of cancer.[29] A 2013 meta-analysis reported an increased risk of solid cancers in the upper aerodigestive tract including the esophagus, lung, liver, and pancreas. However, after adjusting for cigarette smoking and alcohol abuse, they were unable to replicate the increased risk of lung, esophagus, or urinary tract cancer, suggesting an associated rather than an independent risk in patients with psoriasis. The risk of squamous cell carcinoma is increased in patients treated with psoralen combined with ultraviolet A (PUVA), which has been accepted by most studies but was not tested in our study.[30] More prospective studies are needed to investigate this controversial issue.

Psoriatic arthritis can lead to joint destruction, deformity, reduced functional status, and an increased risk of death.[31] Undiagnosed psoriatic arthritis is common among patients with psoriasis, ranging from 10% to 40% in previous studies.[32] In our study, the rate of psoriasis combined with arthritis was 9.7%, but only 2% of patients had psoriatic arthritis, falling within the upper range of the 1.3% to 34.7% reported by the WHO global report on psoriasis. This may be attributed to genetic differences and diagnostic criteria or physicians failing to examine joint symptoms in patients without active complaints of joint pain in the dermatology outpatient clinic. Psoriatic arthritis usually develops 8 to 10 years after the onset of psoriasis, and a delay in diagnosis of 6 months can lead to peripheral joint damage and functional disability.[33] Our study found that the psoriatic arthritis group patients were older and had a higher CCL index compared to patients without arthritis, indicating longer disease duration and worse prognosis. Our findings are consistent with prior reports that a higher prevalence of cardiovascular disease and associated risk factors, such as diabetes and other chronic diseases, in patients with PsA compared with psoriasis patients in the community.[34] Multiple comorbidities in a single patient can make selecting therapeutic agents challenging due to safety concerns and create challenges in assessing the functional impact of PsA. Therefore, early diagnosis and treatment are crucial to improve patient outcomes. Screening for psoriatic arthritis soon after the diagnosis of psoriasis may lead to earlier identification, allowing for earlier treatment and prevention of joint damage and disability.

This study confirms that common complications may also occur in psoriasis patients, and these conditions may affect their own health and social interactions. It filled a gap in the epidemiological data of psoriasis comorbidities in China, providing insights on the understanding of the condition's causes, quality of life, healthcare trends, and research priorities. Additionally, the study highlights the importance of identifying environmental

factors that could influence psoriasis and its comorbidities, which can inform policy decisions and quantify the financial burden to society. However, the study has some limitations due to the retrospective studies based on health databases. Firstly, the temporal trajectory of psoriasis could not be fully determined, requiring a more extensive dataset to identify the optimal time to intervene and reduce the risk of comorbidities. Secondly, there may be potential selection bias since the control population consisted only of patients who visited the hospital, who may themselves have co-morbidities or high-risk factors for these conditions. Thirdly, the study was based on a regional database rather than a national medical insurance database, and patient mobility may have caused some patients with psoriasis from other regions not to seek treatment for other diseases in Tianjin, which may have impacted the data. It is important to emphasize that the results of the sensitivity analysis are partially consistent with the main analysis method, which suggests that the results obtained through the main analysis are more reliable. Inconsistent diseases are also given priority to the main analysis, but the level of evidence may be lower. Further exploration is needed to determine whether the prevalence of diseases such as hyperthyroidism, chronic kidney disease, and cerebrovascular disease decreases in psoriasis patients. Overall, this study provides valuable insights into the burden of comorbidities in patients with psoriasis in China and highlights the need for early diagnosis and management of these comorbidities to improve patient outcomes. It will be important for future studies to address these limitations and to use a more representative sample to validate these findings. Nonetheless, this study highlights the need for a comprehensive approach to the management of patients with psoriasis.

Conclusion

This study represents the most comprehensive and extensive cross-sectional investigation of psoriasis comorbidities conducted in certain regions of China. The results reveal a high

prevalence of comorbidities, including cardiovascular diseases, metabolic diseases, infections, psychiatric disorders, and psoriatic arthritis, which is consistent with findings from other countries. More attention should be given to early screening for patients with psoriatic arthritis because of its high prevalence and poor prognosis. These findings highlight the need for dermatologists to be aware of the high prevalence of these comorbidities in Chinese psoriasis patients, to provide optimal care. In conclusion, the high prevalence of comorbidities emphasizes the importance of better treatment options and therapeutic management to improve clinical outcomes and reduce the burden of psoriasis in China.

Strengths and limitations of this study

This study confirms that common complications may also occur in psoriasis patients, and these conditions may affect their own health and social interactions. It filled a gap in the epidemiological data of psoriasis comorbidities in China.

The study was based on a regional database rather than a national medical insurance database, and patient mobility may have caused some patients with psoriasis from other regions not to seek treatment for other diseases in Tianjin, which may have impacted the data.

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Author Contributions

TY Zhang and Y Guo led the writing, reviewing, and editing of the manuscript. K Zhang, L Fan, J Ma, Y Li, X Wang, Q Zhou, and Q Zhao contributed towards conceptualization,

reviewing, and editing of the manuscript. H Wang and S Hou led the conceptualization and administration of this project and also contributed towards reviewing and editing the manuscript.

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Competing interests

None declared.

Patient and public involvement

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References

1 Griffiths CEM, Walt JMVD, Ashcroft DM, *et al*. The global state of psoriasis disease epidemiology: a workshop report. *Brit J Dermatol* 2017;177:e4-7.

2 Bu J, Ding RL, Zhou LJ, *et al*. Epidemiology of Psoriasis and Comorbid Diseases: A Narrative Review. *Front Immunol* 2022;13:880201.

3 Takeshita J, Grewal S, Langan SM, *et al*. Psoriasis and comorbid diseases: Epidemiology. *J Am Acad Dermatol* 2017;76:377-90.

4 Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. *J Eur Acad Dermatol* 2012;26:3-11.

5 Dauden E, Blasco AJ, Bonanad C, *et al*. Position statement for the management of comorbidities in psoriasis. *J Eur Acad Dermatol* 2018;32:2058-73.

6 Liu SM, Yan ZR, Liu Q. The Burden of Psoriasis in China and Global Level from 1990 to 2019: A Systematic Analysis from the Global Burden of Disease Study 2019. *Biomed Res Int* 2022;2022:3461765.

7 Li J, Yu MW, Wang YW, *et al*. Prevalence of psoriasis and associated risk factors in China: protocol of a nationwide, population-based, cross-sectional study. *BMJ open* 2019;9:e027685.

8 Enos CW, O'Connell KA, Harrison RW, *et al*. Geographic Variations in Biologic Therapy and Disease Characteristics: A Pilot-Study in the Corrona Psoriasis Registry. *J Drugs Dermatol* 2020;19:1119-22.

9 Rahier JF, Moutschen M, Gompel AV, *et al*. Vaccinations in patients with immune-mediated inflammatory diseases. *Rheumatology* 2010;49:1815-27.

10 Gunes AT, Fetil E, Akarsu S, *et al*. Possible Triggering Effect of Influenza Vaccination

on Psoriasis. *J Immunol Res* 2015;2015:258430.

11 Ohmura S, Hanai S, Ishihara R, *et al*. A case of psoriatic spondyloarthritis exacerbation triggered by COVID - 19 messenger RNA vaccine. *J Eur Acad Dermatol* 2022;36:e427-9.

12 Valenzuela F, Cruz CDLA, Lecaros C, *et al*. Comorbidities in Chilean Psoriasis Patients-a Global Healthcare Study on Psoriasis. *Clin Exp Dermatol* 2022;47:2234-41.

13 Prignano F, Ricceri F, Pescitelli L, *et al*. Itch in psoriasis: epidemiology, clinical aspects and treatment options. *Clin Cosmet Inv Derm* 2009;2:9-13.

14 Shah K, Mellars L, Changolkar A, *et al*. Real-world burden of comorbidities in US patients with psoriasis. *J Am Acad Dermatol* 2017;77:287-92.

15 Dagenais GR, Leong DP, Rangarajan S, *et al*. Variations in common diseases, hospital admissions, and deaths in middle-aged adults in 21 countries from five continents (PURE): a prospective cohort study. *Lancet* 2020;395:785-94.

16 Wang LM, Peng W, Zhao ZP, *et al*. Prevalence and Treatment of Diabetes in China, 2013-2018. *Jama-J Am Med Assoc* 2021;326:2498-506.

17 Wu JJ, Feldman SR, Koo J, *et al*. Epidemiology of mental health comorbidity in psoriasis. *J Dermatol Treat* 2018;29:487-95.

18 Kurd SK, Troxel AB, Crits-Christoph P, *et al*. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. *Arch Dermatol* 2010;146:891-5.

19 Pompili M, Innamorati M, Trovarelli S, *et al*. Suicide risk and psychiatric comorbidity in patients with psoriasis. *J Int Med Res* 2016;44:61-6.

20 Egeberg A, Hansen PR, Gislason GH, *et al*. Risk of self-harm and nonfatal suicide attempts, and completed suicide in patients with psoriasis: a population-based cohort

study. *Brit J Dermatol* 2016;175:493-500.

21 Krishnan R, Cella D, Leonardi C, *et al*. Effects of etanercept therapy on fatigue and symptoms of depression in subjects treated for moderate to severe plaque psoriasis for up to 96 weeks. *Brit J Dermatol* 2007;157:1275-7.

22 Hedin CRH, Sonkoly E, Eberhardson M, *et al*. Inflammatory bowel disease and psoriasis: modernizing the multidisciplinary approach. *J Intern Med* 2021;290:257-78.

23 Puig L, Costanzo A, Muñoz-Elías EJ, *et al*. The biological basis of disease recurrence in psoriasis: a historical perspective and current models. *Brit J Dermatol* 2022;186:773-81.

24 Singh R, Koppu S, Perche PO, *et al*. The Cytokine Mediated Molecular Pathophysiology of Psoriasis and Its Clinical Implications. *Int J Mol Sci* 2021;22:12793.

25 Gisondi P, Giglio MD Cozzi A, *et al*. Psoriasis, the liver, and the gastrointestinal tract. *Dermatol Ther* 2010;23:155-9.

26 Alwis NMWDE, Day CP. Non-alcoholic fatty liver disease: the mist gradually clears. *J Hepatol* 2008;48:S104-12.

27 Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: causal effect or epiphenomenon? *Diabetologia* 2008;51:1947-53.

28 Rosenberg P, Urwitz H, Johannesson A, *et al*. Psoriasis patients with diabetes type 2 are at high risk of developing liver fibrosis during methotrexate treatment. *J Hepatol* 2007;46:1111-8.

29 Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell* 2010;140:883-99.

30 Pouplard C, Brenaut E, Horreau C, *et al*. Risk of cancer in psoriasis: a systematic review

and meta-analysis of epidemiological studies. *J Eur Acad Dermatol* 2013;27:36-46.

31 Gladman DD, Antoni C, Mease P, *et al*. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64:14-7.

32 Villani AP, Rouzaud M, Sevrain M, *et al*. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. *J Am Acad Dermatol* 2015;73:242-8.

33 Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic Arthritis and Burden of Disease: Patient Perspectives from the Population-Based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) Survey. *Rheumatol Ther* 2016;3:91-102.

34 Haroon M, Gallagher P, Fitzgerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045-50.

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Medical Comorbidities among Psoriasis Patients in Tianjin Adults: A cross-sectional analysis of the Health Database study

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Abstract

Objectives:

This study aims to examine the prevalence of comorbidities in adult patients with psoriasis and compare them with those in control subjects without psoriasis in Tianjin, China.

Design:

Cross-sectional study.

Participants:

The participants were established by identifying all patients (age ≥ 18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019.

Setting:

The study group consisted of 20,678 adult patients with psoriasis, and a comparison group was created after 1:1 propensity score matching. Logistic regression analyses were conducted to examine the risk of 22 comorbidities for these two groups.

Results:

Patients with psoriasis had a significantly higher prevalence of 11 comorbidities and a lower prevalence of 2 comorbidities within 12 months of follow-up. Our results also showed that the proportion of psoriatic arthritis might account for approximately 2% of all psoriasis patients. This psoriatic arthritis group had a higher average age and CCI index score (2.27 > 1.62, P < 0.001) than the non-arthritis group.

Conclusions:

This study showed that psoriasis in Tianjin is associated with various comorbidities. It also emphasizes the importance of clinical treatment in improving therapeutic effects and reducing the burden of psoriasis in China.

Strengths and limitations of this study:

- This study involved a large cohort of participants (n=20,678) for cross-sectional analysis.
- To mitigate potential confounding factors, subjects were matched 1:1 based on propensity scores in each group.
- Odds ratios (ORs) were adjusted for confounding variables to assess the independent relationship between medical comorbidities in patients with psoriasis compared to the control group using sensitivity analysis.
- The cross-sectional design of this study limited our ability to establish causal inferences regarding psoriasis and comorbidities.
- Due to incomplete electronic medical records in the database, the impact of severity and other potential variables on comorbidities could not be observed.

Keywords: psoriasis, psoriatic arthritis (PsA), comorbidity, epidemiology, Chinese Han

Introduction

Psoriasis is an immune-mediated condition that affects not only the skin but also extracutaneous systems. The disease burden is likely greater than reported due to the associated comorbidities [1], including cardiometabolic, gastrointestinal, renal, malignancy, infection, mental, and ocular diseases, and psoriatic arthritis (PsA) [2,3]. The abnormal immune response that causes psoriasis leads to systemic inflammation and a higher prevalence of comorbidities compared to the general population [4]. Understanding these comorbidities is crucial for better disease management and reducing the burden on individuals and society [5].

According to the "Global Burden of Disease study" in 2019, the prevalence of psoriasis in China is estimated to be 0.56% [6], suggesting based on the estimated population of China in 2023, which is approximately 1.4 billion people, a prevalence rate of 0.56% would correspond to over 7 million individuals with psoriasis in the country. Despite China having the largest population and the most prevalent cases of psoriasis [7], epidemiological studies on psoriasis prevalence and comorbidity risk are rare. Available data mainly come from the USA and Europe [1], but baseline disease characteristics and comorbidity frequencies may differ between geographic regions [8], including China. The World Health Organization (WHO) has recently released a report to bring attention to the public health impact of psoriasis. The report emphasizes that obtaining quality data on the epidemiology of psoriasis is a crucial area of research globally better to understand the size and distribution of the problem. Such data are essential for disease control and appropriate healthcare planning.

Hence, to address the gap in epidemiological data on the prevalence of psoriasis comorbidities in China, we conducted a retrospective study to determine the prevalence of various comorbidities in adult patients with psoriasis. Our study also compared these prevalences with those of control subjects without psoriasis in Tianjin.

Methods

Study Design

This study utilized data from the Inspur Health Database in Tianjin to examine the prevalence of comorbidities in adult patients with psoriasis compared to a control group. The study and control groups were established by identifying all patients (age≥18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019. Patients with two or more psoriasis-related diagnoses were selected as the study group, while those who had never received a psoriasis diagnosis were classified as the control group. The incidence date for the

psoriasis cohort was defined as the date of the first psoriasis diagnosis, while the index date for the control group was defined as the first hospital visit during the recognition period. After excluding individuals with abnormal age, visiting frequency, or missing data, 20,678 subjects were included in each group following 1:1 propensity score matching. Follow-up continued until the end of the study period on 31 October 2020. The baseline period encompassed data from at least 12 months prior to the incidence or index date, while the follow-up period comprised data from at least months after the incidence or index date. The flow of participants through the study is illustrated in a consort diagram in Figure 1.

Outcome

In this study, we focused on several health outcomes of interest, including hypertension, dyslipidemia, diabetes, hyperuricemia, obesity, metabolic syndrome, myocardial infarction, coronary atherosclerotic heart disease, cerebrovascular disease, peripheral vascular disease, inflammatory bowel diseases, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), infection, thyroid disease (including autoimmune thyroid disease, hypothyroidism, hyperthyroidism, thyroiditis, and thyroid cancer), psychiatric diseases, rheumatoid arthritis, arthritis, acquired immune deficiency syndrome (AIDS), lymphoma, and malignancy. The ICD-10 diagnostic codes chosen for each outcome were based on medical judgment.

Statistical Analysis

Categorical variables were reported as frequency and percentage, while continuous variables were summarized using the maximum, minimum, mean, standard deviation, median, and interquartile range. Due to the non-normal distribution of constant data, the Wilcoxon rank sum test or Kruskal-Wallis rank sum test was used to compare group differences, as appropriate.

The $\chi 2$ or Fisher's exact test was used to compare categorical variables between groups. A P-value of less than 0.05 was considered statistically significant.

To address potential confounding factors, a propensity score matching analysis was conducted. A logistic regression model was developed, including age, sex, hospital visited, and type of medical insurance as covariates to generate scores, with age as the primary matching variable. One-to-one nearest-neighbor matching was performed using a caliper width of 0.05. A standardized mean difference (SMD) value of less than 0.2 was considered a good match.

Sensitivity analysis

To assess the robustness of our results, we constructed a logistic regression model and a corresponding forest plot to investigate any differences in the prevalence of the comorbidities of interest between the study and control groups over the follow-up period. The dependent variable was whether individuals developed the relevant outcomes during this period, while the independent variable was the group (psoriasis group vs. control group), as well as the presence of the target comorbidities at baseline. We obtained the odds ratio (OR) and its 95% confidence interval (CI), with statistical significance defined as a two-sided P-value of less than 0.05.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Results

The distribution of baseline characteristics between psoriasis and non-psoriasis groups before and after propensity score matching (PSM) is presented in Table 1. Among the 41,296 sampled patients, the mean ± SD age was 45.37 ± 16.4 years, with 47% and 44.7% being female in the

control and psoriasis groups, respectively. No significant differences were observed between these two groups based on gender, age, type of health insurance, and hospital grade.

Table 1 Differences in Baseline Characteristics between Psoriasis Patients and Controls before and after PSM.

	Before PSM				After PSM			
	Control group, n=82430[1]	Psoriasis group, n=29949[1]	P[2]	SMD	Control group, n=21138[1]	Psoriasis group, n=21138[1]	P[2]	SMD
Sex Female Male	37616 (45.6) 44814(54.4)	12677 (42.3) 17272(57.7)	<0.001	0.067	9938 (47.0) 11200(53)	9449 (44.7) 11689(55.3)	<0.001	0.046
Age (mean (SD))	46.86 (16.81)	43.54 (16.55)	<0.001	0.199	45.37 (16.40)	45.37 (16.40)	1	<0.001
Type of payouts			<0.001	0.255			0.029	0.026
medical insurance payouts	68095 (82.6)	27295 (91.1)			18601 (88.0)	18504 (87.5)		
off-site medical insurance payouts	987 (1.2)	159 (0.5)			116 (0.5)	157 (0.7)		

self-paying	13348 (16.2)	2495 (8.3)			2421 (11.5)	2477 (11.7)		
Hospital grade = tertiary hospital （%）	65452 (79.4)	26104 (87.2)	<0.001	0.209	17436 (82.5)	17303 (81.9)	0.093	0.016

[1]n (%)

[2]Wilcoxon Rank-Sum Test; The χ^2 test of independence.

The prevalence of comorbidities in patients with and without psoriasis is shown in Table 2 with the primary analysis methods of Pearson $\chi 2$ independence test and Fisher's exact test. The results indicate that patients with psoriasis had a significantly higher prevalence of 11 comorbidities, including hypertension, dyslipidemia, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, inflammatory bowel disease, nonalcoholic fatty liver disease (NAFLD), infection, psychiatric disorders, rheumatoid arthritis, and arthritis. On the other hand, patients with psoriasis had a considerably lower prevalence of 2 comorbidities, including hyperthyroidism and malignant tumor, within 12 months of the follow-up period. The sensitivity analysis showed that psoriasis patients had significantly higher probability of developing dyslipidemia (OR [CI 95%] 1.11 [1.04 – 1.19], P = 0.003), hyperuricemia (OR [CI 95%] 1.50 [1.34 – 1.81], P < 0.001), peripheral vascular disease (OR [CI 95%] 1.17 [1.02 – 1.34], P = 0.024), infection (OR [CI 95%] 1.54 [1.48 – 1.60], P < 0.001), psychiatric disorders (OR [CI 95%] 1.14 [1.05 – 1.74], P < 0.001), and rheumatoid arthritis (OR [CI 95%] 3.09 [2.44 – 3.95], P < 0.001), arthritis (OR [CI 95%] 1.61 [1.48 – 1.74], P < 0.001), while they had significantly lower probability of developing malignancy (OR [CI 95%] 0.71 [0.61-0.84], P <

0.001), cerebrovascular disease (OR [CI 95%] 0.92 [0.85-1.00], P = 0.04), and chronic kidney disease (OR [CI 95%] 0.89 [0.81-0.98], P = 0.017), compared to the control group during the 12-month follow-up period. These results are presented in Figure 2.

Table 2 Prevalence of medical comorbidities in patients with psoriasis vs. comparison of two groups in baseline and 12 months follow-up period.

	Baseline			12 months follow-up period		
Variable	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[3]	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[3]
Hypertension	2,773 (13%)	3,408 (16%)	<0.001	3,256 (16%)	3,613 (17%)	<0.001
Dyslipidemia	1,518 (7.3%)	2,020 (9.8%)	<0.001	1,957 (9.5%)	2,316 (11%)	<0.001
Hyperuricemia	126 (0.6%)	201 (1.0%)	<0.001	187 (0.9%)	296 (1.4%)	<0.001
Peripheral Vascular Disease	350 (1.7%)	474 (2.3%)	<0.001	423 (2.0%)	530 (2.6%)	<0.001
Infection	7,813 (38%)	9,538 (46%)	<0.001	8,258 (40%)	10,733 (52%)	<0.001
Psychiatric Diseases	958 (4.6%)	1,346 (6.5%)	<0.001	1,356 (6.6%)	1,687 (8.2%)	<0.001
Rheumatoid Arthritis	58 (0.3%)	213 (1.0%)	<0.001	93 (0.4%)	353 (1.7%)	<0.001
Arthritis	926 (4.5%)	1,816 (8.8%)	<0.001	1,092 (5.3%)	2,004 (9.7%)	<0.001
Coronary Atherosclerotic Heart Disease	2,188 (11%)	2,571 (12%)	<0.001	2,567 (12%)	2,727 (13%)	0.019

Non-alcoholic Fatty Liver Disease (NAFLD)	291 (1.4%)	408 (2.0%)	<0.001	341 (1.6%)	404 (2.0%)	0.02
inflammatory bowel diseases	34 (0.2%)	54 (0.3%)	0.033	36 (0.2%)	55 (0.3%)	0.046
Hyperthyroidis-m	154 (0.7%)	121 (0.6%)	0.046	196 (0.9%)	150 (0.7%)	0.013
Malignancy	269 (1.3%)	306 (1.5%)	0.12	468 (2.3%)	393 (1.9%)	0.01
Hypothyroidis-m	224 (1.1%)	292 (1.4%)	0.003	314 (1.5%)	327 (1.6%)	0.6
Thyroid Cancer	11 (<0.1%)	23 (0.1%)	0.04	22 (0.1%)	29 (0.1%)	0.3
Cerebrovascul-ar Disease	1,276 (6.2%)	1,383 (6.7%)	0.032	1,551 (7.5%)	1,489 (7.2%)	0.2
Chronic Kidney Disease (CKD)	773 (3.7%)	852 (4.1%)	0.046	1,035 (5.0%)	966 (4.7%)	0.11
AIDS	19 (<0.1%)	12 (<0.1%)	0.2	27 (0.1%)	16 (<0.1%)	0.093
Myocardial Infarction	131 (0.6%)	151 (0.7%)	0.2	123 (0.6%)	147 (0.7%)	0.14
Diabetes	1,379 (6.7%)	1,472 (7.1%)	0.071	1,560 (7.5%)	1,629 (7.9%)	0.2
Autoimmune Thyroid Disease	14 (<0.1%)	24 (0.1%)	0.1	29 (0.1%)	41 (0.2%)	0.2
Lymphoma	14 (<0.1%)	12 (<0.1%)	0.7	24 (0.1%)	17 (<0.1%)	0.3

Obesity	16 (<0.1%)	23 (0.1%)	0.3	41 (0.2%)	33 (0.2%)	0.4
Metabolic Syndrome	5 (<0.1%)	2 (<0.1%)	0.5	2 (<0.1%)	0 (0%)	0.5
Thyroiditis	59 (0.3%)	82 (0.4%)	0.052	98 (0.5%)	104 (0.5%)	0.7
Thyroid Disease	740 (3.6%)	774 (3.7%)	0.4	902 (4.4%)	892 (4.3%)	0.8
Nonalcoholic Steatohepatitis (NASH)	0 (0%)	4 (<0.1%)	0.12	1 (<0.1%)	0 (0%)	>0.9

We further analyzed psoriasis patients into those with or without psoriatic arthritis. There was 2% psoriatic arthritis in all of psoriasis patients. Meanwhile, the average age was higher in psoriatic arthritis group than in the non-arthritis group ($P < 0.001$). No gender difference was observed ($P = 0.4$). Moreover, patients with psoriatic arthritis were more likely to have comorbidities such as hypertension, dyslipidemia, diabetes, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, NAFLD, chronic kidney disease, and rheumatoid arthritis. These results are shown in Table 3. Additionally, we compared the CCI index in two groups during the 12-month follow-up period using the Wilcoxon rank sum test. The psoriatic arthritis group had a distinct higher CCI index score ($2.27 > 1.62$, $P < 0.001$).

Table 3 Comorbidities in patients with psoriatic arthritis vs. without psoriatic arthritis group.

	12 months follow-up period		
Variable	Psoriasis without arthritis, n = 28,240[1]	Psoriatic arthritis, n = 631[1]	*P*-value[3]
Arthritis	1,678 (5.9%)	560 (89%)	<0.001
Infection	14,287 (51%)	251 (40%)	<0.001

Rheumatoid Arthritis	232 (0.8%)	147 (23%)	<0.001
Hypertension	3,984 (14%)	120 (19%)	<0.001
Coronary Atherosclerotic Heart Disease	2,965 (10%)	86 (14%)	0.011
Dyslipidemia	2,540 (9.0%)	83 (13%)	<0.001
Diabetes	1,747 (6.2%)	68 (11%)	<0.001
Chronic Kidney Disease (CKD)	1,094 (3.9%)	46 (7.3%)	<0.001
Hyperuricemia	324 (1.1%)	29 (4.6%)	<0.001
Non-alcoholic Fatty Liver Disease (NAFLD)	447 (1.6%)	23 (3.6%)	<0.001
Peripheral Vascular Disease	569 (2.0%)	22 (3.5%)	0.01
Hyperthyroidism	170 (0.6%)	8 (1.3%)	0.062
Thyroid Disease	990 (3.5%)	30 (4.8%)	0.093
Psychiatric Diseases	1,885 (6.7%)	52 (8.2%)	0.12
Autoimmune Thyroid Disease	40 (0.1%)	2 (0.3%)	0.2
Hypothyroidism	351 (1.2%)	5 (0.8%)	0.3
Acquired Immune Deficiency Syndrome (AIDS)	18 (<0.1%)	1 (0.2%)	0.3
Thyroid Cancer	30 (0.1%)	1 (0.2%)	0.5
Malignancy	428 (1.5%)	8 (1.3%)	0.6
Myocardial Infarction	152 (0.5%)	4 (0.6%)	0.6
Thyroiditis	108 (0.4%)	3 (0.5%)	0.7
Cerebrovascular Disease	1,649 (5.8%)	37 (5.9%)	>0.9

Lymphoma	20 (<0.1%)	0 (0%)	>0.9
Inflammatory Bowel Diseases	60 (0.2%)	1 (0.2%)	>0.9
Obesity	36 (0.1%)	0 (0%)	>0.9

Discussion

It is widely recognized that psoriasis patients usually suffer a heavy economic and mental burden. It affects not only the skin level but also multiple systems and organs. Numerous epidemiological data on psoriasis have been collected from European countries, the U.K. and the U.S.A [1] that addressed comorbidities are pretty common in psoriasis patients, however, there is little few information on Asian populations. This study aimed to proceed with a large retrospective study based on the Inspur Tianjin Health Database to assess the comorbidities in psoriasis patients in Tianjin and provide more insights on psoriasis in the Han nationality. Due to the COVID-19 outbreak, the time for us to supplement and optimize data and analysis results has been extended, and it was not until recently that all of it was completed.

Our current study found that the comorbidity with the highest prevalence among psoriasis patients was infection, with a significantly higher prevalence than that of the control group (52% > 40%, $P < 0.001$). Psoriasis patients are at an increased risk of infection, which may be due to treatment with immunomodulatory or immunosuppressive drugs [9]. Vaccinations may prevent specific infections, but they can also trigger and exacerbate psoriasis, as studies have shown in relation to flu vaccination [10]. There have also been reports of psoriatic disease exacerbation triggered by COVID-19 mRNA vaccination, with the mechanism similar to that of other vaccines in that vaccination induces IL-6, which stimulates Th17 cells to produce IL-22, a significant contributor to keratinocyte proliferation in psoriasis [11]. Increasing

epidemiological studies have recently shown a close correlation between psoriasis and metabolic syndrome and cardiovascular factors. Our findings are consistent with these results, with the most prevalent comorbidities being hypertension (17%), hyperlipidemia (11%), diabetes mellitus (7.9%), and coronary heart disease (13%). The origin of the association between psoriasis and cardiovascular factors remains uncertain. However, it is plausible to consider that chronic low-grade systemic inflammation and concomitant pro-inflammatory cytokine activity may contribute to vascular damage and increased cardiovascular risk. The exact role of the IL-23/IL-17 axis in atherosclerosis is still debated, but studies have shown an accumulation of IL-17-producing cells and elevated levels of IL-17A in atherosclerotic lesions [12,13]. Additionally, besides individual genetic predisposition, changing metabolites may elucidate the underlying mechanism linking psoriasis and cardiovascular diseases [14]. Although there was no significant difference between the two groups, the prevalence of diabetes mellitus was slightly higher in the psoriasis group than in the control group. The two diseases share a common genetic etiology and numerous pathophysiological mechanisms connected to an upregulation of pro-inflammatory cytokines, adipokines, receptors for peptide-1-glucagon-like (GLP-1 R), and incretin [15]. It is noteworthy that the emergence of IL-17/23 inhibitory monoclonal antibodies has revolutionized the therapeutic approach to psoriasis, with increasing scientific evidence supporting their use as first-Line therapy in patients with cardiovascular comorbidities and metabolic syndrome [16]. Psoriasis is associated with various negative impacts on mental health, including increased risks of anxiety, depression, low self-esteem, alexithymia, stress, self-harm, and suicidality [17]. Patients with psoriasis experience greater mental health comorbidity burdens [18,19], a recent large case-control study from Denmark evaluated the occurrence of mental health disorders by reviewing patient records and found that mental health disorders were observed in 3.1% of patients with psoriasis compared to 2.2% of

controls [20]. This finding is consistent with our results showing that the prevalence of psychiatric disorders was significantly higher in psoriasis patients (8.2% vs. 6.6%, P＜0.05). Some research focuses on the impact of psychiatric complications during psoriasis treatment [21]. Dermatologists need to screen patients with psoriasis for psychiatric comorbidities and provide appropriate mental health support. Inflammatory bowel disease (IBD) has been caused attention among comorbidities of psoriasis, with a prevalence about 0.3% [22]. There is growing evidence that they could interact with each other. Our results confirm that the prevalence of psoriasis in our study group is significantly higher than that of the control group (0.3% > 0.2%, P=0.046), which is consistent with other studies. There are many overlaps in pathophysiological mechanisms include extracellular tumor necrosis factor, IL-23, IL-17 signaling pathways, and intracellular JAK-STAT pathway, cAMP signaling pathway, and ROR-γ T/Th17 axis between the two conditions, consequently, drugs targeting these common pathways have become a hot topic in treating these two comorbidities [23,24]. Non-alcoholic fatty liver disease (NAFLD), is now regarded as the hepatic manifestation of metabolic syndrome. The relationship between psoriasis and NAFLD was independent of other hepatic risk factors, such as potentially hepatotoxic anti-psoriatic therapy and alcohol consumption [25]. Our results confirm that the prevalence of NAFLD in psoriasis patients is significantly higher than in controls (2.0% > 1.6%, P=0.02). NAFLD might actively contribute to the severity of psoriasis through the release of pathogenic mediators from the inflamed liver [26], the systemic release of pro-inflammatory/pro-atherogenic mediators from the steatotic liver is also one of the underlying mechanisms by which NAFLD may contribute to accelerated atherogenesis [27]. It is worth noting that the presence of NAFLD should be taken into consideration when choosing therapy, as some anti-psoriatic drugs are potentially hepatotoxic [28].

Our study found a lower incidence of malignant tumors compared to the control group (1.9% ＜2.3%, P=0.01), which contrasts with some other studies. Chronic inflammation and impaired immune surveillance have been suggested to be linked to an increased risk of cancer [29]. A 2013 meta-analysis reported an increased risk of solid cancers in the upper aerodigestive tract including the esophagus, lung, liver, and pancreas. However, after adjusting for cigarette smoking and alcohol abuse, they were unable to replicate the increased risk of lung, esophagus, or urinary tract cancer, suggesting an associated rather than an independent risk in patients with psoriasis. The risk of squamous cell carcinoma is increased in patients treated with psoralen combined with ultraviolet A (PUVA), which has been accepted by most studies but was not tested in our study [30]. More prospective studies are needed to investigate this controversial issue.

Psoriatic arthritis can lead to joint destruction, deformity, reduced functional status, and an increased risk of death [31]. Undiagnosed psoriatic arthritis is common among patients with psoriasis, ranging from 10% to 40% in previous studies [32]. In our study, the rate of psoriasis combined with arthritis was 9.7%only 2% of patients had psoriatic arthritis, falling within the upper range of the 1.3% to 34.7% reported by the WHO global report on psoriasis. This may be attributed to genetic differences and diagnostic criteria or physicians failing to examine joint symptoms in patients without active complaints of joint pain in the dermatology outpatient clinic. Psoriatic arthritis usually develops 8 to 10 years after the onset of psoriasis, and a delay in diagnosis of 6 months can lead to peripheral joint damage and functional disability [33]. Our study found that the psoriatic arthritis group patients were older and had a higher CCL index compared to patients without arthritis, indicating longer disease duration and worse prognosis. Our findings are consistent with prior reports that a higher prevalence of cardiovascular disease and associated risk factors, such as diabetes and other chronic diseases, in patients with PsA

compared with psoriasis patients in the community [34]. Multiple comorbidities in a single patient can make selecting therapeutic agents challenging due to safety concerns and create challenges in assessing the functional impact of PsA. Therefore, early diagnosis and treatment are crucial to improve patient outcomes. Screening for psoriatic arthritis soon after diagnosing psoriasis may lead to earlier identification, allowing for earlier treatment and prevention of joint damage and disability.

This study confirms that common complications may also occur in psoriasis patients, which may affect their health and social interactions. It filled a gap in the epidemiological data of psoriasis comorbidities in China, providing insights on the understanding of the condition's causes, quality of life, healthcare trends, and research priorities. Additionally, the study highlights the importance of identifying environmental factors that could influence psoriasis and its comorbidities, which can inform policy decisions and quantify the financial burden to society. However, the study has some limitations due to the retrospective studies based on health databases. Firstly, the temporal trajectory of psoriasis could not be fully determined, requiring a more extensive dataset to identify the optimal time to intervene and reduce the risk of comorbidities. Secondly, there may be potential selection bias since the control population consisted only of patients who visited the hospital, who may themselves have co-morbidities or high-risk factors for these conditions. Thirdly, the study was based on a regional database rather than a national medical insurance database, and patient mobility may have caused some patients with psoriasis from other regions not to seek treatment for other diseases in Tianjin, which may have impacted the data. Fourthly, the project commenced in 2021, a time when Chinese hospitals lacked comprehensive electronic medical record systems for patient visits. Consequently, we were unable to evaluate the influence of factors such as psoriasis severity, smoking history, and alcohol consumption on comorbidities. Additionally, the predetermined

one-year follow-up period was relatively brief. As a result, the current findings do not furnish adequate evidence to establish a relationship between psoriasis therapies and comorbidities. It is important to emphasize that the sensitivity analysis results are partially consistent with the main analysis method, which suggests that the results obtained through the main analysis are more reliable. Inconsistent diseases are also given priority in the main analysis, but the level of evidence may be lower.

Further exploration is needed to determine whether the prevalence of diseases such as hyperthyroidism, chronic kidney disease, and cerebrovascular disease decreases in psoriasis patients. Overall, this study provides valuable insights into the burden of comorbidities in patients with psoriasis in China and highlights the need for early diagnosis and management of these comorbidities to improve patient outcomes. It will be important for future studies to address these limitations and to use a more representative sample to validate these findings. Nonetheless, this study highlights the need for a comprehensive approach to the management of patients with psoriasis.

Conclusion

This study represents the most comprehensive and extensive cross-sectional investigation of psoriasis comorbidities conducted in certain regions of China. The results reveal a high prevalence of comorbidities, including cardiovascular diseases, metabolic diseases, infections, psychiatric disorders, and psoriatic arthritis, which is consistent with findings from other countries. More attention should be given to early screening for patients with psoriatic arthritis because of its high prevalence and poor prognosis. These findings highlight the need for dermatologists to be aware of the high prevalence of these comorbidities in Chinese psoriasis patients, to provide optimal care. In conclusion, the high prevalence of comorbidities

emphasizes the importance of better treatment options and therapeutic management to improve clinical outcomes and reduce the burden of psoriasis in China.

Contributors

Y Zhang and Y Guo led the writing, reviewing, and editing of the manuscript. K Zhang, L Fan, J Ma, Y Li, Q Zhou, and Q Zhao contributed to the conceptualization, reviewing, and editing of the manuscript. H Wang and S Hou led the conceptualization and administration of this project and also contributed to reviewing and editing the manuscript.

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Competing interests

None declared.

Patient consent for publication

Patient informed consents were waived due to the retrospective design.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and received approval from the Medical Ethics Committee of Tianjin Medical University General Hospital (approval number: IRB2021-WZ-171).

Provenance and peer review

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Data availability statement

Not applicable.

References

1 Griffiths CEM, Walt JMVD, Ashcroft DM, *et al*. The global state of psoriasis disease epidemiology: a workshop report. *Brit J Dermatol* 2017;177:e4-7.

2 Bu J, Ding RL, Zhou LJ, *et al*. Epidemiology of Psoriasis and Comorbid Diseases: A Narrative Review. *Front Immunol* 2022;13:880201.

3 Takeshita J, Grewal S, Langan SM, *et al*. Psoriasis and comorbid diseases: Epidemiology. *J Am Acad Dermatol* 2017;76:377-90.

4 Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. *J Eur Acad Dermatol* 2012;26:3-11.

5 Dauden E, Blasco AJ, Bonanad C, *et al*. Position statement for the management of comorbidities in psoriasis. *J Eur Acad Dermatol* 2018;32:2058-73.

6 Liu SM, Yan ZR, Liu Q. The Burden of Psoriasis in China and Global Level from 1990 to 2019: A Systematic Analysis from the Global Burden of Disease Study 2019. *Biomed Res Int* 2022;2022:3461765.

7 Li J, Yu MW, Wang YW, *et al*. Prevalence of psoriasis and associated risk factors in China: protocol of a nationwide, population-based, cross-sectional study. *BMJ open* 2019;9:e027685.

8 Enos CW, O'Connell KA, Harrison RW, *et al*. Geographic Variations in Biologic Therapy and Disease Characteristics: A Pilot-Study in the Corrona Psoriasis Registry.

J Drugs Dermatol 2020;19:1119-22.

9 Rahier JF, Moutschen M, Gompel AV, *et al*. Vaccinations in patients with immune-mediated inflammatory diseases. *Rheumatology* 2010;49:1815-27.

10 Gunes AT, Fetil E, Akarsu S, *et al*. Possible Triggering Effect of Influenza Vaccination on Psoriasis. *J Immunol Res* 2015;2015:258430.

11 Ohmura S, Hanai S, Ishihara R, *et al*. A case of psoriatic spondyloarthritis exacerbation triggered by COVID - 19 messenger RNA vaccine. *J Eur Acad Dermatol* 2022;36:e427-9.

12 Choi H, Uceda DE, Dey AK, *et al*. Treatment of psoriasis with biologic therapy is associated with improvement of coronary artery plaque lipid-rich necrotic core: results from a prospective, observational study. *Circ Cardiovasc Imaging* 2020;13:e011199.

13 Stebut EV, Reich K, Thaçi D, *et al*. Impact of secukinumab on endothelial dysfunction and other cardiovascular disease parameters in psoriasis patients over 52 weeks. *J Invest Dermatol* 2019;139:1054–62.

14 Jia Y, Gan Y, He C, *et al*. The mechanism of skin lipids influencing skin status. *J Dermatol Sci* 2018;89:112–9.

15 Wan MT, Shin DB, Hubbard RA, *et al*. Psoriasis and the risk of diabetes: a prospective population-based cohort study. *J Am Acad Dermatol* 2018;78:315–22.e1.

16 Trovato E, Rubegni P, Prignano F. Place in therapy of anti-IL-17 and 23 in psoriasis according to the severity of comorbidities: a focus on cardiovascular disease and metabolic syndrome. *Expert Opin Biol Ther* 2022;22:1443-48.

17 Wu JJ, Feldman SR, Koo J, *et al*. Epidemiology of mental health comorbidity in psoriasis. *J Dermatol Treat* 2018;29:487-95.

18 Kurd SK, Troxel AB, Crits-Christoph P, *et al*. The risk of depression, anxiety, and

suicidality in patients with psoriasis: a population-based cohort study. *Arch Dermatol* 2010;146:891-5.

19 Pompili M, Innamorati M, Trovarelli S, *et al*. Suicide risk and psychiatric comorbidity in patients with psoriasis. *J Int Med Res* 2016;44:61-6.

20 Egeberg A, Hansen PR, Gislason GH, *et al*. Risk of self-harm and nonfatal suicide attempts, and completed suicide in patients with psoriasis: a population-based cohort study. *Brit J Dermatol* 2016;175:493-500.

21 Krishnan R, Cella D, Leonardi C, *et al*. Effects of etanercept therapy on fatigue and symptoms of depression in subjects treated for moderate to severe plaque psoriasis for up to 96 weeks. *Brit J Dermatol* 2007;157:1275-7.

22 Hedin CRH, Sonkoly E, Eberhardson M, *et al*. Inflammatory bowel disease and psoriasis: modernizing the multidisciplinary approach. *J Intern Med* 2021;290:257-78.

23 Puig L, Costanzo A, Muñoz-Elías EJ, *et al*. The biological basis of disease recurrence in psoriasis: a historical perspective and current models. *Brit J Dermatol* 2022;186:773-81.

24 Singh R, Koppu S, Perche PO, *et al*. The Cytokine Mediated Molecular Pathophysiology of Psoriasis and Its Clinical Implications. *Int J Mol Sci* 2021;22:12793.

25 Gisondi P, Giglio MD Cozzi A, *et al*. Psoriasis, the liver, and the gastrointestinal tract. *Dermatol Ther* 2010;23:155-9.

26 Alwis NMWDE, Day CP. Non-alcoholic fatty liver disease: the mist gradually clears. *J Hepatol* 2008;48:S104-12.

27 Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: causal effect or epiphenomenon? *Diabetologia* 2008;51:1947-53.

28 Rosenberg P, Urwitz H, Johannesson A, *et al*. Psoriasis patients with diabetes type 2 are at high risk of developing liver fibrosis during methotrexate treatment. *J Hepatol* 2007;46:1111-8.

29 Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell* 2010;140:883-99.

30 Pouplard C, Brenaut E, Horreau C, *et al*. Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. *J Eur Acad Dermatol* 2013;27:36-46.

31 Gladman DD, Antoni C, Mease P, *et al*. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64:14-7.

32 Villani AP, Rouzaud M, Sevrain M, *et al*. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. *J Am Acad Dermatol* 2015;73:242-8.

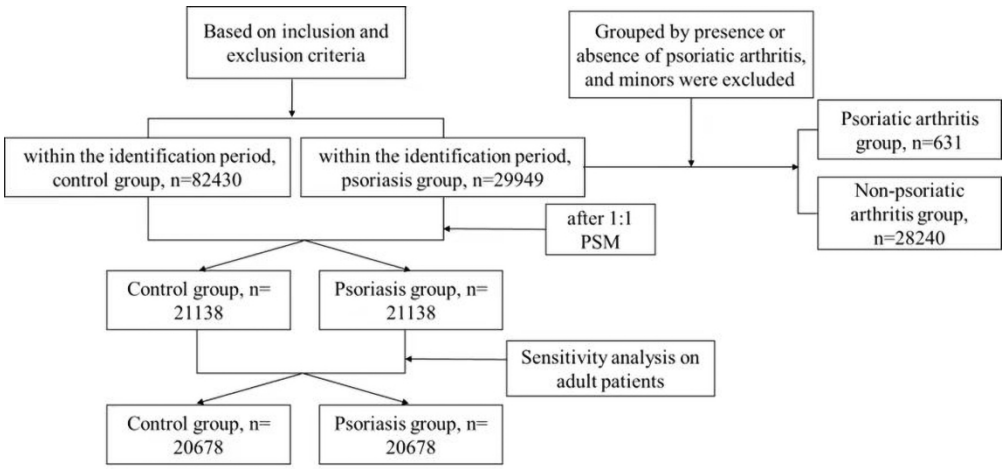
33 Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic Arthritis and Burden of Disease: Patient Perspectives from the Population-Based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) Survey. *Rheumatol Ther* 2016;3:91-102.

34 Haroon M, Gallagher P, Fitzgerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045-50.

Figure legend:

Figure 1 - A consort diagram to show the study process.

Figure 2 - Adjusted odds ratios (ORs) of medical comorbidities in patients with psoriasis vs. comparison group by sensitivity analysis (OR>1 indicates that patients with psoriasis have greater incidence).



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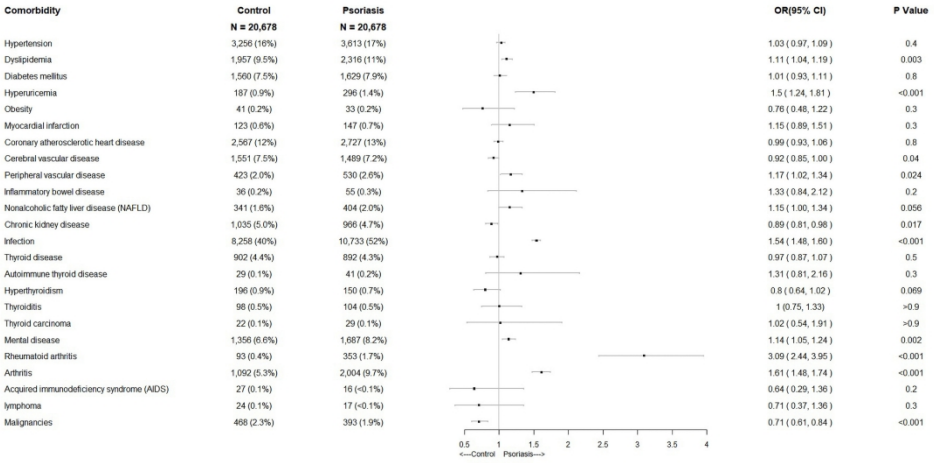

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Comorbidities among adult patients with psoriasis in Tianjin: A cross-sectional analysis of the Health Database study

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Abstract

Objectives:

This study aims to examine the prevalence of comorbidities in adult patients with psoriasis and compare them with those in control subjects without psoriasis in Tianjin, China.

Design:

Cross-sectional study.

Participants:

The participants were established by identifying all patients (age ≥ 18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019.

Setting:

The study group consisted of 20,678 adult patients with psoriasis, and a comparison group was created after 1:1 propensity score matching. Logistic regression analyses were conducted to examine the risk of 22 comorbidities for these two groups.

Results:

Patients with psoriasis had a significantly higher prevalence of 11 comorbidities and a lower prevalence of 2 comorbidities within 12 months of follow-up. Our results also showed that the proportion of psoriatic arthritis might account for approximately 2% of all psoriasis patients. This psoriatic arthritis group had a higher average age and CCI index score (2.27 > 1.62, P < 0.001) than the non-arthritis group.

Conclusions:

This study showed that psoriasis in Tianjin is associated with various comorbidities. It also emphasizes the importance of clinical treatment in improving therapeutic effects and reducing the burden of psoriasis in China.

Strengths and limitations of this study:

- This study involved a large cohort of participants (n=20,678) for cross-sectional analysis.
- To mitigate potential confounding factors, subjects were matched 1:1 based on propensity scores in each group.
- Odds ratios (ORs) were adjusted for confounding variables to assess the independent relationship between medical comorbidities in patients with psoriasis compared to the control group using sensitivity analysis.
- The cross-sectional design of this study limited our ability to establish causal inferences regarding psoriasis and comorbidities.
- Due to incomplete electronic medical records in the database, the impact of severity and other potential variables on comorbidities could not be observed.

Keywords: psoriasis, psoriatic arthritis (PsA), comorbidity, epidemiology, Chinese Han

Introduction

Psoriasis is an immune-mediated condition that affects not only the skin but also extracutaneous systems. The disease burden is likely greater than reported due to the associated comorbidities [1], including cardiometabolic, gastrointestinal, renal, malignancy, infection, mental, and ocular diseases, and psoriatic arthritis (PsA) [2,3]. The abnormal immune response that causes psoriasis leads to systemic inflammation and a higher prevalence of comorbidities compared to the general population [4]. Understanding these comorbidities is crucial for better disease management and reducing the burden on individuals and society [5].

According to the "Global Burden of Disease study" in 2019, the prevalence of psoriasis in China is estimated to be 0.56% [6], suggesting based on the estimated population of China in 2023, which is approximately 1.4 billion people, a prevalence rate of 0.56% would correspond to over 7 million individuals with psoriasis in the country. Despite China having the largest population and the most prevalent cases of psoriasis [7], epidemiological studies on psoriasis prevalence and comorbidity risk are rare. Available data mainly come from the USA and Europe [1], but baseline disease characteristics and comorbidity frequencies may differ between geographic regions [8], including China. The World Health Organization (WHO) has recently released a report to bring attention to the public health impact of psoriasis. The report emphasizes that obtaining quality data on the epidemiology of psoriasis is a crucial area of research globally better to understand the size and distribution of the problem. Such data are essential for disease control and appropriate healthcare planning.

Hence, to address the gap in epidemiological data on the prevalence of psoriasis comorbidities in China, we conducted a retrospective study to determine the prevalence of various comorbidities in adult patients with psoriasis. Our study also compared these prevalences with those of control subjects without psoriasis in Tianjin.

Methods

Study Design

This study utilized data from the Inspur Health Database in Tianjin to examine the prevalence of comorbidities in adult patients with psoriasis compared to a control group. The study and control groups were established by identifying all patients (age≥18 years) who visited hospitals and clinics in Tianjin between 1 January 2016 and 31 October 2019. Patients with two or more psoriasis-related diagnoses were selected as the study group, while those who had never received a psoriasis diagnosis were classified as the control group. The incidence date for the

psoriasis cohort was defined as the date of the first psoriasis diagnosis, while the index date for the control group was defined as the first hospital visit during the recognition period. After excluding individuals with abnormal age, visiting frequency, or missing data, 20,678 subjects were included in each group following 1:1 propensity score matching. Follow-up continued until the end of the study period on 31 October 2020. The baseline period encompassed data from at least 12 months prior to the incidence or index date, while the follow-up period comprised data from at least months after the incidence or index date. The flow of participants through the study is illustrated in a consort diagram in Figure 1.

Outcome

In this study, we focused on several health outcomes of interest, including hypertension, dyslipidemia, diabetes, hyperuricemia, obesity, metabolic syndrome, myocardial infarction, coronary atherosclerotic heart disease, cerebrovascular disease, peripheral vascular disease, inflammatory bowel diseases, non-alcoholic fatty liver disease (NAFLD), chronic kidney disease (CKD), infection, thyroid disease (including autoimmune thyroid disease, hypothyroidism, hyperthyroidism, thyroiditis, and thyroid cancer), psychiatric diseases, rheumatoid arthritis, arthritis, acquired immune deficiency syndrome (AIDS), lymphoma, and malignancy. The ICD-10 diagnostic codes chosen for each outcome were based on medical judgment.

Statistical Analysis

Categorical variables were reported as frequency and percentage, while continuous variables were summarized using the maximum, minimum, mean, standard deviation, median, and interquartile range. Due to the non-normal distribution of constant data, the Wilcoxon rank sum test or Kruskal-Wallis rank sum test was used to compare group differences, as appropriate.

The $\chi 2$ or Fisher's exact test was used to compare categorical variables between groups. A P-value of less than 0.05 was considered statistically significant.

To address potential confounding factors, a propensity score matching analysis was conducted. A logistic regression model was developed, including age, sex, hospital visited, and type of medical insurance as covariates to generate scores, with age as the primary matching variable. One-to-one nearest-neighbor matching was performed using a caliper width of 0.05. A standardized mean difference (SMD) value of less than 0.2 was considered a good match.

Sensitivity analysis

To assess the robustness of our results, we constructed a logistic regression model and a corresponding forest plot to investigate any differences in the prevalence of the comorbidities of interest between the study and control groups over the follow-up period. The dependent variable was whether individuals developed the relevant outcomes during this period, while the independent variable was the group (psoriasis group vs. control group), as well as the presence of the target comorbidities at baseline. We obtained the odds ratio (OR) and its 95% confidence interval (CI), with statistical significance defined as a two-sided P-value of less than 0.05.

Patient and public involvement

Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

Results

The distribution of baseline characteristics between psoriasis and non-psoriasis groups before and after propensity score matching (PSM) is presented in Table 1. Among the 41,296 sampled patients, the mean ± SD age was 45.37 ± 16.4 years, with 47% and 44.7% being female in the

control and psoriasis groups, respectively. No significant differences were observed between these two groups based on gender, age, type of health insurance, and hospital grade.

Table 1 Differences in Baseline Characteristics between Psoriasis Patients and Controls before and after PSM.

	Before PSM				After PSM			
	Control group, n=82,430[1]	Psoriasis group, n=29,949[1]	P[2]	SMD	Control group, n=21,138[1]	Psoriasis group, n=21,138[1]	P[2]	SMD
Sex			<0.001	0.067			<0.001	0.046
Female	37,616 (45.6)	12,677 (42.3)			9,938 (47.0)	9,449 (44.7)		
Male	44,814 (54.4)	17,272 (57.7)			11,200 (53.0)	11,689 (55.3)		
Age (mean (SD))	46.86 (16.81)	43.54 (16.55)	<0.001	0.199	45.37 (16.40)	46.37 (16.40)	1	<0.001
Type of Payouts			<0.001	0.255			0.029	0.026
Medical Insurance Payouts	68,095 (82.6)	27,295 (91.1)			18,601 (88.0)	18,504 (87.5)		
Off-site Medical Insurance Payouts	987 (1.2)	159 (0.5)			116 (0.5)	107 (0.7)		
Self-paying	13,348 (16.2)	2,495 (8.3)			2,421 (11.5)	2,477 (11.7)		
Hospital Grade			<0.001	0.209			0.093	0.016
Tertiary Hospital (%)	65,452 (79.4)	26,104 (87.2)			17,436 (82.5)	17,303 (81.9)		
Non-Tertiary Hospital (%)	16,978 (20.6)	3,845 (12.8)			3,702 (17.5)	3,835 (18.1)		

[1]n (%)

[2]Wilcoxon Rank-Sum Test; The χ^2 test of independence.

The prevalence of comorbidities in patients with and without psoriasis is shown in Table 2 and STable 1 with the primary analysis methods of Pearson $\chi 2$ independence test and Fisher's exact test. The results indicate that patients with psoriasis had a significantly higher prevalence of 11 comorbidities, including hypertension, dyslipidemia, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, inflammatory bowel disease, nonalcoholic fatty liver disease (NAFLD), infection, psychiatric disorders, rheumatoid arthritis, and arthritis. On the other hand, patients with psoriasis had a considerably lower prevalence of 2 comorbidities, including hyperthyroidism and malignant tumor, within 12 months of the follow-up period. The sensitivity analysis showed that psoriasis patients had significantly higher probability of developing dyslipidemia (OR [CI 95%] 1.11 [1.04 – 1.19], P = 0.003), hyperuricemia (OR [CI 95%] 1.50 [1.34 – 1.81], P < 0.001), peripheral vascular disease (OR [CI 95%] 1.17 [1.02 – 1.34], P = 0.024), infection (OR [CI 95%] 1.54 [1.48 – 1.60], P < 0.001), psychiatric disorders (OR [CI 95%] 1.14 [1.05 – 1.74], P < 0.001), and rheumatoid arthritis (OR [CI 95%] 3.09 [2.44 – 3.95], P < 0.001), arthritis (OR [CI 95%] 1.61 [1.48 – 1.74], P < 0.001), while they had significantly lower probability of developing malignancy (OR [CI 95%] 0.71 [0.61-0.84], P < 0.001), cerebrovascular disease (OR [CI 95%] 0.92 [0.85-1.00], P = 0.04), and chronic kidney disease (OR [CI 95%] 0.89 [0.81-0.98], P = 0.017), compared to the control group during the 12-month follow-up period. These results are presented in Figure 2.

Table 2 Prevalence of medical comorbidities in patients with psoriasis vs. comparison of two groups in baseline and 12 months follow-up period.

	Baseline			12 months follow-up period		
Variable	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[2]	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[2]
Hypertension	2,773 (13%)	3,408 (16%)	<0.001	3,256 (16%)	3,6[illegible] (17%)	<0.001
Dyslipidemia	1,518 (7.3%)	2,020 (9.8%)	<0.001	1,957 (9.5%)	2,3[illegible] (11%)	<0.001
Hyperuricemia	126 (0.6%)	201 (1.0%)	<0.001	187 (0.9%)	296 (1.4%)	<0.001
Peripheral Vascular Disease	350 (1.7%)	474 (2.3%)	<0.001	423 (2.0%)	536 (2.6%)	<0.001
Infection	7,813 (38%)	9,538 (46%)	<0.001	8,258 (40%)	10,733 (52%)	<0.001
Psychiatric Diseases	958 (4.6%)	1,346 (6.5%)	<0.001	1,356 (6.6%)	1,687 (8.2%)	<0.001
Rheumatoid Arthritis	58 (0.3%)	213 (1.0%)	<0.001	93 (0.4%)	359 (1.7%)	<0.001
Arthritis	926 (4.5%)	1,816 (8.8%)	<0.001	1,092 (5.3%)	2,054 (9.9%)	<0.001
Coronary Atherosclerotic Heart Disease	2,188 (11%)	2,571 (12%)	<0.001	2,567 (12%)	2,787 (13%)	0.019
Non-alcoholic Fatty Liver Disease (NAFLD)	291 (1.4%)	408 (2.0%)	<0.001	341 (1.6%)	404 (2.0%)	0.020
Inflammatory Bowel Diseases	34 (0.2%)	54 (0.3%)	0.033	36 (0.2%)	55 (0.3%)	0.046
Hyperthyroidism	154 (0.7%)	121 (0.6%)	0.046	196 (0.9%)	150 (0.7%)	0.013
Malignancy	269 (1.3%)	306 (1.5%)	0.120	468 (2.3%)	393 (1.9%)	0.010
Hypothyroidism	224 (1.1%)	292 (1.4%)	0.003	314 (1.5%)	327 (1.6%)	0.6

Cerebrovascular Disease	1,276 (6.2%)	1,383 (6.7%)	0.032	1,551 (7.5%)	1,489 (7.2%)	0.2
Chronic Kidney Disease (CKD)	773 (3.7%)	852 (4.1%)	0.046	1,035 (5.0%)	966 (4.7%)	0.114
Myocardial Infarction	131 (0.6%)	151 (0.7%)	0.2	123 (0.6%)	147 (0.7%)	0.143
Diabetes	1,379 (6.7%)	1,472 (7.1%)	0.071	1,560 (7.5%)	1,619 (7.9%)	0.2

[1]n (%)

[2]Fisher's exact test; The χ^2 test of independence.

We further analyzed psoriasis patients into those with or without psoriatic arthritis. There was 2% psoriatic arthritis in all of psoriasis patients. Meanwhile, the average age was higher in psoriatic arthritis group than in the non-arthritis group ($P < 0.001$). No gender difference was observed ($P = 0.4$). Moreover, patients with psoriatic arthritis were more likely to have comorbidities such as hypertension, dyslipidemia, diabetes, hyperuricemia, coronary atherosclerotic heart disease, peripheral vascular disease, NAFLD, chronic kidney disease, and rheumatoid arthritis. These results are shown in Table 3. Additionally, we compared the CCI index in two groups during the 12-month follow-up period using the Wilcoxon rank sum test. The psoriatic arthritis group had a distinct higher CCI index score ($2.27 > 1.62$, $P < 0.001$).

Table 3 Comorbidities in patients with psoriatic arthritis vs. without psoriatic arthritis group.

	12 months follow-up period		
Variable	Psoriasis without arthritis, n = 28,240[1]	Psoriatic arthritis, n = 631[1]	*P*-value[3]
Arthritis	1,678 (5.9%)	560 (89%)	<0.001
Infection	14,287 (51%)	251 (40%)	<0.001
Rheumatoid Arthritis	232 (0.8%)	147 (23%)	<0.001
Hypertension	3,984 (14%)	120 (19%)	<0.001
Coronary Atherosclerotic Heart Disease	2,965 (10%)	86 (14%)	0.011
Dyslipidemia	2,540 (9.0%)	83 (13%)	<0.001
Diabetes	1,747 (6.2%)	68 (11%)	<0.001
Chronic Kidney Disease (CKD)	1,094 (3.9%)	46 (7.3%)	<0.001
Hyperuricemia	324 (1.1%)	29 (4.6%)	<0.001

Non-alcoholic Fatty Liver Disease (NAFLD)	447 (1.6%)	23 (3.6%)	<0.001
Peripheral Vascular Disease	569 (2.0%)	22 (3.5%)	0.01
Hyperthyroidism	170 (0.6%)	8 (1.3%)	0.062
Thyroid Disease	990 (3.5%)	30 (4.8%)	0.093
Psychiatric Diseases	1,885 (6.7%)	52 (8.2%)	0.12
Autoimmune Thyroid Disease	40 (0.1%)	2 (0.3%)	0.2
Hypothyroidism	351 (1.2%)	5 (0.8%)	0.3
Acquired Immune Deficiency Syndrome (AIDS)	18 (<0.1%)	1 (0.2%)	0.3
Thyroid Cancer	30 (0.1%)	1 (0.2%)	0.5
Malignancy	428 (1.5%)	8 (1.3%)	0.6
Myocardial Infarction	152 (0.5%)	4 (0.6%)	0.6
Thyroiditis	108 (0.4%)	3 (0.5%)	0.7
Cerebrovascular Disease	1,649 (5.8%)	37 (5.9%)	>0.9
Lymphoma	20 (<0.1%)	0 (0%)	>0.9
Inflammatory Bowel Diseases	60 (0.2%)	1 (0.2%)	>0.9
Obesity	36 (0.1%)	0 (0%)	>0.9

Discussion

It is widely recognized that psoriasis patients usually suffer a heavy economic and mental burden. It affects not only the skin level but also multiple systems and organs. Numerous epidemiological data on psoriasis have been collected from European

countries, the U.K. and the U.S.A [1] that addressed comorbidities are pretty common in psoriasis patients, however, there is little few information on Asian populations. This study aimed to proceed with a large retrospective study based on the Inspur Tianjin Health Database to assess the comorbidities in psoriasis patients in Tianjin and provide more insights on psoriasis in the Han nationality. Due to the COVID-19 outbreak, the time for us to supplement and optimize data and analysis results has been extended, and it was not until recently that all of it was completed.

Our current study found that the comorbidity with the highest prevalence among psoriasis patients was infection, with a significantly higher prevalence than that of the control group (52% > 40%, $P < 0.001$). Psoriasis patients are at an increased risk of infection, which may be due to treatment with immunomodulatory or immunosuppressive drugs [9]. Vaccinations may prevent specific infections, but they can also trigger and exacerbate psoriasis, as studies have shown in relation to flu vaccination [10]. There have also been reports of psoriatic disease exacerbation triggered by COVID-19 mRNA vaccination, with the mechanism similar to that of other vaccines in that vaccination induces IL-6, which stimulates Th17 cells to produce IL-22, a significant contributor to keratinocyte proliferation in psoriasis [11]. Increasing epidemiological studies have recently shown a close correlation between psoriasis and metabolic syndrome and cardiovascular factors. Our findings are consistent with these results, with the most prevalent comorbidities being hypertension (17%), hyperlipidemia (11%), diabetes mellitus (7.9%), and coronary heart disease (13%). The origin of the association between psoriasis and cardiovascular factors remains uncertain. However, it is plausible to consider that chronic low-grade systemic inflammation and concomitant pro-inflammatory cytokine activity may contribute to vascular damage and increased cardiovascular risk. The exact role of the IL-23/IL-17 axis in atherosclerosis is still debated, but studies have shown an

accumulation of IL-17-producing cells and elevated levels of IL-17A in atherosclerotic lesions [12,13]. Additionally, besides individual genetic predisposition, changing metabolites may elucidate the underlying mechanism linking psoriasis and cardiovascular diseases [14]. Although there was no significant difference between the two groups, the prevalence of diabetes mellitus was slightly higher in the psoriasis group than in the control group. The two diseases share a common genetic etiology and numerous pathophysiological mechanisms connected to an upregulation of pro-inflammatory cytokines, adipokines, receptors for peptide-1-glucagon-like (GLP-1 R), and incretin [15]. It is noteworthy that the emergence of IL-17/23 inhibitory monoclonal antibodies has revolutionized the therapeutic approach to psoriasis, with increasing scientific evidence supporting their use as first-Line therapy in patients with cardiovascular comorbidities and metabolic syndrome [16]. Psoriasis is associated with various negative impacts on mental health, including increased risks of anxiety, depression, low self-esteem, alexithymia, stress, self-harm, and suicidality [17]. Patients with psoriasis experience greater mental health comorbidity burdens [18,19], a recent large case-control study from Denmark evaluated the occurrence of mental health disorders by reviewing patient records and found that mental health disorders were observed in 3.1% of patients with psoriasis compared to 2.2% of controls [20]. This finding is consistent with our results showing that the prevalence of psychiatric disorders was significantly higher in psoriasis patients (8.2% vs. 6.6%, $P < 0.05$). Some research focuses on the impact of psychiatric complications during psoriasis treatment [21]. Dermatologists need to screen patients with psoriasis for psychiatric comorbidities and provide appropriate mental health support. Inflammatory bowel disease (IBD) has been caused attention among comorbidities of psoriasis, with a prevalence about 0.3% [22]. There is growing evidence that they could interact with each other. Our results confirm that the prevalence of psoriasis in our study group is significantly higher than that of the control group

(0.3% > 0.2%, P=0.046), which is consistent with other studies. There are many overlaps in pathophysiological mechanisms include extracellular tumor necrosis factor, IL-23, IL-17 signaling pathways, and intracellular JAK-STAT pathway, cAMP signaling pathway, and ROR-γ T/Th17 axis between the two conditions, consequently, drugs targeting these common pathways have become a hot topic in treating these two comorbidities [23,24]. Non-alcoholic fatty liver disease (NAFLD), is now regarded as the hepatic manifestation of metabolic syndrome. The relationship between psoriasis and NAFLD was independent of other hepatic risk factors, such as potentially hepatotoxic anti-psoriatic therapy and alcohol consumption [25]. Our results confirm that the prevalence of NAFLD in psoriasis patients is significantly higher than in controls (2.0% > 1.6%, P=0.020). NAFLD might actively contribute to the severity of psoriasis through the release of pathogenic mediators from the inflamed liver [26], the systemic release of pro-inflammatory/pro-atherogenic mediators from the steatotic liver is also one of the underlying mechanisms by which NAFLD may contribute to accelerated atherogenesis [27]. It is worth noting that the presence of NAFLD should be taken into consideration when choosing therapy, as some anti-psoriatic drugs are potentially hepatotoxic [28].

Our study found a lower incidence of malignant tumors compared to the control group (1.9% ＜2.3%, P=0.01), which contrasts with some other studies. Chronic inflammation and impaired immune surveillance have been suggested to be linked to an increased risk of cancer [29]. A 2013 meta-analysis reported an increased risk of solid cancers in the upper aerodigestive tract including the esophagus, lung, liver, and pancreas. However, after adjusting for cigarette smoking and alcohol abuse, they were unable to replicate the increased risk of lung, esophagus, or urinary tract cancer, suggesting an associated rather than an independent risk in patients with psoriasis. The risk of squamous cell carcinoma is increased in patients treated with psoralen

combined with ultraviolet A (PUVA), which has been accepted by most studies but was not tested in our study [30]. More prospective studies are needed to investigate this controversial issue.

Psoriatic arthritis can lead to joint destruction, deformity, reduced functional status, and an increased risk of death [31]. Undiagnosed psoriatic arthritis is common among patients with psoriasis, ranging from 10% to 40% in previous studies [32]. In our study, the rate of psoriasis combined with arthritis was 9.7%only 2% of patients had psoriatic arthritis, falling within the upper range of the 1.3% to 34.7% reported by the WHO global report on psoriasis. This may be attributed to genetic differences and diagnostic criteria or physicians failing to examine joint symptoms in patients without active complaints of joint pain in the dermatology outpatient clinic. Psoriatic arthritis usually develops 8 to 10 years after the onset of psoriasis, and a delay in diagnosis of 6 months can lead to peripheral joint damage and functional disability [33]. Our study found that the psoriatic arthritis group patients were older and had a higher CCL index compared to patients without arthritis, indicating longer disease duration and worse prognosis. Our findings are consistent with prior reports that a higher prevalence of cardiovascular disease and associated risk factors, such as diabetes and other chronic diseases, in patients with PsA compared with psoriasis patients in the community [34]. Multiple comorbidities in a single patient can make selecting therapeutic agents challenging due to safety concerns and create challenges in assessing the functional impact of PsA. Therefore, early diagnosis and treatment are crucial to improve patient outcomes. Screening for psoriatic arthritis soon after diagnosing psoriasis may lead to earlier identification, allowing for earlier treatment and prevention of joint damage and disability.

This study confirms that common complications may also occur in psoriasis patients, which may affect their health and social interactions. It filled a gap in the epidemiological data of

psoriasis comorbidities in China, providing insights on the understanding of the condition's causes, quality of life, healthcare trends, and research priorities. Additionally, the study highlights the importance of identifying environmental factors that could influence psoriasis and its comorbidities, which can inform policy decisions and quantify the financial burden to society. However, the study has some limitations due to the retrospective studies based on health databases. Firstly, the temporal trajectory of psoriasis could not be fully determined, requiring a more extensive dataset to identify the optimal time to intervene and reduce the risk of comorbidities. Secondly, there may be potential selection bias since the control population consisted only of patients who visited the hospital, who may themselves have co-morbidities or high-risk factors for these conditions. Thirdly, the study was based on a regional database rather than a national medical insurance database, and patient mobility may have caused some patients with psoriasis from other regions not to seek treatment for other diseases in Tianjin, which may have impacted the data. Fourthly, the project commenced in 2021, a time when Chinese hospitals lacked comprehensive electronic medical record systems for patient visits. Consequently, we were unable to evaluate the influence of factors such as psoriasis severity, smoking history, and alcohol consumption on comorbidities. Additionally, the predetermined one-year follow-up period was relatively brief. As a result, the current findings do not furnish adequate evidence to establish a relationship between psoriasis therapies and comorbidities. It is important to emphasize that the sensitivity analysis results are partially consistent with the main analysis method, which suggests that the results obtained through the main analysis are more reliable. Inconsistent diseases are also given priority in the main analysis, but the level of evidence may be lower.

Further exploration is needed to determine whether the prevalence of diseases such as hyperthyroidism, chronic kidney disease, and cerebrovascular disease decreases in psoriasis

patients. Overall, this study provides valuable insights into the burden of comorbidities in patients with psoriasis in China and highlights the need for early diagnosis and management of these comorbidities to improve patient outcomes. It will be important for future studies to address these limitations and to use a more representative sample to validate these findings. Nonetheless, this study highlights the need for a comprehensive approach to the management of patients with psoriasis.

Conclusion

This study represents the most comprehensive and extensive cross-sectional investigation of psoriasis comorbidities conducted in certain regions of China. The results reveal a high prevalence of comorbidities, including cardiovascular diseases, metabolic diseases, infections, psychiatric disorders, and psoriatic arthritis, which is consistent with findings from other countries. More attention should be given to early screening for patients with psoriatic arthritis because of its high prevalence and poor prognosis. These findings highlight the need for dermatologists to be aware of the high prevalence of these comorbidities in Chinese psoriasis patients, to provide optimal care. In conclusion, the high prevalence of comorbidities emphasizes the importance of better treatment options and therapeutic management to improve clinical outcomes and reduce the burden of psoriasis in China.

Contributors

Y Zhang and Y Guo led the writing, reviewing, and editing of the manuscript. K Zhang, L Fan, J Ma, Y Li, Q Zhou, and Q Zhao contributed to the conceptualization, reviewing, and editing of the manuscript. H Wang and S Hou led the conceptualization and administration of this project and also contributed to reviewing and editing the manuscript.

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Competing interests

None declared.

Patient consent for publication

Patient informed consents were waived due to the retrospective design.

Ethics approval

The study was conducted in accordance with the Declaration of Helsinki and received approval from the Medical Ethics Committee of Tianjin Medical University General Hospital (approval number: IRB2021-WZ-171).

Provenance and peer review

Not commissioned; externally peer reviewed.

Data availability statement

Not applicable.

References

1 Griffiths CEM, Walt JMVD, Ashcroft DM, *et al*. The global state of psoriasis disease epidemiology: a workshop report. *Brit J Dermatol* 2017;177:e4-7.

2 Bu J, Ding RL, Zhou LJ, *et al*. Epidemiology of Psoriasis and Comorbid Diseases: A

Narrative Review. *Front Immunol* 2022;13:880201.

3 Takeshita J, Grewal S, Langan SM, *et al*. Psoriasis and comorbid diseases: Epidemiology. *J Am Acad Dermatol* 2017;76:377-90.

4 Reich K. The concept of psoriasis as a systemic inflammation: implications for disease management. *J Eur Acad Dermatol* 2012;26:3-11.

5 Dauden E, Blasco AJ, Bonanad C, *et al*. Position statement for the management of comorbidities in psoriasis. *J Eur Acad Dermatol* 2018;32:2058-73.

6 Liu SM, Yan ZR, Liu Q. The Burden of Psoriasis in China and Global Level from 1990 to 2019: A Systematic Analysis from the Global Burden of Disease Study 2019. *Biomed Res Int* 2022;2022:3461765.

7 Li J, Yu MW, Wang YW, *et al*. Prevalence of psoriasis and associated risk factors in China: protocol of a nationwide, population-based, cross-sectional study. *BMJ open* 2019;9:e027685.

8 Enos CW, O'Connell KA, Harrison RW, *et al*. Geographic Variations in Biologic Therapy and Disease Characteristics: A Pilot-Study in the Corrona Psoriasis Registry. *J Drugs Dermatol* 2020;19:1119-22.

9 Rahier JF, Moutschen M, Gompel AV, *et al*. Vaccinations in patients with immune-mediated inflammatory diseases. *Rheumatology* 2010;49:1815-27.

10 Gunes AT, Fetil E, Akarsu S, *et al*. Possible Triggering Effect of Influenza Vaccination on Psoriasis. *J Immunol Res* 2015;2015:258430.

11 Ohmura S, Hanai S, Ishihara R, *et al*. A case of psoriatic spondyloarthritis exacerbation triggered by COVID - 19 messenger RNA vaccine. *J Eur Acad Dermatol* 2022;36:e427-9.

12 Choi H, Uceda DE, Dey AK, *et al*. Treatment of psoriasis with biologic therapy is

associated with improvement of coronary artery plaque lipid-rich necrotic core: results from a prospective, observational study. *Circ Cardiovasc Imaging* 2020;13:e011199.

13 Stebut EV, Reich K, Thaçi D, *et al*. Impact of secukinumab on endothelial dysfunction and other cardiovascular disease parameters in psoriasis patients over 52 weeks. *J Invest Dermatol* 2019;139:1054–62.

14 Jia Y, Gan Y, He C, *et al*. The mechanism of skin lipids influencing skin status. *J Dermatol Sci* 2018;89:112–9.

15 Wan MT, Shin DB, Hubbard RA, *et al*. Psoriasis and the risk of diabetes: a prospective population-based cohort study. *J Am Acad Dermatol* 2018;78:315–22.e1.

16 Trovato E, Rubegni P, Prignano F. Place in therapy of anti-IL-17 and 23 in psoriasis according to the severity of comorbidities: a focus on cardiovascular disease and metabolic syndrome. *Expert Opin Biol Ther* 2022;22:1443-48.

17 Wu JJ, Feldman SR, Koo J, *et al*. Epidemiology of mental health comorbidity in psoriasis. *J Dermatol Treat* 2018;29:487-95.

18 Kurd SK, Troxel AB, Crits-Christoph P, *et al*. The risk of depression, anxiety, and suicidality in patients with psoriasis: a population-based cohort study. *Arch Dermatol* 2010;146:891-5.

19 Pompili M, Innamorati M, Trovarelli S, *et al*. Suicide risk and psychiatric comorbidity in patients with psoriasis. *J Int Med Res* 2016;44:61-6.

20 Egeberg A, Hansen PR, Gislason GH, *et al*. Risk of self-harm and nonfatal suicide attempts, and completed suicide in patients with psoriasis: a population-based cohort study. *Brit J Dermatol* 2016;175:493-500.

21 Krishnan R, Cella D, Leonardi C, *et al*. Effects of etanercept therapy on fatigue and symptoms of depression in subjects treated for moderate to severe plaque psoriasis for

up to 96 weeks. *Brit J Dermatol* 2007;157:1275-7.

22 Hedin CRH, Sonkoly E, Eberhardson M, *et al*. Inflammatory bowel disease and psoriasis: modernizing the multidisciplinary approach. *J Intern Med* 2021;290:257-78.

23 Puig L, Costanzo A, Muñoz-Elías EJ, *et al*. The biological basis of disease recurrence in psoriasis: a historical perspective and current models. *Brit J Dermatol* 2022;186:773-81.

24 Singh R, Koppu S, Perche PO, *et al*. The Cytokine Mediated Molecular Pathophysiology of Psoriasis and Its Clinical Implications. *Int J Mol Sci* 2021;22:12793.

25 Gisondi P, Giglio MD Cozzi A, *et al*. Psoriasis, the liver, and the gastrointestinal tract. *Dermatol Ther* 2010;23:155-9.

26 Alwis NMWDE, Day CP. Non-alcoholic fatty liver disease: the mist gradually clears. *J Hepatol* 2008;48:S104-12.

27 Targher G, Marra F, Marchesini G. Increased risk of cardiovascular disease in non-alcoholic fatty liver disease: causal effect or epiphenomenon? *Diabetologia* 2008;51:1947-53.

28 Rosenberg P, Urwitz H, Johannesson A, *et al*. Psoriasis patients with diabetes type 2 are at high risk of developing liver fibrosis during methotrexate treatment. *J Hepatol* 2007;46:1111-8.

29 Grivennikov SI, Greten FR, Karin M. Immunity, inflammation, and cancer. *Cell* 2010;140:883-99.

30 Pouplard C, Brenaut E, Horreau C, *et al*. Risk of cancer in psoriasis: a systematic review and meta-analysis of epidemiological studies. *J Eur Acad Dermatol* 2013;27:36-46.

31 Gladman DD, Antoni C, Mease P, *et al*. Psoriatic arthritis: epidemiology, clinical features, course, and outcome. *Ann Rheum Dis* 2005;64:14-7.

32 Villani AP, Rouzaud M, Sevrain M, *et al*. Prevalence of undiagnosed psoriatic arthritis among psoriasis patients: Systematic review and meta-analysis. *J Am Acad Dermatol* 2015;73:242-8.

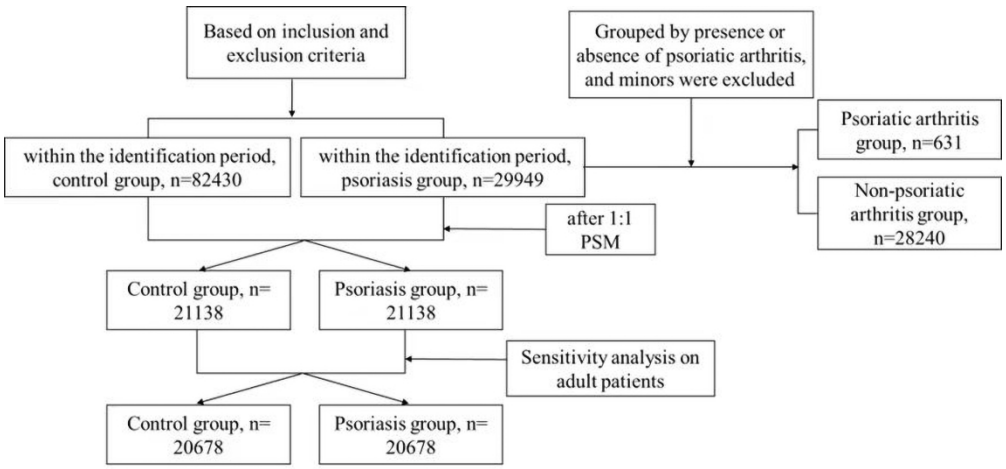
33 Kavanaugh A, Helliwell P, Ritchlin CT. Psoriatic Arthritis and Burden of Disease: Patient Perspectives from the Population-Based Multinational Assessment of Psoriasis and Psoriatic Arthritis (MAPP) Survey. *Rheumatol Ther* 2016;3:91-102.

34 Haroon M, Gallagher P, Fitzgerald O. Diagnostic delay of more than 6 months contributes to poor radiographic and functional outcome in psoriatic arthritis. *Ann Rheum Dis* 2015;74:1045-50.

Figure legend:

Figure 1 - A consort diagram to show the study process.

Figure 2 - Adjusted odds ratios (ORs) of medical comorbidities in patients with psoriasis vs. comparison group by sensitivity analysis (OR>1 indicates that patients with psoriasis have greater incidence).



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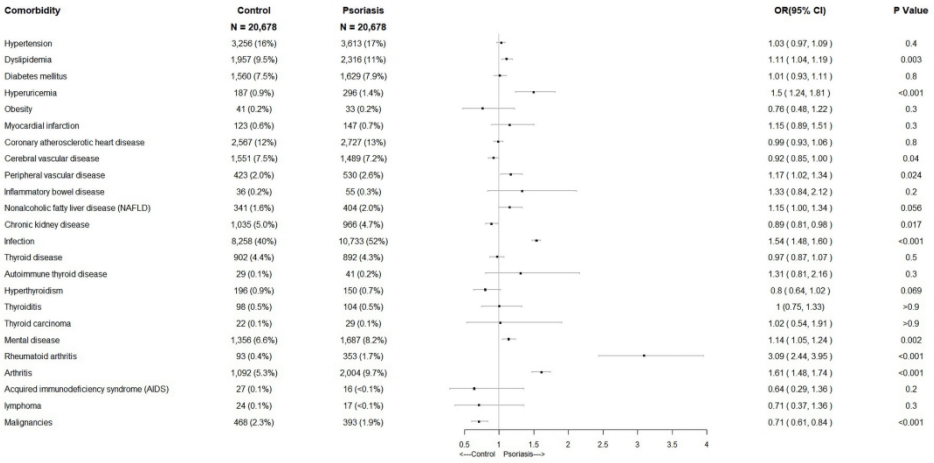

STable 1 Prevalence of medical comorbidities in patients with psoriasis vs. comparison of two groups in baseline and 12 months follow-up period.

	Baseline			12 months follow-up period		
Variable	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[2]	Control group, n = 20,678[1]	Psoriasis group, n = 20,678[1]	*p*-value[2]
Thyroid Cancer	11 (<0.1%)	23 (0.1%)	0.040	22 (0.1%)	29 (0.1%)	0.3
AIDS	19 (<0.1%)	12 (<0.1%)	0.2	27 (0.1%)	16 (<0.1%)	0.093
Autoimmune Thyroid Disease	14 (<0.1%)	24 (0.1%)	0.1	29 (0.1%)	41 (0.2%)	0.2
Lymphoma	14 (<0.1%)	12 (<0.1%)	0.7	24 (0.1%)	17 (<0.1%)	0.3
Obesity	16 (<0.1%)	23 (0.1%)	0.3	41 (0.2%)	33 (0.2%)	0.4
Metabolic Syndrome	5 (<0.1%)	2 (<0.1%)	0.5	2 (<0.1%)	0 (0%)	0.5
Thyroiditis	59 (0.3%)	82 (0.4%)	0.052	98 (0.5%)	104 (0.5%)	0.7
Thyroid Disease	740 (3.6%)	774 (3.7%)	0.4	902 (4.4%)	892 (4.3%)	0.8
Nonalcoholic Steatohepatitis (NASH)	0 (0%)	4 (<0.1%)	0.125	1 (<0.1%)	0 (0%)	>0.9

[1]n (%)

[2]Fisher's exact test; The χ^2 test of independence.