Obesity and dyslipidemia in patients with psoriasis
A case–control study
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Abstract
The aim of this study was to conduct a more comprehensive analysis of the association between psoriasis and abnormal lipid metabolism.

The case–control study included 222 psoriatic patients and 445 non-psoriatic control patients matched for age and gender. Clinical parameters included age, gender, and body mass index (BMI). Serum lipid levels were recorded and included cholesterol (CHO), triglycerides (TG), low-density lipoprotein (LDL), high density lipoprotein (HDL), phospholipids (PLIP), free fatty acids (FFA), lipoprotein (a) [Lp(a)], and apolipoproteins (apoA1, apoB, and apoE). Statistical analysis was carried out through the IBM Statistical Package for the Social Studies version 23.0.

Compared with controls, levels of BMI and the prevalence of obesity were significantly higher in psoriatic patients. The results revealed that when compared to controls, significant elevation of serum TG (P < .001) and Lp(a) (P = .022) was observed. Levels of HDL (P < .001) and apoA1 (P < .001) were significantly lower in psoriatic patients. There was no significant difference in CHO (P = .367), LDL (P = .400), apoB (P = .294), apoE (P = .554), PLIP (P = .931) and FFA (P = .554) between patients and controls. The levels of CHO, TG, PLIP, FFA, and apoE were positively correlated with BMI level.

Dyslipidemia was more common in psoriatic patients, compared with non-psoriatic controls.

Abbreviations: apo = apolipoproteins, BMI = body mass index, CHO = cholesterol, CI = confidence interval, CVD = cardiovascular disease, FFA = free fatty acids, HDL = high density lipoprotein, LDL = low-density lipoprotein, Lp (a) = lipoprotein (a), OR = odds ratio, PA = psoriasis arthritis, PE = erythroderma psoriasis, PLIP = phospholipids, SD = standard deviation, TG = triglycerides.

Keywords: apolipoprotein, body mass index, lipid metabolism, obesity, psoriasis

1. Introduction
Psoriasis is a common chronic recurrent inflammatory skin disease with unknown etiology. Genetic, metabolic and immunologic factors play an important role in the pathogenesis of psoriasis. Beyond the skin, psoriasis is often associated with comorbidities such as metabolic syndrome. Obesity, as a component of the metabolic syndrome, is an important comorbidity.[1] Increasing evidence has demonstrated the association of psoriasis and inflammatory bowel disease, metabolic syndrome, dyslipidemia, cardiovascular diseases, and so on. Armstrong et al[2] performed a systematic review on the association between psoriasis and dyslipidemia and found that most studies presented significant associations between psoriasis and dyslipidemia.[5] However, there are also a few studies that indicated no significant associations between psoriasis and dyslipidemia.[6-7] Apolipoproteins are the protein part of lipoproteins and are involved in the transport and metabolism of cholesterol (CHO), triglycerides (TG), and other lipids. In psoriatic patients, different results concerning apolipoproteins (apoA1, apoB, and apoE) have been found.[8-10] In addition, in recent years, the establishment of a clear association between psoriasis and obesity coincided with a growing awareness that both diseases are chronic inflammatory processes. The aim of this study was to investigate the association of obesity and abnormal lipid metabolism with psoriasis in Chinese patients, and we proposed the hypothesis that the prevalence of dyslipidemia and obesity was higher in patients with psoriasis than that in the controls.

2. Methods
2.1. Subjects
This hospital-based case–control study was performed in 222 psoriatic patients who were admitted to the hospital from January 2015 to September 2017. Patients who had received
systemic therapy during the prehospital phase were excluded. The control group comprised 445 hospitalized non-psoriatic individuals referred with cosmetic complaints or superficial skin masses, without a personal or family history of psoriasis. The patients and controls had no history of systemic diseases (including coronary heart disease, diabetes, hyperlipidemia, obstructive liver disease, and endocrine diseases). There was no history of lipid-lowering medication in any of the patients and controls. This work was approved by the ethics committee of China-Japan Friendship Hospital.

Hypertension was identified when a diagnosis of hypertension was made previously or when blood pressure was ≥140/90 mmHg. The criteria for hypertension was from Chinese Guidelines for the Management of Hypertension in 2010.[11] Hyperlipidemia was defined as a CHO 6.2 mmol/L or greater, TG 2.26 mmol/L or greater, low-density lipoprotein (LDL) 4.14 mmol/L or greater, or high-density lipoprotein (HDL) 1.04 mmol/L or less. The criteria for dyslipidemia was from Chinese guideline for the management of dyslipidemia in adults in 2016.[12] Diabetes was defined as fasting glycaemia greater than or equal to 6.11 mmol/L, hypoglycemic treatment, or both. The criteria for hyperglycaemia was from Chinese guideline for Type 2 Diabetes in 2017.[13] The weight classification for body mass index (BMI) in Chinese adults was as follows: a BMI between 18.5 and 23.9 is normal, a BMI between 24 and 27.9 is overweight, and a BMI greater than 28 is a diagnosis of obesity.

2.2. Data collection
Clinical information about the age, gender, height, weight, and BMI of all participants and the type of psoriasis by patient group was registered. BMI was calculated as weight (kg)/[height in m²].

Biological examinations included serum levels of CHO, TG, LDL, HDL, free fatty acids (FFA), lipoprotein (a) [Lp(a)], apoA1, apoB, and apoE from the electronic medical records system.

2.3. Statistical analysis
Data were analyzed using the IBM Statistical Package for the Social Studies version 23.0 (Statistical Package for the Social Studies [SPSS] Inc., Chicago, IL). For the descriptive analysis: normally distributed quantitative variables were expressed as the mean ± standard deviation (SD). For the univariate analysis: categorical variables were studied using the chi-square test, and the comparison of averages was done with Student t test. A correlation analysis of quantitative variables was performed by the Pearson correlation test. A multivariable logistic regression analysis was performed to identify the factors independently associated with psoriasis.

3. Results
3.1. Demographic data
In this case-control study, 222 psoriatic patients (146 men and 76 women) and 445 non-psoriatic individuals as the control group (273 men and 172 women) were enrolled for investigation. The patient group included 186 individuals with psoriasis vulgaris (PV), 22 with psoriasis arthritis (PA), 9 with pustular psoriasis (PUS) and 5 with erythroderma psoriasis (PE). The age range of both groups was 16 to 80 years. The mean age of the patients and controls was 51.60 (SD = 14.50) and 49.80 (SD = 14.07) years, respectively. There was no significant difference in the age and gender of cases and controls (P = .125 and P = .266). The descriptive subject characteristics are given in Table 1.

3.2. Obesity and BMI
The prevalence of obesity in the patient group (20.3%) was higher than that in the control group (11.9%), P = .004. The prevalence of obesity in the patients with psoriasis and the controls is presented in Figure 1. The association between psoriasis and obesity might exist. The result of regression model presented that psoriasis might increase the risk for obesity, odds ratio (OR) 1.88 [95% confidence interval (CI) 1.22–2.91, P = .004]. However, this association was not significant after adjusting for potential confounders with multivariable logistic regression (OR = 1.60 [95% CI 0.85–2.99, P = .144]). We calculated the numerical BMI value of all participants, and the level was significantly higher in patients with psoriasis (24.82 ± 3.69 kg/m²) than in controls (24.12 ± 3.51 kg/m²), P = .017. Psoriasis was strongly associated with high level of BMI (OR = 1.06, 95% CI 1.009–1.105; P = .018).

3.3. Serum lipids and apolipoproteins
The serum lipid levels and apolipoproteins in both patient and control groups are presented in Table 2. The serum CHO was 4.49 ± 1.03 mmol/L in cases and 4.56 ± 0.83 mmol/L in controls.

Data are presented as means ± SD or percentages. Differences are tested by the unpaired t test or the χ² test. P value with an asterisk (*) was statistically significant. BMI = body mass index.

Table 1
The main descriptive characteristics of participants.

| Clinical characteristics | Patients (n = 222) | Control Subjects (n = 445) | P value |
|--------------------------|-------------------|---------------------------|---------|
| Sex, Male/Female         | 146/76            | 273/172                   | .266    |
| Age (yr), (Mean ± SD)    | 51.59 ± 14.50     | 49.80 ± 14.07             | .125    |
| BMI, kg/m²                | 24.82 ± 3.69      | 24.12 ± 3.51              | .017    |
| Obesity, n (%)           | 45 (20.3%)        | 53 (11.9%)                | .004    |
| Current Smoker, n (%)    | 87 (39.2%)        | 109 (24.5%)               | <.001   |
| Current Drinker, n (%)   | 49 (22.1%)        | 91 (20.4%)                | .628    |
| Hyperlipidemia, n (%)    | 94 (44.1%)        | 117 (26.3%)               | <.001   |
| Hypertension, n (%)      | 75 (33.8%)        | 111 (24.9%)               | .016    |
| Diabetics, n (%)         | 39 (17.6%)        | 50 (11.2%)                | .023    |

Figure 1. Prevalence of hyperlipidemia and obesity in psoriatic patients and control subjects. *P < .05 for the significant difference between 2 groups.
There was no significance (P = .367). The TG level in cases was 1.83 ± 1.55 mmol/L and in controls was 1.29 ± 0.67 mmol/L. The elevation of TG was significant (P < .001) in cases. In cases, the mean level of HDL was 1.02 ± 0.37 mmol/L, which was significantly lower than the mean level (1.17 ± 0.31 mmol/L) in controls, P < .001. The elevation of LDL was noted in cases; however, the difference was not significant (P = .400). The levels of PLIP and FFA between cases and controls were not significantly different (P = .931, P = .554). The prevalence of hyperlipidemia in psoriatic patients (44.1%) was significantly higher than that in individuals without psoriasis (26.3%), which might be seen in Figure 1. The multivariable logistic regression analysis of psoriatic patients versus non-psoriatic individuals is presented in Table 3. Hyperlipidemia was independently associated with psoriasis after adjusting for potential confounders (BMI, obesity, smoking, hypertension, and diabetes).

The level of apoA1 (1.20 ± 0.29 g/L) in the psoriatic patients was significantly lower than that (1.31 ± 0.28 g/L) in the control subjects (P < .001). Compared with the controls, the Lp(a) (0.19 ± 0.23 g/L) levels were increased in the patients (P = .028). However, the levels of apoB and apoE in cases were not significantly different than those in controls (P = .294 and P = .05).

### 3.4. The correlation between BMI and lipid parameters

The levels of CHO (r = 0.203, P = .002), TG (r = 0.296, P < .001), PLIP (r = 0.201, P = .003), FFA (r = 0.147, P = .028), and apoE (r = 0.244, P < .001) had a positive correlation with the BMI level. The concentration of HDL (r = −0.137, P = .042) had a negative correlation with the BMI level. However, LDL (r = 0.13, P = .052), apoA1 (r = −0.088, P = .191), apoB (r = −0.017, P = .804) and Lp(a) (r = −0.038, P = .574) were not significantly correlated with the BMI level.

### 4. Discussion

The relationship between obesity and psoriasis is probably bidirectional, with obesity predisposing individuals to psoriasis and psoriasis leading to obesity.[14] On 1 hand, psoriatic patients did have a higher propensity for obesity. Various mechanisms might lead to obesity in psoriatic patients, such as progressive social isolation, poor eating habits, depression, increased alcohol consumption, decreased physical activity and so on. On the other hand, obesity predisposes patients to psoriasis. Setty et al.[15] demonstrated this hypothesis and found that a linear correlation between BMI and risk of incident psoriasis existed. In our study, the prevalence of obesity in psoriatic patients was higher than in non-psoriatic controls. However, it was not significant after adjusting for potential confounders with multivariable logistic regression. The BMI level in patients was positively correlated with the concentration of the serum CHO, TG, PLIP, apoE, and FFA levels, which suggested that abnormal lipid metabolism might be associated with the elevation of BMI or obesity.

In this study, the significantly higher levels of TG, Lp(a), BMI and lower levels of HDL, apoA1 were observed in psoriatic patients. Abnormal lipid metabolism may be associated with psoriasis. In most studies, compared to a control group, a significantly elevated level of CHO, LDL, and TG in psoriatic patients was demonstrated.[8,16,17] Moreover, there was a lower level of HDL in the serum of psoriatic patients.[17] FFA is released from adipose tissue, and serum FFA levels are higher in obese individuals compared with lean individuals.[18] The results of studies that investigated FFA levels in psoriatic patients are contradictory.[19,20] A few studies revealed no differences in serum lipid levels between the psoriatic patients and healthy populations.[21] Our study revealed that significant elevation of TG was observed; whereas compared with the controls, the HDL level was lower in the psoriatic patients, which is consistent with most previous studies. However, the concentration of CHO, LDL, and FFA was not significantly different between cases and controls.

The studies concerning the level of serum PLIP in psoriatic patients presented different results. A decrease in concentration of total serum PLIP was observed.[22] There was also an increased level of some fractions of serum PLIP, such as lyssolecithin and palmitic acid.[23] However, some reports do not present any differences in the level of serum phospholipids between the psoriatic patients and the healthy control group.[19] We detected no difference in serum PLIP between cases and controls.

Lp(a) and apolipoprotein may be associated with psoriasis. On 1 hand, Lp(a) levels are increased in chronic inflammatory diseases, such as rheumatoid arthritis, systemic lupus erythematosus and so on. Elevated Lp(a) is a risk factor for cardiovascular disease (CVD).[24] Lp(a) plays a role in stimulating platelet aggregation, alteration of fibrin clot structure, inhibiting the tissue factor pathway inhibitor, promoting endothelial dysfunction and phospholipid oxidation, which may increase CVD risk.[25] Lp(a) may play a role in psoriasis, and many studies revealed that when compared with healthy controls, Lp(a) levels
were significantly higher in patients with psoriasis.\textsuperscript{[26]} Our result was consistent with previous studies and showed that the level of Lp (a) in psoriasis was significantly higher in patients with psoriasis. The patients with psoriasis tend to have an increased risk of CVD,\textsuperscript{[27]} and Lp(a) may contribute to the association between psoriasis and CVD.

In addition, elevated levels of apoA1 and apoB were detected in the serum of psoriatic patients compared to the serum of control group individuals.\textsuperscript{[18,28]} However, there are also contrary results showing decreased levels of apolipoproteins.\textsuperscript{[19]} ApoA1 plays an important role in the reverse cholesterol transport from the peripheral cells to the liver, and a lower level of apoA1 is associated with a higher risk of atherosclerosis. The lower serum level of apoA1 in the inflammatory tissues might lead to the reduction of circulating HDL and thus increase the risk of cardiovascular disease in psoriatic patients.\textsuperscript{[19]} In our study, the apoA1 level was significantly decreased in the psoriatic patients, and there was a strong correlation between apoA1 and HDL ($r=0.584$, $P<.001$). An elevated level of apoB is associated with the increased risk of atherosclerosis because of its role in cholesterol accumulation in the endothelium. The level of apoB in our patient group was higher than in the control group, but there was no significant difference. ApoE is essential for the normal transformation and metabolic processes involved in lipoproteins, and it also modulates TG and LDL levels.\textsuperscript{[30]} Veletza et al.\textsuperscript{[30]} found that the downregulation of apoE expression and the normalization of the apoE level preceded clinical improvement, suggesting that the apoE gene might play a role in psoriasis. In contrast, no significant elevation of apoE in patients was noted, but the levels of TG ($r=0.630$, $P<.001$) and LDL ($r=0.265$, $P<.001$) in psoriasis were positively correlated with apoE.

Inflammation may be a common pathogenic factor for psoriasis and dyslipidemia. Psoriasis is a chronic inflammatory disease characterized by increased Th1 and Th17 cells,\textsuperscript{[31]} and the systemic inflammation of patients may contribute to the development of psoriasis and lipid disturbance. Certain cytokines implicated in psoriasis, such as interleukin 1 (IL-1), IL-6 and TNF-\alpha, also play important roles in the dysregulation and elevation of serum lipids.\textsuperscript{[32]} Some studies have found that IL-1, IL-6, and TNF-\alpha may be involved in the inhibition of lipoprotein lipase activity, therefore decreasing triglyceride clearance and increasing triglyceride levels.\textsuperscript{[33,34]} Moreover, these cytokines may elevate lipid levels by increasing lipolysis and stimulating fatty acid synthesis.\textsuperscript{[35,36]} FFA dose-dependently enhanced the secretion of the pro-inflammatory cytokines IL-6 and IL-8.\textsuperscript{[37]} The increased levels of FFAs might be a predisposing factor promoting Th1/Th17-mediated inflammation, such as psoriasis.\textsuperscript{[38]}

Our study also had some limitations. First, this study was a hospital-based study, and there might be selection bias. Second, the information on the psoriasis area and severity index (PASI) was incomplete, so we did not analyze the correlation between serum lipids and PASI. Third, the sample size was not sufficiently large. Further studies are needed to illustrate the association and mechanisms between psoriasis and dyslipidemia.

5. Conclusion

In conclusion, dyslipidemia was more common in psoriatic patients than in controls, and psoriasis might be associated with the abnormal lipid metabolism. In the clinic, psoriatic patients should be screened and treated for lipid abnormalities, which would be conducive to treatment of psoriasis.

Author contributions

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