BMC Immunology

RESEARCH

Open Access

Pre-treatment plasma retinol binding protein 4 level and its change after treatments predict systemic treatment response in psoriasis patients

Runting Niu[1], Zhijia Li[2*], Wanqing Jiang[1], Qingyan Yang[3], Xinfei Duan[4*], Lixiao Sun[5], Zhijie Cheng[6], Junhui Huang[7], Lihong Li[1], Junge Ma[1], Taiping Hu[8], Lijuan Zhou[8], Juan Du[1], Chang Wang[1] and Feifei Liu[8]

Abstract

Background Retinol binding protein 4 (RBP4) is a mediator of inflammation and related to skin lesion formation, which suggests its engagement in psoriasis pathology and progression. This study intended to explore the change in RBP4 after systemic treatments, and its ability to predict treatment response in psoriasis patients.

Methods This prospective study enrolled 85 psoriasis patients and 20 healthy subjects. Plasma RBP4 was detected by enzyme-linked immunosorbent assay at baseline and 12th week (W12) after systemic treatments in psoriasis patients, as well as after enrollment in healthy subjects. Psoriasis Area and Severity Index (PASI) 75 and PASI 90 were evaluated at W12 in psoriasis patients.

Results RBP4 at baseline was higher in psoriasis patients than in healthy subjects [median (interquartile range): 13.39 (9.71–22.92) versus 9.59 (6.57–13.72) μg/mL] ($P=0.003$). In psoriasis patients, 50 (58.8%) patients achieved PASI 75 at W12, and 25 (29.4%) patients achieved PASI 90 at W12. RBP4 was decreased at W12 compared to its level at baseline ($P<0.001$). Lower RBP4 at baseline predicted achieving PASI 75 at W12 ($P=0.038$). Greater RBP4 change (baseline-W12) precited achieving PASI 75 ($P=0.036$) and PASI 90 ($P=0.045$) at W12. Receiver operating characteristic curves suggested that after adjustment for all clinical features, RBP4 at baseline and RBP4 change (baseline-W12) had an acceptable ability to predict PASI 75 and PASI 90 at W12 with all area under curve values > 0.7.

Conclusion Plasma RBP4 is decreased after systemic treatments, and its low baseline level and greater decline after treatments predict good treatment response in psoriasis patients.

Keywords Psoriasis, Retinol binding protein 4, Longitudinal change, Systemic treatments, Treatment response

*Correspondence:
Zhijia Li
jiaozai648871@163.com
Xinfei Duan
xfduan_hd@163.com

Full list of author information is available at the end of the article

Introduction

Psoriasis is a chronic autoimmune skin disease characterized by abnormal skin cell proliferation, which typically manifests as a red and raised area of plaques on the skin covered with a silvery-white scale [1]. Globally, the incidence of psoriasis varies from 30.3 to 321.0 per 100,000 person-years, and the prevalence of psoriasis ranges from 0.14 to 1.99% [2]. Systemic treatments, including conventional systemic agents and biologic agents, are common treatment strategies for psoriasis patients [3–5]. However, the response to systemic treatments is still unsatisfactory in some psoriasis patients, and the Psoriasis Area and Severity Index (PASI) 90 response rate ranges from 12.2 to 72% after 10 to 16 weeks [6–8]. Subsequently, psoriasis patients who do not respond to systemic treatments would suffer from disease progression and reduced quality of life [5]. Therefore, investigating potential markers that estimate response to systemic treatments may help to improve the management of psoriasis patients.

Retinol binding protein 4 (RBP4), the specific transport protein of the lipophilic vitamin A with a molecular weight of about 21 kDa, is primarily derived from hepatocytes and adipocytes [9–12]. Previous studies found that RBP4 might be related to psoriatic skin lesion formation and was a mediator of inflammation, suggesting a potential involvement of RBP4 in psoriasis pathology and progression [13, 14]. As reported by a previous study, RBP4 protein was accumulated in psoriatic skin lesions, and this study also proposed a physiological role of RBP4 in psoriasis: the demand for vitamin A in psoriatic skin lesions was elevated. In response, RBP4 transferred retinol to lesional skin. After that, retinol was metabolized into retinoic acid, which further activated downstream pathways that facilitated keratinocyte proliferation and aggravated psoriasis [14]. More importantly, some clinical studies have reported the variation of RBP4 after treatments in psoriasis patients [15–18]. For instance, a study discovered that RBP4 was reduced after 6 months of adalimumab treatment in psoriasis patients [18]. Another study disclosed that after 3 months of acitretin treatment, RBP4 was decreased in psoriasis patients [15]. However, RBP4 was not influenced by phototherapy or topical treatment in psoriasis patients [16, 17]. Based on the above evidence, we deduced that RBP4 might predict response to systemic treatments in psoriasis patients. However, relevant evidence is scarce.

Therefore, the current study aimed to investigate the longitudinal change in RBP4 after systemic treatments, and its ability to predict treatment response in psoriasis patients.

Methods

Patients and healthy subjects

This prospective, observational cohort study enrolled 85 psoriasis patients who were in the active state of the disease (PASI score ≥ 8) and needed systemic treatment (conventional systemic agents or biologic agents). Patients who met all of the following criteria were included: (1) clinically diagnosed as psoriasis [19]; (2) PASI score ≥ 8; (3) needed systemic treatment (conventional systemic agents or biologic agents); (4) could be followed up for 12 weeks; (5) could provide the blood samples. Patients who met one of the following criteria were excluded: (1) concomitant infections; (2) concomitant hematological diseases; (3) pregnant or lactating women. The study enrolled 20 age-sex-matched healthy subjects during the same period. The inclusion criteria were: (1) physical examination results were normal; (2) could provide the blood samples. The exclusion criteria were the same as the psoriasis patients. This study was approved by the Ethics Committee of HanDan Central Hospital. Psoriatic patients and healthy subjects signed an informed consent form.

Clinical characteristics collection

Clinical characteristics of psoriasis patients such as age, gender, body mass index (BMI), psoriasis duration, disease involving arthritis, conventional systemic agents, and biologic agents were collected after enrollment. The clinical characteristics of healthy subjects such as age, gender, and BMI were also collected.

Blood sample collection and RBP4 detection

Blood samples were collected from patients at baseline (before the start of systemic treatment) and the 12th week (±2 weeks) of follow-up (W12). Blood samples from healthy subjects were also collected after enrollment. All blood samples were centrifuged in a centrifuge at 1500 rpm for 10 min at 4 °C. The plasma was obtained and then stored at -80 °C until testing. In this study, RBP4 levels in plasma were detected using an Enzyme-linked immunosorbent assay (ELISA) kit purchased from R&D, USA. The experimental procedure was performed in strict accordance with the instructions.

PASI score evaluation

PASI scores were assessed at baseline (before the start of systemic treatment) and W12. PASI 75 and PASI 90 for the patients were calculated. The PASI score was evaluated in four sections: head, trunk, upper extremities, and lower extremities, which accounted for 10%, 30%, 20%, and 40% of the total score, respectively. The percentage of skin with psoriasis in that section was calculated and categorized on a scale of 0–6. The severity of psoriasis (erythema, induration, scale) was assessed separately for each

section on a scale of 0–4. The total score ranging from 0 to 72. The higher the score, the more severe the psoriasis [20]. PASI 75/90 was defined as the PASI≥75%/90% improvement from the baseline [21].

Statistical analysis

SPSS 26.0 (IBM, USA) was used for the data analysis. Patients who lacked blood samples or PASI score at W12 were excluded from this study analysis, and a total of 85 patients were finally included. The comparative analyses were performed through the student's t, Mann-Whitney U, Chi-square, and Wilcoxon Signed Rank tests. The Correlation analysis was done using the Spearman test. The distinguishing efficiency of RBP4 at baseline between psoriasis and healthy subjects was analyzed by receiver operating characteristic (ROC). A logistic regression analysis model was used to find the factors associated with the PASI 75/90. The predictive efficacy of RBP4 at baseline and decreased RBP4 level for PASI 75/90 were analyzed by ROC. *P* values less than 0.05 were considered statistically different.

The study developed 4 logistic regression models. The logistic regression model 1 was an unadjusted logistic regression of RBP4 at baseline or decreased RBP4 level. In model 2, age and male were adjusted. In model 3, age, male, and BMI were adjusted. In model 4, all clinical characteristics in our study were adjusted.

Table 1 Clinical characteristics

Clinical characteristics	Psoriasis patients (*N*=85)	Healthy subjects (*N*=20)	*P* value
Age (years), mean ± SD	41.7 ± 11.5	38.1 ± 9.2	0.201
Male, n (%)	45 (52.9)	10 (50.0)	0.813
BMI (kg/m^2), mean ± SD	25.9 ± 3.7	23.3 ± 2.3	< 0.001
Psoriasis duration (years), mean ± SD	13.3 ± 6.7	-	-
PASI score, median (IQR)	12.9 (10.6–18.0)	-	-
Disease involving arthritis, n (%)	16 (18.8)	-	-
Conventional systemic agents, n (%)	58 (68.2)	-	-
MTX	28 (32.9)	-	-
CyA	19 (22.4)	-	-
Acitretin	11 (12.9)	-	-
Biologic agents, n (%)	39 (45.9)	-	-
TNF inhibitor	28 (32.9)	-	-
IL-12/23 inhibitor	7 (8.2)	-	-
IL-17 inhibitor	4 (4.7)	-	-

SD, standard deviation; BMI, body mass index; PASI, psoriasis area and severity index; IQR, interquartile range; MTX, methotrexate; CyA, cyclosporin A; TNF, tumor necrosis factor; IL, interleukin

Results

Clinical information of psoriasis patients and healthy subjects

The mean age was 41.7 ± 11.5 years in psoriasis patients and 38.1 ± 9.2 years in healthy subjects (*P*=0.201). There were 45 (52.9%) male psoriasis patients and 10 (50.0%) male healthy subjects (*P*=0.813). The BMI was increased in psoriasis patients compared to healthy subjects (*P*<0.001) (Table 1).

In psoriasis patients, the mean psoriasis duration was 13.3 ± 6.7 years. The median [interquartile range (IQR)] PASI score was 12.9 (10.6–18.0). Sixteen (18.8%) psoriasis patients were found to have disease involving arthritis. Moreover, 58 (68.2%) patients received conventional systemic agents, and 39 (45.9%) patients received biologic agents. Regarding conventional systemic agents, 28 (32.9%), 19 (22.4%), and 11 (12.9%) patients received methotrexate (MTX), cyclosporin A (CyA), and acitretin, respectively. Regarding biologic agents, 28 (32.9%), 7 (8.2%), and 4 (4.7%) patients received tumor necrosis factor (TNF) inhibitor, interleukin (IL)-12/23 inhibitor, and IL-17 inhibitor, respectively (Table 1).

Comparison of RBP4 at baseline between psoriasis patients and healthy subjects

RBP4 at baseline was higher in psoriasis patients than in healthy subjects [median (IQR): 13.39 (9.71–22.92) versus 9.59 (6.57–13.72) μg/mL] (*P*=0.003) (Fig. 1A). The ROC curve suggested that RBP4 at baseline had an acceptable ability to discriminate psoriasis patients from healthy subjects with an area under curve (AUC) [95% confidence interval (CI)] of 0.717 (0.597–0.837) (Fig. 1B). After adjustment for age, gender, and BMI, RBP4 at baseline had a good ability to discriminate psoriasis patients from healthy subjects [AUC (95% CI): 0.794 (0.693–0.894)] (Fig. 1C).

Correlation of RBP4 at baseline with clinical features in psoriasis patients

RBP4 at baseline was positively correlated with disease involving arthritis in psoriasis patients (*r*=0.234, *P*=0.031). Meanwhile, RBP4 at baseline showed a trend to be positively correlated with BMI in psoriasis patients but did not achieve statistical significance (*r*=0.194, *P*=0.075). However, RBP4 at baseline was not correlated with other clinical features in psoriasis patients (all *P*>0.05) (Table 2).

Relationship of RBP4 at baseline and RBP4 change (baseline-W12) with systemic treatment response at W12 in psoriasis patients

A total of 50 (58.8%) psoriasis patients achieved PASI 75 at W12, and 25 (29.4%) psoriasis patients achieved PASI 90 at W12 (Fig. 2A). RBP4 at W12 was lower than its

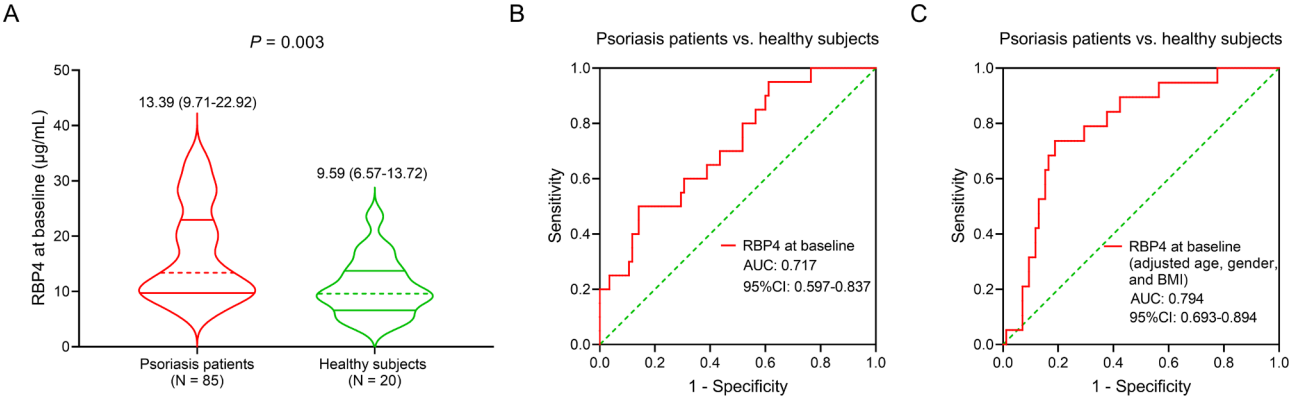

Fig. 1 RBP4 in psoriasis patients and healthy subjects. Comparison of RBP4 between psoriasis patients and healthy subjects (**A**). ROC curves of RBP4 at baseline (**B**) and RBP4 at baseline (adjusted age, gender, and BMI) (**C**) for discriminating psoriasis patients from healthy subjects

Table 2 Correlation between RBP4 at baseline and clinical characteristics in psoriasis patients

Clinical characteristics	RBP4 at baseline (μg/mL)	
	r value	*P* value
Age (years)	0.152	0.166
Male	0.085	0.439
BMI (kg/m^2)	0.194	0.075
Psoriasis duration (years)	0.044	0.692
PASI score	0.171	0.117
Disease involving arthritis	0.234	0.031
Conventional systemic agents	-0.110	0.315
Biologic agents	0.020	0.858

RBP4, retinol binding protein 4; BMI, body mass index; PASI, psoriasis area and severity index

level at baseline [median (IQR): 11.10 (6.88–16.28) versus 13.39 (9.71–22.93) μg/mL] ($P<0.001$). The median (IQR) RBP4 change (baseline-W12) was 2.87 (0.47–7.82) μg/mL (Fig. 2B).

RBP4 at baseline was lower in psoriasis patients who achieved PASI 75 at W12 than those who did not achieve that ($P=0.038$). However, RBP4 at baseline was not different between psoriasis patients who achieved PASI 90 at W12 and those who did not achieve that ($P=0.130$) (Fig. 2C). RBP4 change (baseline-W12) was greater in psoriasis patients who achieved PASI 75 at W12 than those who did not achieve that ($P=0.036$); it was also greater in patients who achieved PASI 90 at W12 than those who did not achieve that ($P=0.045$) (Fig. 2D).

Comparison of RBP4 before and after treatments in psoriasis patients

RBP4 at W12 was lower than its level at baseline in patients receiving MTX ($P<0.001$) and acitretin ($P=0.041$). However, there was no difference in RBP4 at W12 and baseline in patients receiving CyA ($P=0.601$). Regarding biologic agents, RBP4 at W12 was lower than its level at baseline in patients receiving TNF inhibitor ($P<0.001$) and IL-12/23 inhibitor ($P=0.018$). However, there was no difference in RBP4 at W12 and baseline in patients receiving IL-17 inhibitor ($P=0.144$) (**Supplementary Table 1**).

Subgroup analysis of the prognostic value of RBP4 based on treatment regimens in psoriasis patients

Subgroup analysis revealed that RBP4 at baseline showed a decreasing trend in patients receiving MTX ($P=0.078$) and TNF inhibitor ($P=0.084$) who achieved PASI 75 at W12 compared to those who did not achieve it, but it did not reach statistical significance. Additionally, RBP4 at baseline was numerically decreased in patients receiving CyA who achieved PASI 90 at W12 compared to those who did not achieve it, but without statistical significance ($P=0.057$). Moreover, the RBP4 change (baseline-W12) was greater in patients receiving CyA who achieved PASI 75 at W12 than those who did not achieve that, but it did not reach statistical significance ($P=0.099$) (**Supplementary Table 2**).

ROC curves of RBP4 at baseline and RBP4 change (baseline-W12) for systemic treatment response at W12 in psoriasis patients

ROC curves were applied to analyze the abilities of RBP4 at baseline to predict PASI 75 (Fig. 3A-D) and PASI 90 (Fig. 3E-H) at W12 in psoriasis patients. After adjustment for all clinical characteristics, RBP4 at baseline had an acceptable ability to predict PASI 75 [AUC (95% CI): 0.762 (0.654–0.871)] (Fig. 3D) and PASI 90 [AUC (95% CI): 0.828 (0.721–0.935)] (Fig. 3H) at W12 in psoriasis patients.

The abilities of RBP4 change (baseline-W12) to predict PASI 75 (Fig. 3I-L) and PASI 90 (Fig. 3M-P) at W12 in psoriasis patients were also analyzed. After adjustment for all clinical characteristics, RBP4 change (baseline-W12) had a certain ability to predict PASI 75 [AUC (95% CI): 0.717 (0.600-0.834)] (Fig. 3L) and PASI 90 [AUC

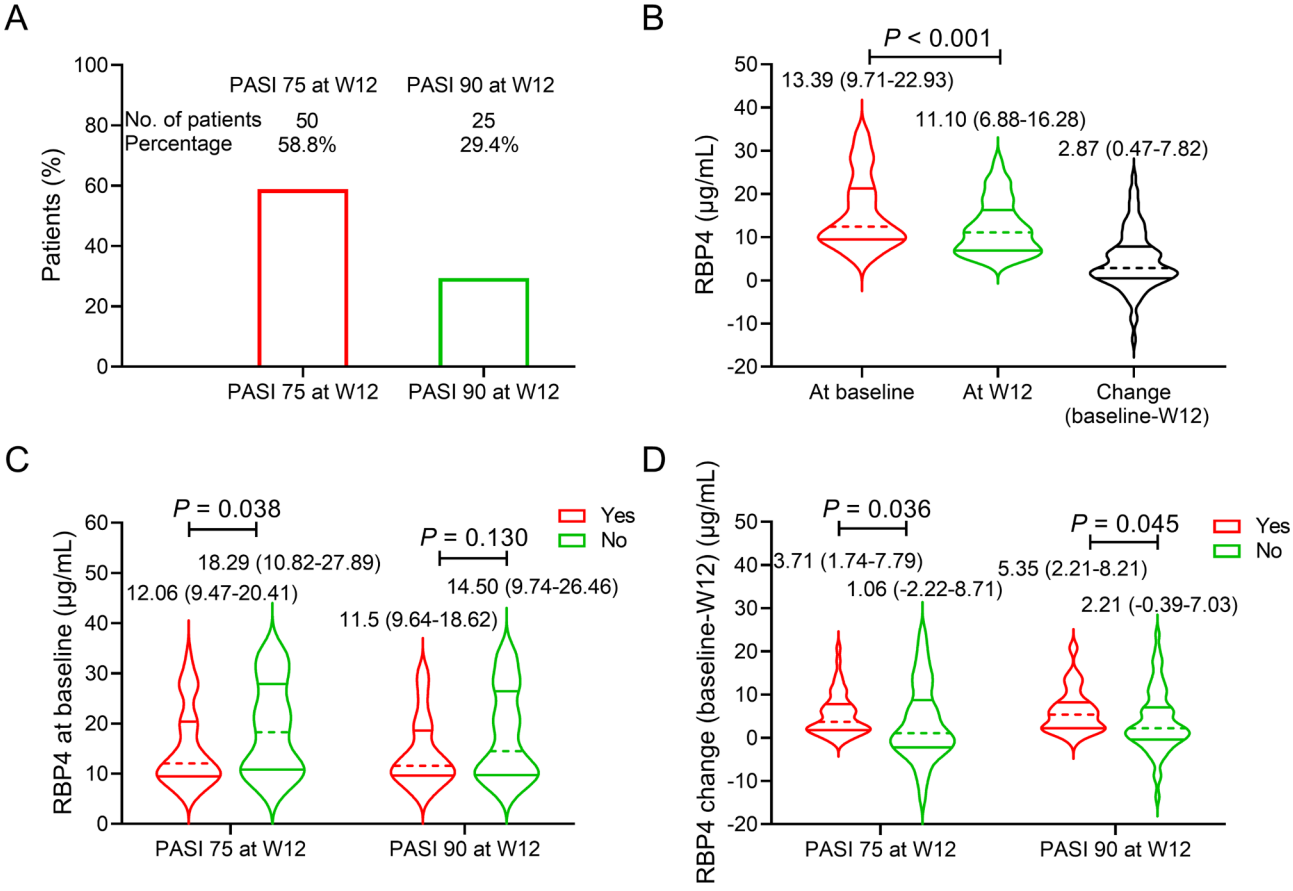

Fig. 2 Relationship of RBP4 at baseline and RBP4 change (baseline-W12) with PASI 75 and PASI 90 at W12 in psoriasis patients. PASI 75 and PASI 90 at W12 in psoriasis patients (**A**). Comparison of RB4 at baseline and W12; the data of RBP4 change (baseline-W12) in psoriasis patients (**B**). RBP4 at baseline (**C**) and RBP4 change (baseline-W12) (**D**) for predicting PASI 75 and PASI 90 at W12 in psoriasis patients

(95% CI): 0.785 (0.675–0.895)] (Fig. 3P) at W12 in psoriasis patients.

Logistic regression models for systemic treatment response at W12 in psoriasis patients

Model 1 (unadjusted) suggested that RBP4 at baseline was negatively associated with PASI 75 at W12 [odds ratio (OR)=0.946, P=0.039]. Model 4 (adjusted all clinical characteristics in our study) disclosed that RBP4 at baseline was negatively and independently associated with PASI 75 at W12 (OR=0.923, P=0.019). Meanwhile, only model 4 (adjusted all clinical characteristics in our study) revealed that RBP4 at baseline was negatively and independently associated with PASI 90 at W12 (OR=0.920, P=0.038) (Table 3).

Regarding RBP4 change (baseline-W12), models 1, 2, 3, and 4 suggested that RBP4 change (baseline-W12) was not associated with PASI 75 or PASI 90 at W12 in psoriasis patients (all P>0.05) (Table 4).

Discussion

RBP4 is dysregulated in patients with autoimmune diseases according to previous studies [16, 22–24]. In terms of psoriasis, previous studies found that RBP4 was increased in psoriasis patients compared to healthy controls [16, 24, 25]. In line with these previous studies [16, 24, 25], we also discovered that RBP4 at baseline was higher in psoriasis patients compared to healthy subjects. The potential explanations would be that: (1) the increase in RBP4 might be related to psoriatic skin lesion formation [14]. (2) RBP4 could also regulate stimulated by retinoic acid (STRA)6, c-Jun N-terminal protein kinase (JNK), and toll-like receptor 4 (TLR4) to amplify inflammation, thereby inducing psoriasis [26–28]. Thus, an increase in RBP4 was discovered in psoriasis patients compared to healthy controls. Another finding was that, after adjustment for age, gender, and BMI, RBP4 at baseline had a good ability to estimate psoriasis risk. This finding suggested that the detection of RBP4 might assist in diagnosing psoriasis. It should be clarified that only 20 healthy subjects were enrolled in this study, which might affect the statistical power.

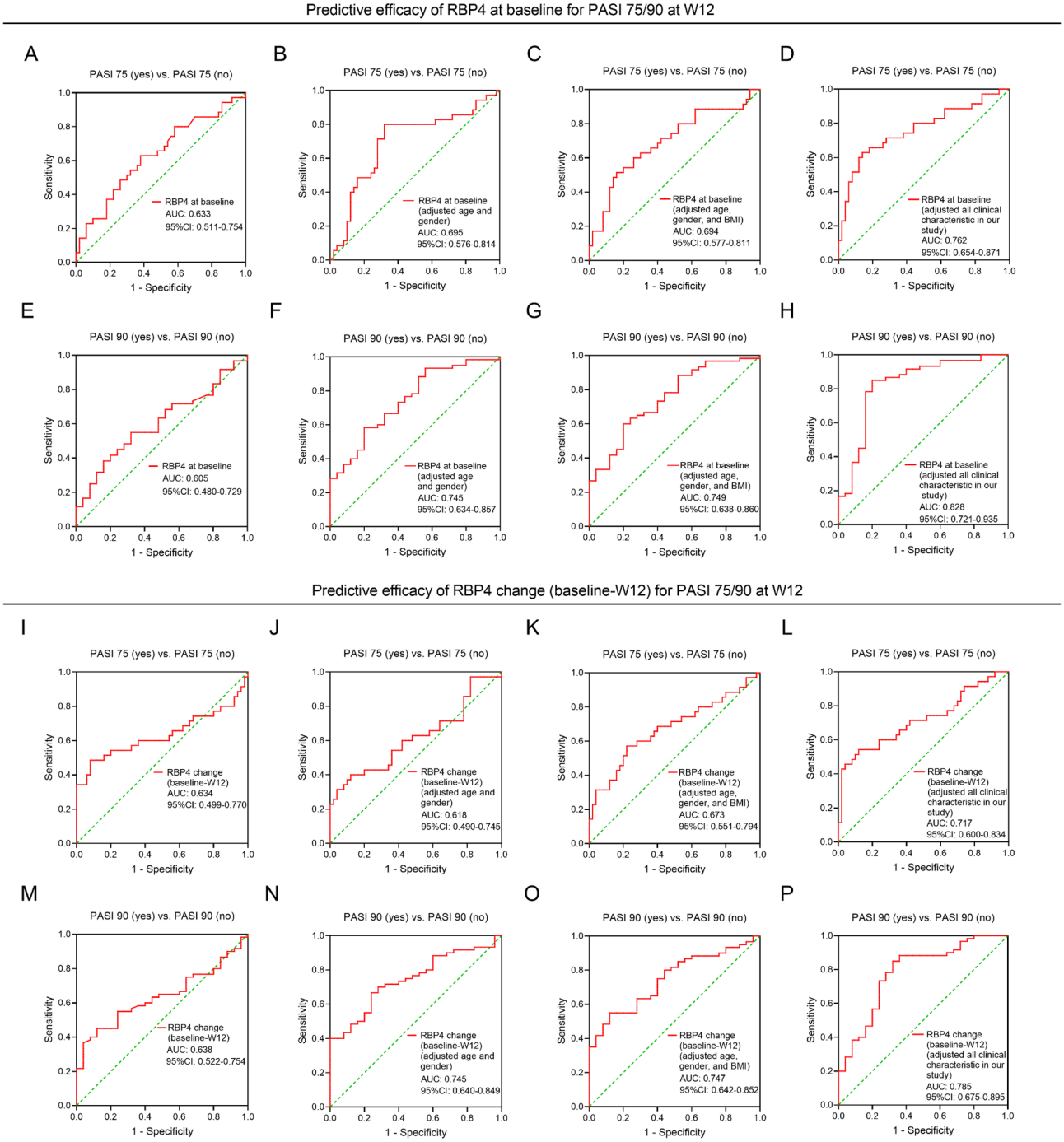

Fig. 3 Predictive ability of RBP4 at baseline and RBP4 change (baseline-W12) for PASI 75 and PASI 90 at W12 in psoriasis patients. Predictive ability of RBP4 at baseline for PASI 75 in psoriasis patients (**A**). Predictive ability of RBP4 at baseline adjusted age and gender (**B**), adjusted age, gender, and BMI (**C**), and adjusted all clinical characteristics in our study (**D**) for PASI 75 in psoriasis patients. Predictive ability of RBP4 at baseline for PASI 90 in psoriasis patients (**E**). Predictive ability of RBP4 at baseline adjusted age and gender (**F**), adjusted age, gender, and BMI (**G**), and adjusted all clinical characteristics in our study (**H**) for PASI 90 in psoriasis patients. Predictive ability of RBP4 change (baseline-W12) for PASI 75 in psoriasis patients (**I**). Predictive ability of RBP4 change (baseline-W12) adjusted age and gender (**J**), adjusted age, gender, and BMI (**K**), and adjusted all clinical characteristics in our study (**L**) for PASI 75 in psoriasis patients. Predictive ability of RBP4 change (baseline-W12) for PASI 90 in psoriasis patients (**M**). Predictive ability of RBP4 change (baseline-W12) adjusted age and gender (**N**), adjusted age, gender, and BMI (**O**), and adjusted all clinical characteristics in our study (**P**) for PASI 90 in psoriasis patients

Table 3 Association between RBP4 at baseline and PASI 75/90 at W12

Factors	*P* value	OR	95%CI
Logistic regression analysis models of PASI 75 at W12			
Model 1 (unadjusted)			
RBP4 at baseline (μg/mL)	0.039	0.946	0.898–0.997
Model 2 (adjusted age and gender)			
RBP4 at baseline (μg/mL)	0.065	0.951	0.901–1.003
Model 3 (adjusted age, gender, and BMI)			
RBP4 at baseline (μg/mL)	0.113	0.957	0.906–1.010
Model 4 (adjusted all clinical characteristics in our study)			
RBP4 at baseline (μg/mL)	0.019	0.923	0.863–0.987
Logistic regression analysis models of PASI 90 at W12			
Model 1 (unadjusted)			
RBP4 at baseline (μg/mL)	0.079	0.946	0.888–1.006
Model 2 (adjusted age and gender)			
RBP4 at baseline (μg/mL)	0.101	0.945	0.884–1.011
Model 3 (adjusted age, gender, and BMI)			
RBP4 at baseline (μg/mL)	0.119	0.947	0.885–1.014
Model 4 (adjusted all clinical characteristics in our study)			
RBP4 at baseline (μg/mL)	0.038	0.920	0.850–0.995

PASI 75, psoriasis area and severity index ≥ 75% improvement; PASI 90, psoriasis area and severity index ≥ 90% improvement; W12, 12th week (±2 weeks) of follow-up; OR, odds ratio; CI, confidence interval; RBP4, retinol binding protein 4; BMI, body mass index

Table 4 Association between RBP4 change (baseline-W12) and PASI 75/90 at W12

Factors	*P* value	OR	95%CI
Logistic regression analysis models of PASI 75 at W12			
Model 1 (unadjusted)			
RBP4 change (baseline-W12) (μg/mL)	0.179	1.048	0.979–1.122
Model 2 (adjusted age and gender)			
RBP4 change (baseline-W12) (μg/mL)	0.172	1.050	0.979–1.125
Model 3 (adjusted age, gender, and BMI)			
RBP4 change (baseline-W12) (μg/mL)	0.156	1.053	0.981–1.130
Model 4 (adjusted all clinical characteristics in our study)			
RBP4 change (baseline-W12) (μg/mL)	0.375	1.036	0.958–1.120
Logistic regression analysis models of PASI 90 at W12			
Model 1 (unadjusted)			
RBP4 change (baseline-W12) (μg/mL)	0.146	1.054	0.982–1.131
Model 2 (adjusted age and gender)			
RBP4 change (baseline-W12) (μg/mL)	0.177	1.055	0.976–1.140
Model 3 (adjusted age, gender, and BMI)			
RBP4 change (baseline-W12) (μg/mL)	0.167	1.056	0.977–1.142
Model 4 (adjusted all clinical characteristics in our study)			
RBP4 change (baseline-W12) (μg/mL)	0.374	1.045	0.949–1.151

RBP4, retinol binding protein 4; W12, 12th week (±2 weeks) of follow-up; PASI 75, psoriasis area and severity index ≥ 75% improvement; PASI 90, psoriasis area and severity index ≥ 90% improvement; OR, odds ratio; CI, confidence interval; BMI, body mass index

The current study also discovered that RBP4 at baseline showed a trend to be positively correlated with BMI in psoriasis patients, but it did not achieve statistical significance. We speculated that a potential reason would be that RBP4 could regulate adipogenesis, lipid accumulation, and insulin resistance, which might contribute to an increase in BMI [26, 29–31]. Therefore, RBP4 showed a trend of positive correlation with BMI in psoriasis patients. In addition, we also found that RBP4 was positively correlated with psoriasis involving arthritis. A possible explanation would be that RBP4 could induce an inflammatory response in chondrocytes and synoviocytes, which triggered joint destruction [32]. Thus, there was a positive correlation between RBP4 and psoriasis involving arthritis in psoriasis patients.

The change in RBP4 after treatments in psoriasis patients has been revealed by previous studies [15–18]. Some studies reported that RBP4 remained unchanged after phototherapy or topical treatment in psoriasis patients [16, 17]. However, after systemic treatments (acitretin treatment and anti-TNF-α treatment), RBP4 was decreased in psoriasis patients [15, 18]. In line with the two previous studies [15, 18], our study also found that RBP4 was decreased after systemic treatments in psoriasis patients. A possible reason behind this might be that RBP4 was predominantly secreted by adipocytes [33], and systemic treatments might influence the structure of adipocytes, thereby decreasing the production of RBP4 [15]. Moreover, it was discovered that lower RBP4 at baseline and its greater change after treatment were related to achieving response to systemic treatments in psoriasis patients, which was further validated by our ROC curves. A potential reason might be that decreased RBP4 might attenuate psoriatic skin lesion formation, which might promote the efficacy of systemic treatments [14].

Several limitations should be noted in this study. (1) The number of psoriasis patients and healthy subjects was unmatched. Thus, the level of RBP4 in psoriasis patients and healthy subjects should be further explored. (2) The follow-up duration should be prolonged to investigate the ability of RBP4 to predict long-term response to systemic treatments in psoriasis patients. (3) The number of psoriasis patients was small, which limited the statistical power. Further studies should consider enrolling more psoriasis patients. (4) The specific reason behind the decrease in RBP4 after systemic treatments should be investigated in cellular or animal experiments.

Conclusions

In conclusion, plasma RBP4 is reduced after systemic treatments, and its lower basal level and greater change after treatments predict satisfactory systemic treatment response in psoriasis patients. Our findings provide a reference that the detection of RBP4 predicts treatment response in psoriasis patients receiving systemic treatments, which helps to stratify these patients and improve their management.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12865-024-00647-7.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
Not applicable.

Author contributions
RN: Conceptualization, Formal Analysis, Methodology, Project administration, Supervision, Writing – original draft, Writing – review & editing. ZL: Conceptualization, Formal Analysis, Resources, Supervision, Writing – original draft, Writing – review & editing. WJ: Data curation, Methodology, Resources, Supervision, Writing – original draft, Writing – review & editing. QY: Formal Analysis, Investigation, Resources, Supervision, Writing – review & editing. XD: Conceptualization, Formal Analysis, Investigation, Methodology, Supervision, Writing – review & editing. LS: Data curation, Investigation, Resources, Supervision, Writing – review & editing. ZC: Data curation, Investigation, Resources, Supervision, Writing – review & editing. JH: Formal Analysis, Investigation, Resources, Supervision, Writing – review & editing. LL: Data curation, Methodology, Resources, Writing – original draft, Writing – review & editing. JM: Data curation, Methodology, Resources, Writing – original draft, Writing – review & editing. TH: Data curation, Investigation, Resources, Supervision, Writing – review & editing. LZ: Data curation, Investigation, Resources, Supervision, Writing – review & editing. JD: Data curation, Methodology, Resources, Writing – original draft, Writing – review & editing. CW: Data curation, Methodology, Resources, Writing – original draft, Writing – review & editing. FL: Data curation, Investigation, Resources, Supervision, Writing – review & editing.

Funding
None.

Data availability
The datasets used and/or analysed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was approved by the Ethics Committee of HanDan Central Hospital. Psoriatic patients and healthy subjects signed an informed consent form.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

Author details
[1]Department of Dermatology, HanDan Central Hospital, Handan 056000, China
[2]Department of Oncology, Affiliated Hospital of Hebei University of Engineering, Handan 056002, China
[3]Departement of General Surgery, Affiliated Hospital of Hebei University of Engineering, Handan 056002, China
[4]Department of Neurology, HanDan Central Hospital, Handan 056000, China
[5]Department of Critical Care Medicine, HanDan Central Hospital, Handan 056000, China
[6]Department of Emergency Medicine, HanDan Central Hospital, Handan 056000, China
[7]Department of Dermatology, Xingtai Third Hospital, Xingtai 054001, China
[8]Department of Medicalcosmetology, HanDan Central Hospital, Handan 056000, China

Received: 11 June 2024 / Accepted: 12 August 2024
Published online: 21 August 2024

References

1. Walter K, Psoriasis. JAMA. 2022;327(19):1936.
2. Parisi R, Iskandar IYK, Kontopantelis E, Augustin M, Griffiths CEM, Ashcroft DM, Global Psoriasis A. National, regional, and worldwide epidemiology of psoriasis: systematic analysis and modelling study. BMJ. 2020;369:m1590.
3. Sbidian E, Chaimani A, Guelimi R, Garcia-Doval I, Hua C, Hughes C, Naldi L, Kinberger M, Afach S, Le Cleach L. Systemic pharmacological treatments for chronic plaque psoriasis: a network meta-analysis. Cochrane Database Syst Rev. 2023;7(7):CD011535.
4. Garner KK, Hoy KDS, Carpenter AM. Psoriasis: Recognition and Management Strategies. Am Fam Physician. 2023;108(6):562–73.
5. Lee HJ, Kim M. Challenges and Future trends in the treatment of Psoriasis. Int J Mol Sci. 2023;24(17).
6. Griffiths CEM, Armstrong AW, Gudjonsson JE, Barker J. Psoriasis Lancet. 2021;397(10281):1301–15.
7. Armstrong AW, Puig L, Joshi A, Skup M, Williams D, Li J, Betts KA, Augustin M. Comparison of Biologics and oral treatments for Plaque psoriasis: a Meta-analysis. JAMA Dermatol. 2020;156(3):258–69.
8. Armstrong AW, Soliman AM, Betts KA, Wang Y, Gao Y, Puig L, Augustin M. Comparative efficacy and relative ranking of biologics and oral therapies for moderate-to-severe Plaque Psoriasis: A Network Meta-analysis. Dermatol Ther (Heidelb). 2021;11(3):885–905.
9. Steinhoff JS, Lass A, Schupp M. Retinoid Homeostasis and Beyond: How Retinol Binding Protein 4 Contributes to Health and Disease. Nutrients. 2022; 14(6).
10. Huang H, Xu C. Retinol-binding protein-4 and nonalcoholic fatty liver disease. Chin Med J (Engl). 2022;135(10):1182–89.
11. Colantuoni V, Romano V, Bensi G, Santoro C, Costanzo F, Raugei G, Cortese R. Cloning and sequencing of a full length cDNA coding for human retinol-binding protein. Nucleic Acids Res. 1983;11(22):7769–76.
12. Oluwamodupe C, Adeleye AO. Targeting retinol-binding protein 4 (RBP4) in the management of Cardiometabolic diseases. Cardiovasc Toxicol. 2023;23(9–10):285–94.
13. Moraes-Vieira PM, Yore MM, Sontheimer-Phelps A, Castoldi A, Norseen J, Aryal P, Simonyte Sjodin K, Kahn BB. Retinol binding protein 4 primes the NLRP3 inflammasome by signaling through toll-like receptors 2 and 4. Proc Natl Acad Sci U S A. 2020;117(49):31309–18.
14. Wang HM, Wu C, Jiang YY, Wang WM, Jin HZ. Retinol and vitamin A metabolites accumulate through RBP4 and STRA6 changes in a psoriasis murine model. Nutr Metab (Lond). 2020;17:5.
15. Karadag AS, Ertugrul DT, Kalkan G, Bilgili SG, Celik HT, Takci Z, Balahoroglu R, Calka O. The effect of acitretin treatment on insulin resistance, retinol-binding protein-4, leptin, and adiponectin in psoriasis vulgaris: a noncontrolled study. Dermatology. 2013;227(2):103–8.
16. Romani J, Caixas A, Ceperuelo-Mallafre V, Carrascosa JM, Ribera M, Rigla M, Vendrell J, Luelmo J. Circulating levels of lipocalin-2 and retinol-binding protein-4 are increased in psoriatic patients and correlated with baseline PASI. Arch Dermatol Res. 2013;305(2):105–12.
17. Baran A, Swiderska M, Flisiak I. The effect of topical treatment and psoriasis severity on serum retinol-binding protein-4 levels. J Dermatolog Treat. 2016;27(2):114–9.
18. Pina T, Genre F, Lopez-Mejias R, Armesto S, Ubilla B, Mijares V, Dierssen-Sotos T, Corrales A, Gonzalez-Lopez MA, Gonzalez-Vela MC, et al. Anti-TNF-alpha therapy reduces retinol-binding protein 4 serum levels in non-diabetic patients with psoriasis: a 6-month prospective study. J Eur Acad Dermatol Venereol. 2016;30(1):92–5.
19. Committee on Psoriasis CSoD. Guideline for the diagnosis and treatment of psoriasis in China (2018 simplified edition). Chin J Dermatology. 2019;52(4):223–30.
20. Blauvelt A, Papp KA, Griffiths CE, Randazzo B, Wasfi Y, Shen YK, Li S, Kimball AB. Efficacy and safety of guselkumab, an anti-interleukin-23 monoclonal antibody, compared with adalimumab for the continuous treatment of patients with moderate to severe psoriasis: results from the phase III, double-blinded, placebo- and active comparator-controlled VOYAGE 1 trial. J Am Acad Dermatol. 2017;76(3):405–17.
21. Ritchlin CT, Coates LC, McInnes IB, Mease PJ, Merola JF, Tanaka Y, Asahina A, Gossec L, Gottlieb AB, Warren RB, et al. Bimekizumab treatment in biologic

DMARD-naive patients with active psoriatic arthritis: 52-week efficacy and safety results from the phase III, randomised, placebo-controlled, active reference BE OPTIMAL study. Ann Rheum Dis. 2023;82(11):1404–14.
22. Wei Y, Xia N, Zhang W, Huang J, Ren Z, Zhu L, Zhang Z, Yang L. Serum retinol-binding protein 4 is associated with insulin resistance in patients with early and untreated rheumatoid arthritis. Joint Bone Spine. 2019;86(3):335–41.
23. Go DJ, Lee JY, Kang MJ, Lee EY, Lee EB, Yi EC, Song YW. Urinary vitamin D-binding protein, a novel biomarker for lupus nephritis, predicts the development of proteinuric flare. Lupus. 2018;27(10):1600–15.
24. Gul FC, Cicek D, Kaman D, Demir B, Nazik H. Changes of serum lipocalin-2 and retinol binding protein-4 levels in patients with psoriasis and Behcet's disease. Eur J Dermatol. 2015;25(2):195–7.
25. Bakry OA, Shoeib MA, Gayed IM, Menoufy AS. Retinol binding protein 4 in non obese psoriatic cases. J Clin Diagn Res. 2016;10(8):WL01–2.
26. Gokulakrishnan K, Pandey GK, Sathishkumar C, Sundararajan S, Durairaj P, Manickam N, Mohan V, Balasubramanyam M. Augmentation of RBP4/STRA6 signaling leads to insulin resistance and inflammation and the plausible therapeutic role of vildagliptin and metformin. Mol Biol Rep. 2021;48(5):4093–106.
27. Moraes-Vieira PM, Yore MM, Dwyer PM, Syed I, Aryal P, Kahn BB. RBP4 activates antigen-presenting cells, leading to adipose tissue inflammation and systemic insulin resistance. Cell Metab. 2014;19(3):512–26.
28. Norseen J, Hosooka T, Hammarstedt A, Yore MM, Kant S, Aryal P, Kiernan UA, Phillips DA, Maruyama H, Kraus BJ, et al. Retinol-binding protein 4 inhibits insulin signaling in adipocytes by inducing proinflammatory cytokines in macrophages through a c-Jun N-terminal kinase- and toll-like receptor 4-dependent and retinol-independent mechanism. Mol Cell Biol. 2012;32(10):2010–9.
29. Muenzner M, Tuvia N, Deutschmann C, Witte N, Tolkachov A, Valai A, Henze A, Sander LE, Raila J, Schupp M. Retinol-binding protein 4 and its membrane receptor STRA6 control adipogenesis by regulating cellular retinoid homeostasis and retinoic acid receptor alpha activity. Mol Cell Biol. 2013;33(20):4068–82.
30. Flores-Cortez YA, Barragan-Bonilla MI, Mendoza-Bello JM, Gonzalez-Calixto C, Flores-Alfaro E, Espinoza-Rojo M. Interplay of retinol binding protein 4 with obesity and associated chronic alterations (review). Mol Med Rep. 2022;26(1).
31. Nono Nankam PA, Bluher M. Retinol-binding protein 4 in obesity and metabolic dysfunctions. Mol Cell Endocrinol. 2021;531:111312.
32. Pazos-Perez A, Pineiro-Ramil M, Franco-Trepat E, Alonso-Perez A, Guillan-Fresco M, Crespo-Golmar A, Lopez-Fagundez M, Aranda JC, Bravo SB, Jorge-Mora A et al. The Hepatokine RBP4 links metabolic diseases to articular inflammation. Antioxid (Basel). 2024;13(1).
33. Ji Y, Song J, Su T, Gu X. Adipokine Retinol binding protein 4 and Cardiovascular diseases. Front Physiol. 2022;13:856298.

Publisher's Note