Original Article

Prevalence and risk of chronic kidney disease in oral lichen planus: a large cross-sectional study from eastern China

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Background: Oral lichen planus (OLP) is a chronic inflammatory mucocutaneous disease which is frequently associated with comorbidities such as diabetes and cardiovascular diseases. However, little is known about the association of OLP with impaired kidney function. To elucidate the possible association of chronic kidney disease (CKD) with OLP and its severity, this study investigated the prevalence of CKD as well as its risk factors in patients with OLP.

Methods: A large prospective cross-sectional study of 1,021 patients with OLP was carried out using questionnaires and laboratory tests available from an oral medicine clinic at a university in eastern China. According to the Kidney Disease: Improving Global Outcomes (KDIGO) diagnostic guideline, CKD was classified based on the estimated glomerular filtration rate (eGFR, <60 mL/min/1.73 m^2) or urinary albumin to creatinine ratio (UACR, >30 mg/g).

Results: The prevalence of CKD in the patients with OLP in this study was 14.3% (95% CI, 12.3–16.6%), which was higher than that in the general Chinese population (10.8%; 95% CI, 10.2–11.3%). The mean values of serum creatinine, eGFR, UACR, and urine N-acetyl-β-D-glucosidase in patients with CKD were significantly higher than those in patients without CKD (all P<0.01). Pearson's correlation analysis revealed that CKD stage and UACR were positively correlated with the severity of OLP (both P<0.001). Importantly, multivariate regression analysis revealed that age ≥58 years old, female sex, and hypertension were independent risk factors for incident CKD and abnormal UACR (>30 mg/g) in patients with OLP (all P<0.01).

Conclusions: This study has reported for the first time that CKD is a comorbidity in patients with OLP. The occurrence and staging of incident CKD are associated with OLP and its severity.

Keywords: Chronic kidney disease (CKD); oral lichen planus (OLP); hypertension; albuminuria; estimated glomerular filtration rate (eGFR)

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Introduction

Lichen planus (LP) is a common chronic inflammatory mucocutaneous disease of probable autoimmune-related etiology (1,2). Oral LP (OLP) affects 0.38% to 2.0% of the general population, occurring mostly in female, middle-aged, and older adults (3). OLP is characterized by a T-cell-mediated immune response against epithelial cells, causing epithelial cell damage and subepithelial persistent accumulation of T lymphocytes (1). In its clinical presentation, OLP ranges from asymptomatic reticular white lichen to symptomatic atrophic-erosive red lichen with symptoms of burning, irritation, and pain (4). Despite a variety of treatments being available, this disease often severely affects patients' quality of life due to its protracted clinical course (4,5) and, in particular, its potential for malignant transformation (6,7). Although the etiology and pathogenesis of OLP remain unclear, it has been reported to be associated with several systemic comorbidities including diabetes mellitus (8) and cardiovascular disease (CVD) (9). Furthermore, it is noteworthy that in clinical practice, a proportion of patients with OLP suffer from renal dysfunction, such as abnormal serum creatinine and urine albumin levels (Figures S1,S2).

Chronic kidney disease (CKD), which includes a variety of renal dysfunction diseases, is a major health problem worldwide due to its high rates of mortality and comorbidity (10). Based on classification by the Kidney Disease Improving Global Outcome (KDIGO) guideline, the prevalence of CKD in China was reported to be 10.8% by one well-recognized study (11). Recently, CKD has been reported to be associated with some chronic inflammatory disorders, such as periodontitis (12,13), rheumatoid arthritis (14), and psoriasis (15). Emerging evidence suggests that immune systems and its components have important roles in the initiation, progression and complications of CKD by systemic inflammation (16). CKD patients are characterized by a complex impairment of the immune system, which combines low-grade chronic inflammation and the inability to mount protective immune responses (17). This chronic inflammation arises possibly from accumulation of proinflammatory cytokines in CKD patients, whom have been characterized by variable accumulation and aberrant activation status of memory T cell subsets (18,19). It is reasonable to assume that aberrant immune response, with an emphasis on T cell-mediated immune dysfunction, related to the potential mechanisms that might link both OLP and CKD. Furthermore, studies on LP have revealed a possible association with hyperuricemia and abnormal creatinine (20,21), with the authors also stating that the involvement of metabolic defects was highly detected in patients with LP compared to controls (20,21). These observations, along with our clinical experience treating patients with OLP, suggest a possible association between kidney dysfunction and LP.

At present, little is known about the association between LP and renal function impairment. Therefore, to examine this relationship, we conducted a large prospective cross-sectional study using the questionnaires and laboratory tests available from an oral medicine clinic at a university in eastern China. We aimed to investigate the prevalence of CKD and its risk factors in patients with OLP in order to elucidate the possible association of CKD with OLP and its severity. We present the following article in accordance with the STROBE reporting checklist (available at http://dx.doi.org/10.21037/atm-21-699).

Methods

Participants

At the time this study was planned, no previous study had evaluated the association between CKD as the primary exposure and OLP as the outcome. We estimated the sample size based on the sample size (n=47,204) in a nationally representative cross-sectional survey of the Chinese population (11). Based on the highest estimated prevalence (2.0%) of OLP in the general population (3), we assumed that 944 individuals (2.0% of 47,204) had OLP. Taking into consideration an alpha of 5% and a relative error of sampling of 10%, we calculated that the present study would require a sample size of 1049. This study was approved by the Institutional Review Board of Shanghai Ninth People's Hospital, Shanghai Jiao Tong University School of Medicine [No. (2016)01]. Written informed consent was obtained from all study participants. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). Patients with a diagnosis of OLP who initially visited the clinic at the Department of Oral Mucosal Diseases of our hospital between April 2016 and March 2018 were prospectively enrolled into this prospective cross-sectional study.

The inclusion criteria for patients were as follows: (I) aged ≥18 years; (II) a clinical and histological diagnosis of OLP which met the modified World Health Organization (WHO) diagnostic criteria (22); and (III) agreed to participate

in the study. The exclusion criteria were as follows: (I) patients who were pregnant; (II) patients diagnosed with periodontitis with a periodontal probing depth of ≥6 mm and clinical attachment loss of ≥6 mm; (III) patients with a history of malignancy or other inflammatory or autoimmune diseases such as psoriasis, vitiligo, Behçet's disease, lupus erythematosus, or rheumatoid arthritis; and (IV) patients who had taken antibiotics, or immunosuppressive or nephrotoxic drugs in the 6 months prior. The antibiotics include aminoglycosides, cephalosporins, quinolones, antitubercular agents; the immunosuppressive drugs include steroids, cyclophosphamide, azathioprine, cyclosporine, methotrexate, chloroquine; the nephrotoxic drugs include non-steroidal anti-inflammatory drugs, lithium, chloroquine, cytotoxic drugs e.g., cisplatinum.

Data collection

The age, sex, and body mass index (BMI) of each participant were recorded. Any medical history of kidney diseases, hypertension, diabetes, or CVD was also recorded, on a standardized computerized database, before laboratory tests of renal function. Blood and urine samples (10 mL) were collected from all participants, and all analyses were carried out at the Department of Clinical Laboratory of our hospital. Serum creatinine was examined using Siemens Dimension RxL Max HM, serum cystatin C and urine N-acetyl-β-D-glucosidase (UNAG) were examined using Siemens ADVIA 2400, urinary albumin, urinary creatinine, and C-reactive protein were examined using Dade Behring BN ProSpec according to these manufacturers' protocols. All laboratory tests were completed on the basis of a standardization and certification programme.

According to the KDIGO stratification risk criteria (23) and the calculation method previously described (11), CKD was classified based on the estimated glomerular filtration rate (eGFR <60 mL/min/1.73 m^2) or urinary albumin to creatinine ratio (UACR >30 mg/g classified as albuminuria). The stratified staging of CKD was also assessed based on the eGFR and UACR according to the classification of the KDIGO statement (23). Further, the disease severity of OLP was assessed using the Thongprasom sign scoring system (24), which has been used in previous studies (25-27). Using this scoring system, patients are given a score of: 0 for normal healthy mucosa; 1 for lesions with only white striae; 2 for mixed keratotic and atrophic or erythematous lesions <1 cm^2 in size; 3 for keratotic and atrophic or erythematous lesions >1 cm^2 in size; 4 for erosive/ulcerative lesions <1 cm^2; and 5 for erosive/ulcerative lesions >1 cm^2.

Statistical analysis

When the expected values were less than 5, differences in quantitative and qualitative variables between 2 groups were calculated by the Student's *t* test and the chi-square (χ^2) test or Fisher's exact test, respectively. Differences in quantitative and qualitative variables between multiple groups were calculated using 1-way analysis of variance and non-parametric tests, respectively. If quantitative variables did not follow a Gaussian distribution, the differences between 2 groups were calculated using the non-parametric test. Pearson's correlation analysis was used to determine the correlation between CKD stratified risk and OLP severity. Logistic regression with random effects model analysis was applied to evaluate odds ratios (OR) with 95% confidence intervals (CIs) and the associations among variables. In the logistic regression, univariate analysis was first performed to obtain the significant variables. To further assess and adjust the influence of each significant variable, multivariate analysis was subsequently performed, and the factors that remained statistically significant were determined. Statistical analysis was performed using SPSS for Windows (version 23.0; SPSS Inc.). All tests were 2-sided, and P values of <0.05 were considered to be statistically significant.

Results

Prevalence of CKD in OLP and renal function analysis

A total of 1,021 eligible patients with OLP, who completed the blood and/or urine laboratory tests, were consecutively enrolled in this prospective cross-sectional study. Among the 1,021 patients were 352 males and 669 females, and the average age was 50.4 years (range, 18–88 years). According to the classification by the KDIGO criteria, 146 patients were identified as OLP with CKD, which translated to a prevalence of 14.3% (95% CI, 12.3–16.6%). Thus, the prevalence of CKD among the patients in our study was significantly (P<0.05; χ^2 test) higher than that (10.8%; 95% CI, 10.2–11.3%) in the general Chinese population (11). Furthermore, the prevalence of eGFR <60 mL/min/1.73 m^2 and UACR >30 mg/g in OLP patients were 2.5% (95% CI, 1.7–3.7%) and 13.0% (95% CI, 11.1–15.2%), respectively. However, the prevalence of eGFR <60 mL/min/1.73 m^2 and UACR >30 mg/g in the general Chinese population were

Table 1 Demographic, oral lesion score and renal function indicators of OLP patients without and with CKD

Characteristic	OLP without CKD	OLP with CKD	P value
No. of patients (n=1,021)	875 (85.7)	146 (14.3)	
Age (y)			<0.001
Mean (SD)	49.2 (13.6)	57.7 (13.4)	
Range	18–88	18–86	
Gender (%)			<0.001
Male	326 (37.3)	26 (17.8)	
Female	549 (62.7)	120 (82.2)	
Body mass index (kg/m^2)			0.908
Mean (SD)	23.4 (3.17)	23.4 (3.05)	
Range	15.1–33.9	17.2–31.3	
OLP lesion score (%)			<0.001
Score 1	317 (38.1)	30 (22.2)	
Score 2	184 (22.1)	29 (21.5)	
Score 3	115 (13.8)	24 (17.8)	
Score 4	99 (11.9)	27 (20.0)	
Score 5	116 (14.0)	25 (18.5)	
Not available	44	11	
Renal function indicators, Mean (SD)			
Serum creatinine (μmol/L)	82.0 (15.2)	88.9 (51.3)	0.002
Serum cystatin C (mg/L)	0.89 (2.84)	0.85 (0.51)	0.841
eGFR (mL/min/1.73 m^2)	87.4 (22.9)	79.1 (23.6)	<0.001
UACR (mg/g)	10.5 (6.2)	100.7 (130.7)	<0.001
UNAG (U/L)	6.26 (6.22)	8.73 (10.53)	<0.001
C-reactive protein (mg/L)	2.71 (2.17)	2.43 (1.59)	0.130

OLP, oral lichen planus; CKD, chronic kidney disease; SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; UNAG, Urine N-acetyl-β-D-glucosidase. Normal range values: serum creatinine, 62–115 μmol/L; serum cystatin C, 0–1 mg/L; eGFR, 80–120 mL/min/1.73 m^2; UACR, 0–30 mg/g; UNAG, 0.3–11.5 U/L; C-reactive protein, 0–10 mg/L.

1.7% (95% CI, 1.5–1.9%) and 9.4% (95% CI, 8.9–10.0%), respectively.

To determine the differences in demographics, oral lesion scores, and renal function indicators, a comparative analysis was performed between OLP patients without CKD (n=875) and with CKD (n=146) (*Table 1*). The mean age (57.7 years) of the patients with CKD was significantly higher than that (49.2 years) of the patients without CKD (P<0.001; Student's *t* test). The proportions of females and patients with OLP lesion scores 3–5 was higher in the CKD group than in the non-CKD group (both P<0.001, χ^2 test). The mean values of serum creatinine, eGFR, UACR, and UNAG in patients with CKD were significantly higher than those in patients without CKD (all P<0.01; Student's *t* test).

Renal function indicators and CKD staging correlated with the severity of OLP

Oral lesion scores were available for 966 of the 1,021 patients with OLP in this study. To analyze the correlation between the severity of OLP and CKD, we compared renal function indicators and CKD staging in 3 groups: mild

Table 2 Correlation of disease severity of OLP (n=966) with renal function indicators and CKD stage

Disease severity of OLP	No. of patients	Mild (Score 1)	Moderate (Scores 2,3)	Severe (Scores 4,5)	P-value
Renal function indicators, Mean (SD)					
Serum creatinine (μmol/L)	939	84.2 (34.1)	83.0 (15.6)	80.9 (16.8)	0.273
Serum cystatin C (mg/L)	919	0.75 (0.31)	1.14 (4.47)	0.77 (0.18)	0.007
eGFR (mL/min/1.73 m^2)	939	88.2 (23.9)	86.9 (25.8)	84.4 (20.9)	0.015
UACR (mg/g)	818	15.5 (34.3)	21.0 (37.5)	39.7 (96.8)	<0.001
UNAG (U/L)	807	5.97 (5.56)	7.39 (8.92)	6.54 (6.64)	0.722
C-reactive protein (mg/L)	934	2.66 (1.70)	2.66 (2.17)	2.48 (1.93)	0.473
eGFR stage (n, %)					0.062
G1 (≥90 mL/min/1.73 m^2)	268	113 (33.2)	81 (23.8)	74 (28.5)	
G2 (60-90 mL/min/1.73 m^2)	648	222 (34.1)	250 (73.5)	177 (68.1)	
G3-5 (<60 mL/min/1.73 m^2)	23	5 (1.5)	9 (2.6)	9 (3.5)	
UACR stage (n, %)					<0.001
A1 (<30 mg/g)	695	264 (91.3)	243 (83.8)	188 (78.7)	
A2 (30–299 mg/g)	113	24 (21.4)	46 (15.9)	43 (18.0)	
A3 (≥300 mg/g)	10	1 (0.3)	1 (0.3)	8 (3.3)	
CKD stratified risk (n, %)					0.002
Low risk (stage 1)	255	108 (31.1)	82 (23.3)	65 (24.3)	
Moderately increased risk (stage 2)	691	236 (68.2)	266 (75.6)	189 (70.5)	
High or higher risk (stage 3–5)	20	2 (0.6)	4 (1.1)	14 (5.2)	

OLP, oral lichen planus; CKD, chronic kidney disease; SD, standard deviation; eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; UNAG, Urine N-acetyl-β-D-glucosidase.

(score: 1), moderate (scores: 2 and 3), and severe (score: 4 and 5) OLP (*Table 2*). The mean value of eGFR significantly decreased in order of mild, moderate, and severe OLP (88.2, 86.9, and 84.4 mL/min/1.73 m^2, respectively; P=0.015). The mean value of UACR significantly increased in order of mild, moderate, and severe OLP (15.5, 21.0, and 39.7 mg/g, respectively; P<0.001; Student's *t* test). Consistently, UACR level was positively correlated with the severity of OLP (P<0.001, Pearson's correlation), while eGFR level was marginally correlated with the severity of OLP (P=0.062, *Table 2*). According to the KDIGO stratified risk criteria, CKD stage was also positively correlated with the severity of OLP (P<0.001, Pearson's correlation).

Risk assessment for CKD occurrence and relevant covariates in OLP

Systemic comorbidity data on hypertension, diabetes, and CVD were available for 675 of the 1,021 patients with OLP in this study. Among these 675 patients, 99 (14.7%) were identified as OLP with CKD. There were no significant differences in demographics, BMI, or CKD prevalence or indicators between the 675 patients with systemic comorbidity data and the 346 patients without these data. Because the mean age of the patients with CKD was 57.7 years old, the patients were divided into two age groups (<58 and ≥58 years old) in the logistic analysis. We performed the statistical evaluation on the differences in BMI and the main lab parameters (serum creatinine, UACR, and eGFR) between the two age groups. The results revealed that BMI (mean, 23.4 *vs.* 23.5, P=0.435) and serum creatinine (mean, 83.3 *vs.* 82.5, P=0.239) were not significantly difference between <58- and ≥58-year-old groups. Notably, eGFR (mean, 89.5 *vs.* 79.4, P=0.003) and UACR (mean, 19.2 *vs.* 38.2, P<0.001) were significantly difference between <58- and ≥58-year-old groups. These

Table 3 Risk assessment for CKD occurrence and relevant covariates with emphasis on comorbidities in 675 patients with OLP

Characteristic (%)	OLP without CKD	OLP with CKD	P value	Univariate analysis		Multivariate analysis	
				OR (95% CI)	P value	Adjusted OR (95% CI)	P value
No. of patients	576 (85.3)	99 (14.7)					
Age group (y)			<0.001				
<58	403 (70.0)	39 (39.4)		1.0 (ref)		1.0 (ref)	
≥58	173 (30.0)	60 (60.6)		3.58 (2.31–5.57)	<0.001	2.47 (1.53–3.98)	<0.001
Gender			<0.001				
Male	218 (37.8)	17 (17.2)		1.0 (ref)		1.0 (ref)	
Female	358 (62.2)	82 (82.8)		2.94 (1.70–5.09)	<0.001	2.39 (1.35–4.21)	0.003
Body mass index (kg/m^2)			0.891				
Mean (SD)	23.7 (3.1)	23.4 (3.1)					
Range	15.1–33.9	17.2–31.3					
Hypertension			<0.001				
No	524 (91.0)	72 (72.7)		1.0 (ref)		1.0 (ref)	
Yes	52 (9.0)	27 (27.3)		3.78 (2.23–6.40)	<0.001	2.16 (1.21–3.85)	0.009
Diabetes			0.001				
No	556 (96.5)	87 (87.9)		1.0 (ref)		1.0 (ref)	
Yes	20 (3.5)	12 (12.1)		3.83 (1.81–8.12)	<0.001	1.96 (0.87–4.44)	0.106
Cardiovascular diseases			0.030				
No	568 (98.6)	94 (94.9)		1.0 (ref)		1.0 (ref)	
Yes	8 (1.4)	5 (5.1)		3.78 (1.21–11.79)	0.022	2.10 (0.62–7.09)	0.231

CKD, chronic kidney disease; OLP, oral lichen planus; SD, standard deviation; OR, odds ratio; CI, confidence interval.

suggested that renal function should corelate with the age factor.

Univariate logistic analysis revealed that age (≥58 years old), sex, hypertension, diabetes, and CVD were significant covariates (*Table 3*). Multivariate analysis revealed that the risk of CKD in OLP patients aged ≥58 years old (adjusted OR, 2.47; 95% CI, 1.53–3.98; P<0.001) was higher than that in patients aged <58 years old. Female OLP patients were at higher risk of CKD than were male patients (adjusted OR, 2.39; 95% CI, 1.35–4.21; P=0.003). The risk of CKD was higher for patients with hypertension (adjusted OR, 2.16; 95% CI, 1.21–3.8; P=0.009) than for those without hypertension. However, diabetes and CVD were not found to be significant covariates, which indicated that neither of them is confounding variables of CKD occurrence in patients with OLP.

CKD is classified based on eGFR <60 mL/min/1.73 m^2 and UACR >30 mg/g. To further investigate whether the relevant covariates affect eGFR or UACR in patients with OLP, logistic regression models were also performed as per the method described above. Multivariate analysis revealed that only age (≥58 years old; adjusted OR, 9.92; 95% CI, 2.08–47.23; P=0.004) was an independent risk factor for eGFR <60 mL/min/1.73 m^2. Furthermore, age (≥58 years old; adjusted OR, 2.35; 95% CI, 1.42–3.90; P=0.001), female sex (adjusted OR, 2.44; 95% CI, 1.34–4.47; P=0.004), and hypertension (adjusted OR, 2.31; 95% CI, 1.27–4.21; P=0.006) were independent risk factors for UACR >30 mg/g in patients with OLP (*Table 4*). These results indicated that hypertension and female sex were independent factors of UACR >30 mg/g and were further associated with the occurrence of CKD in OLP.

Based on the adjusted analyses, the adjusted prevalence of CKD in males (7.2%), patients aged <58 years old (8.8%),

Table 4 Multivariate logistic analyses of risk factors of abnormal eGFR and UACR in OLP patients

Characteristic	eGFR <60 mL/min/1.73 m^2		UACR >30 mg/g	
	Adjusted OR (95% CI)	P value	Adjusted OR (95% CI)	P value
Age (y)				
<58	1.0 (ref)		1.0 (ref)	
≥58	9.92 (2.08–47.23)	0.004	2.35 (1.42–3.90)	0.001
Gender				
Male	1.0 (ref)		1.0 (ref)	
Female	1.43 (0.38–5.37)	0.593	2.44 (1.34–4.47)	0.004
Hypertension				
No	1.0 (ref)		1.0 (ref)	
Yes	1.17 (0.33–4.20)	0.805	2.31 (1.27–4.21)	0.006
Diabetes				
No	1.0 (ref)		1.0 (ref)	
Yes	2.60 (0.63–10.79)	0.187	2.03 (0.87–4.73)	0.100
Cardiovascular disease				
No	1.0 (ref)		1.0 (ref)	
Yes	0.00 (0.00–0.00)	0.999	2.22 (0.63–7.82)	0.217

eGFR, estimated glomerular filtration rate; UACR, urine albumin-to-creatinine ratio; OLP, oral lichen planus; OR, odds ratio; CI, confidence interval.

and patients without hypertension (10.8%) were lower than the overall prevalence of CKD among patients with OLP (14.7%; 95% CI, 12.2–17.5%). Conversely, the adjusted prevalence of CKD in females (18.6%), patients aged ≥58 years old (25.8%), and patients with hypertension (34.2%) were higher than the overall prevalence of CKD among patients with OLP (14.7%; 95% CI, 12.2–17.5%).

Discussion

OLP is a chronic, relapsing disease often associated with systemic comorbidities. Comorbidities of OLP have been preliminarily elucidated and described, mainly in the fields of diabetes and CVD (8,9). Recently, psoriasis has also been robustly demonstrated to be associated with CKD by some well-designed studies (15). Because OLP is an immune-mediated inflammatory mucocutaneous disease (1,2), it is reasonable to speculate that it could also be linked to CKD. However, few data are available regarding renal impairment in patients with OLP. The current study attempted to examine renal impairment using blood and urine tests and to elucidate the possible association between incident CKD and OLP in a large prospective series of patients from eastern China. We also assessed the risk factors for incident CKD in patients with OLP and the relevant covariates after adjustment for comorbidities including diabetes, hypertension, and CVD.

To the best of our knowledge, this study is the first to investigate the renal function indicators and the prevalence and staging of incident CKD in patients with OLP, as well as the disease severity. We performed a comparative analysis with the data from a nationally representative cross-sectional survey of Chinese adults as a control group (11). Arguably, the mean ages of the OLP patients (50.4 years old) and the general Chinese adult group (49.6 years old) were comparable, and female predominance was found in both groups (11). According to the classification of the KDIGO criteria (28), the prevalence and demographic- and comorbidity-adjusted prevalence of CKD in patients with OLP were significantly higher than those in the general Chinese population (11). Importantly, we observed a significant positive correlation between the severity of OLP and renal function indicators and CKD stage (*Table 2*). Since the clinical manifestations and scoring of lesions in the oral

mucosa can be observed relatively easily, it is plausible that the severity of OLP may be useful in detecting individuals at risk and the development of kidney damage, as well as in the staging of CKD. This also suggests that CKD prevention and interference could effectively reduce the incidence and/or severity of OLP.

OLP is frequently linked to systemic comorbidities, including hypertension, diabetes, and CVD (8,9). In our study, 11.7% of patients had hypertension and 4.7% had diabetes; these rates were within the range of those reported for hypertension (11–27%) (28-30) and diabetes (1.6–37.7%) previously (8). Furthermore, the prevalence of patients with CVDs (1.9%) in our study was lower than the prevalence of 7.8% reported in an Italian study (9). These comorbidities can also be observed in patients with CKD (10). The prevalence of comorbidities and risk factors for CKD in OLP can be confounding. Hence, a multivariate logistic regression model, adjusted for age at diagnosis, sex, hypertension, diabetes, and CVD, was performed. Multivariate regression analysis revealed that age ≥58 years old, female sex, and hypertension were independent risk factors for incident CKD in patients with OLP, while diabetes and CVD were not significant factors. Furthermore, multivariate logistic analyses of risk factors for abnormal eGFR and UACR, as the 2 determinants of CKD occurrence, were also performed. We found that female sex and hypertension were independent risk factors for normal eGFR (<60 mL/min/1.73 m^2) but abnormal UACR (>30 mg/g), while age ≥58 years old was an independent risk factor for both. Taken together, these results suggest that hypertension prevention and interference may effectively decrease the incidence of CKD in patients with OLP.

We acknowledge that there are limitations to this study. First, this was a cross-sectional study, which makes inference of a causal relationship between indicators of kidney damage and associated factors impossible. Second, data on systemic comorbidities were not available for all participants, although there were no significant differences in baseline factors or renal function indicators between the patients with and without available data. Third, the calculation of the estimated sample size needed for the study was based on the prevalence of OLP in the general population (3,31), and there was a lack of a contemporaneous control group with which to compare the prevalence of CKD. We adopted national cross-sectional data from Chinese adults with a plausible age- and sex-matched population as the control group (11). Our study is the first to investigate the occurrence and staging of CKD in patients with OLP. However, the patients included only the Chinese population, which limits the generalizability of the results to other ethnicities and races. Our results therefore need to be confirmed by large-scale studies conducted in different geographic and ethnic populations.

In conclusion, this study identified for the first time that CKD is a new incident comorbidity in patients with OLP, with incident CKD occurrence and staging exhibiting significant associations with OLP and its severity. Further studies are necessary to determine whether CKD prevention and interference can effectively reduce the incidence and/or severity of OLP. Additionally, further research is required into the mechanisms underlying the coexistence of OLP and CKD.

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