· Clinical Research ·

Correlation between diabetic retinopathy and *Helicobacter pylori* infection: a cross-sectional retrospective study

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Abstract

● **AIM:** To explore the correlation between diabetic retinopathy (DR) and *Helicobacter pylori* (Hp) infection, based on data from a physical examination population.

● **METHODS:** This cross-sectional retrospective analysis included data of 73 824 health examination participants from December 2018 to December 2019. Participants were divided into the diabetic group and non-diabetic group, non-diabetic retinopathy (NDR) group, non-proliferative diabetic retinopathy (NPDR) group, proliferative diabetic retinopathy (PDR) group, and Hp infection group. Gender, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FPG), glycated hemoglobin A1c (HbA1c), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), and Hp data were recorded to compare the degree of DR lesions and Hp infection. Logistic regression analysis was used to evaluate the correlation between DR and Hp infection.

● **RESULTS:** There was a statistically significant difference between the diabetic and non-diabetic group (χ^2=94.17, P<0.0001). Logistic regression analysis showed that male sex, age, BMI, SBP, TG, LDL-C, and Hp infection were independent risk factors for DR. There was no correlation between the degree of DR lesions and Hp infection (ρ= -0.00339, P=0.7753). Age [odds ratio (OR)=1.035, 95%CI: 1.024, 1.046, P<0.0001] and SBP (OR=1.009, 95%CI: 1.004, 1.015, P=0.0013) were independent risk factors for the degree of DR.

● **CONCLUSION:** There is a significant correlation between DR and Hp infection in the physical examination population. Hp infection is a risk factor for DR, and there is no significant difference between Hp infection and DR of different pathological degrees. Actively eradicating Hp may be of help to prevent DR.

● **KEYWORDS:** diabetic retinopathy; *Helicobacter pylori*; physical examination population; correlation

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INTRODUCTION

Diabetic retinopathy (DR) is a blinding eye disease that seriously affects human eye health. Prevention is the main therapeutic goal, and early diagnosis and standard treatment can effectively improve prognosis. The International Diabetes Federation estimates that the global prevalence of diabetes mellitus (DM) among people aged 20–79y is 10.5% and the global population with DM will reach 783.2 million by 2045[1]. A previous study showed that the global prevalence of DR was 22.27%, by 2045 the global number of people with DR will increase to 160 million[2], posing a huge challenge for ophthalmologists and socio-economic burden around the world. Therefore, early screening and prevention of DR are particularly important.

Helicobacter pylori (Hp) is a pathogenic microorganism colonizing the stomach, which can produce a variety of inflammatory cytokines and can secrete urease and adhesin to cause cell damage[3]. Approximately 50% of people worldwide are infected with Hp, and the Hp infection rate varies due to health and economic conditions and regional differences. In a study involving approximately 400 000 people in 73 countries, the overall prevalence of Hp was 44.3%, and the prevalences were 34.7% and 50.8% in developed countries and in developing countries, respectively[4]. Hp infection is related to systemic multi-system diseases[5-7], such as metabolic diseases and eye diseases including central serous retinal diseases, blepharitis, and open angle glaucoma among others.

Some scholars believe that Hp infection is positively correlated with DM and abnormal glucose tolerance[8]; yet, related studies on Hp infection, DR, and complications of DM are few and controversial. Therefore, this study aimed to analyze the data of 73 824 physical examination participants to explore whether there is a correlation between the occurrence and development of DR and Hp infection, and to provide new ideas for the etiological study of DR and pave the way for future prospective studies.

SUBJECTS AND METHODS

Ethical Approval This study was approved by the Biomedical Research Ethics Committee at the West China Hospital of Sichuan University (Approval No.2021-1597).

Study Design and Population This cross-sectional retrospective study included physical examination participants who underwent non-dilatation fundus photography and a ^{14}C urease breath test at a local hospital from December 2018 to December 2019. We excluded those with blurred fundus images and those with a history of antibiotic use within the last month. The data included basic data, DM data, Hp infection status, and ocular data. The participants were grouped and classified, their data were observed, and the differences between groups were compared. Differences in the occurrence of different degrees of Hp infection and different severities of DR were compared, and the correlation between the occurrence and development of DR and Hp infection was discussed.

Data Collection The physical examination number, name, sex, age, body mass index (BMI), systolic blood pressure (SBP), diastolic blood pressure (DBP), fasting plasma glucose (FPG), glycated hemoglobin A1c (HbA1c), triglycerides (TG), total cholesterol (TC), low-density lipoprotein cholesterol (LDL-C), high-density lipoprotein cholesterol (HDL-C), Hp infection status, and fundus photography results of all participants were recorded. The height and weight of all participants were automatically measured using the SK-V7 ultrasonic physical examination machine, and the BMI was automatically calculated as BMI=weight/height^2 (kg/m^2)[9].

Patients were required to take a labeled ^{14}C urea capsule after 8h of fasting, and we measured the exhaled $^{14}CO_2$ to determine the presence of Hp infection. When the $^{14}CO_2$ level is ≥100 dpm/mmol, Hp infection is considered positive, and when the $^{14}CO_2$ level is <100 dpm/mmol, Hp infection is negative[10].

The DM group was diagnosed as having a history of DM or having an FPG level ≥7.0 mmol/L or HbA1c level ≥6.5% during the current physical examination[11], whereas the non-diabetic group had no history of diabetes and had normal blood FPG and HbA1c levels.

A digital fundus camera (CR-2, Canon, Tokyo, Japan) was used to photograph the fundus without dilatation. A 45° fundus photograph was taken with the macula as the center[12], and a photograph of the other eye was taken after a rest period of approximately 3min. The fundus photography results were divided into three groups according to the guidelines issued by the fundus group of Ophthalmology Society of Chinese Medical Association in 2014: non-diabetic retinopathy (NDR), non-proliferative diabetic retinopathy (NPDR), and proliferative diabetic retinopathy (PDR)[13]. All data were obtained from the general physical examination system of the Health Management Center of the local hospital, and all indicators were collected and recorded by professional personnel.

Statistical Analysis Continuous variables conforming to a normal distribution are expressed as mean±standard deviation. The independent sample *t*-test was used to compare data between two groups; the Chi-square test was used to compare categorical data between two groups; and the R×C Chi-square test was used to compare data in an R×C contingency table. The Fisher exact test was used to analyze categorical data that did not meet the Chi-square test conditions. The Cochran-Mantel-Haenszel Chi-square test was used to analyze rank variables. Spearman rank correlation was used to analyze the correlations of categorical data. The Student-Newman-Keuls (SNK) test was used to perform pairwise comparisons of multiple means and condition numbers, and to conduct characteristic analysis for the diagnosis of multicollinearity. Logistic regression analysis was used as multivariate analysis. SPSS 26.0 software (IBM Corp., Armonk, NY, USA) was used to perform the statistical analyses. All tests were two-sided, and the significance level was set at 0.05.

RESULTS

Baseline Characteristics A total of 129 927 physical examination participants who underwent a physical examination and completed the Hp examination and fundus photography in the health management center of our hospital from December 2018 to December 2019 were included in this study. Their basic information, DM-related information, dpm value on Hp examination, and fundus photography results were sorted and recorded, and 73 824 participants were finally included in the study. There were 66 717 patients in the non-diabetic group and 7107 patients in the diabetic group.

The detection rates for DM and DR were 9.63% and 6.88%, respectively. The average age of the whole population was 44.33±11.59y, and 89.82% were younger than 60 years of age. There were 43 083 (58.36%) men and 30 741 (41.64%) women. The proportion of men, mean age, and values of BMI, SBP, DBP, FPG, HbA1c, TG, TC, and LDL-C were significantly higher in the diabetic group than in the non-diabetic group, and HDL-C levels were lower in the diabetic group than in the non-diabetic group. There were 2340 Hp

Table 1 Comparison of basic data between diabetic group and non-diabetic group in physical examination population

Parameters	Non-diabetic group (*n*=66717)	Diabetic group (*n*=7107)	Test statistic value[a]
Gender (case, %)			χ^2=1457.78
Male	37427 (56.098)	5656 (79.583)	
Female	29290 (43.902)	1451 (20.417)	
Age (y)	43.2866±11.2657	54.1607±9.9722	*t*=-78.18
BMI (kg/m^2)	23.3282±3.2338	25.3825±3.1932	*t*=-50.79
SBP (mm Hg)	117±14.9726	128.8±16.8961	*t*=-58.55
DBP (mm Hg)	72.7505±10.2819	77.7975±10.9235	*t*=-38.99
FPG (mmol/L)	4.972±0.5111	8.3418±2.7223	*t*=-277.05
HbA1c (%)	5.4865±0.3479	7.2855±1.4979	*t*=-233.72
TG (mmol/L)	1.5278±1.2018	2.368±2.1305	*t*=-50.99
TC (mmol/L)	4.8513±0.9066	5.0315±1.1204	*t*=-15.53
LDL-C (mmol/L)	2.9245±0.786	2.9785±0.9146	*t*=-5.41
HDL-C (mmol/L)	1.4237±0.3969	1.2281±0.3449	*t*=39.95
Hp (positive/negative)	18339/48378	2340/4767	χ^2=94.17

1 mm Hg=0.133 kPa. [a]All *P* values were *P*<0.0001 when comparing basic data between the diabetic group and the non-diabetic group. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated hemoglobin A1c; TG: Triglycerides; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; Hp: *Helicobacter pylori.*

infection-positive cases in the diabetic group, and the Hp-positive detection rate was 32.93%; there were 18 339 Hp infection-positive cases in the non-diabetic group, and the detection rate was 27.49% (Table 1).

Univariate and Multivariate Logistic Regression Analyses of DR Univariate analysis of DR in the whole population, with DR as the dependent variable, showed that all independent variables were statistically significant (*P*<0.0001). Sex, age, BMI, SBP, DBP, FPG, HbA1c, TG, TC, LDL-C, and Hp infection were risk factors for DR. Higher HDL-C levels were associated with a lower risk of DR. The condition number and characteristic analysis method were used for multicollinearity diagnosis. LDL-C, TG, and SBP levels were included in the multivariate model. As shown in Table 2, age, BMI, SBP, TG, LDL-C, and Hp infection were associated with DR and were independent risk factors for DR. The risk of DR in the Hp-positive group was 1.15 times higher than that in the Hp-negative group [odds ratio (OR)=1.150, *P*<0.0001].

Comparison of Basic Data of the NDR, NPDR, and PDR Groups There were statistically significant differences in age and values of BMI, SBP, FPG, HbA1c, and HDL-C between the three groups (NDR group, 6618 cases; NPDR group, 467 cases; PDR group, 22 cases, all *P*<0.05; Table 3). The SNK multiple range test was used to compare the statistically significant variables within the groups. Statistically significant differences were found only in the age groups between the PDR, NPDR, and NDR groups (*P*<0.05). The positive detection rates of Hp were 32.97% in the NDR group and 33.62% in the NPDR group. There was one Hp-positive patient in the PDR group, and the positive detection rate was 4.55%. The R×C contingency table Chi-square test was used to compare data between the three groups (*P*=0.3874), and the difference in data was not statistically significant.

Comparison of Different Degrees of Hp Infection in the Diabetic Group In the diabetic group, Hp infection status according to the dpm value was divided into Hp(-) (Hp<100 dpm/tendency), Hp(+) (100≤Hp<500 dpm/tendency), Hp(++) (500≤Hp<1500 dpm/tendency), and Hp(+++) groups (Hp≥1500 dpm/tendency). There were statistically significant differences in sex, age, and values of BMI, DBP, FPG, HbA1c, and HDL-C between the groups (all *P*<0.05; Table 4). In the pairwise comparison of SNK within the groups, the BMI, DBP, and HbA1c values of the Hp(+++) group were statistically significant compared with those of the Hp(++), Hp(+), and Hp(-) groups (*P*<0.005). There was a significant difference in HDL-C values between the Hp(+++) and Hp(+) groups (*P*<0.05), but there was no significant difference in the other groups.

Association Between DR and Hp Infection in the Diabetic Group Among 7107 participants in the diabetic group, the number of those with PDR in the Hp(++) group was 0, and the numbers of those with NPDR and PDR in the Hp(+++) group were both 0. Therefore, correlation analysis was conducted by combining the Hp groups (Table 5). The Spearman rank correlation coefficient was negative, indicating that Hp infection was negatively correlated with the degree of DR lesions; however, the difference was not statistically significant (*P*=0.7753).

Univariate and Multivariate Logistic Regression Analyses of the Degree of DR in the Diabetic Group To further

Table 2 Univariate and multivariate logistic analysis of DR

Parameters	Single factor analysis		Multiple factor analysis	
	P	OR (95%CI)	*P*	OR (95%CI)
Gender (female)	<0.0001	0.328 (0.309, 0.348)	<0.0001	0.512 (0.478, 0.548)
Age (y)	<0.0001	1.090 (1.087, 1.092)	<0.0001	1.088 (1.085, 1.091)
BMI (kg/m^2)	<0.0001	1.196 (1.187, 1.205)	<0.0001	1.101 (1.091, 1.111)
SBP (mm Hg)	<0.0001	1.042 (1.040, 1.043)	<0.0001	1.015 (1.013, 1.016)
DBP (mm Hg)	<0.0001	1.044 (1.042, 1.047)	/	/
FPG (mmol/L)	<0.0001	21.374 (20.001, 22.841)	/	/
HbA1c (%)	<0.0001	898.813 (748.784, 999.999)	/	/
TG (mmol/L)	<0.0001	1.341 (1.322, 1.360)	<0.0001	1.356 (1.321, 1.393)
TC (mmol/L)	<0.0001	1.219 (1.189, 1.250)	/	/
LDL-C (mmol/L)	<0.0001	1.087 (1.055, 1.120)	<0.0001	1.332 (1.225, 1.449)
HDL-C (mmol/L)	<0.0001	0.223 (0.207, 0.240)	/	/
Hp (positive/negative)	<0.0001	1.295 (1.229, 1.365)	<0.0001	1.150 (1.086, 1.218)

1 mm Hg=0.133 kPa. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated hemoglobin A1c; TG: Triglycerides; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; Hp: *Helicobacter pylori*; DR: Diabetic retinopathy; OR: Odds ratio; CI: Confidence interval.

Table 3 Comparison of data among three groups of diabetic patients

Parameters	NDR (n=6618)	NPDR (n=467)	PDR (n=22)	Statistic of test	*P*
Gender (male/female)	5266/1352	374/93	16/6	χ^2=0.0054	0.9416
Age (y)	53.913±9.988^c	57.321±9.064^c	61.545±9.500^{a,b}	F=31.8	<0.0001
BMI (kg/m^2)	25.409±3.207	25.058±2.994	24.176±2.299	F=4.11	0.0165
SBP (mm Hg)	127.909±16.717	131.438±18.939	133.857±16.859	F=10.68	<0.0001
DBP (mm Hg)	77.835±10.818^c	77.498±12.156^c	72.571±13.847^{a,b}	F=2.62	0.073
FPG (mmol/L)	8.300±2.676	8.882±3.220	9.163±3.431	F=10.97	<0.0001
HbA1c (%)	7.263±1.490	7.609±1.587	7.414±0.992	F=7.53	0.0005
TG (mmol/L)	2.371±2.088	2.345±2.684	1.794±1.218	F=0.83	0.4342
TC (mmol/L)	5.031±1.113	5.049±1.215	4.638±1.187	F=1.41	0.2442
LDL-C (mmol/L)	2.981±0.913	2.942±0.933	2.780±0.829	F=0.92	0.3982
HDL-C (mmol/L)	1.2245±0.342	1.2789±0.373	1.2214±0.237	F=5.43	0.0044
Hp (positive, %)	2182 (32.97)	157 (33.62)	1 (4.55)	χ^2=0.7472	0.3874

P<0.05 was considered statistically significant. For SNK pairwise comparison, ^aP<0.05 compared to NDR; ^bP<0.05 compared to NPDR; ^cP<0.05 compared to PDR. NDR: Non-diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated hemoglobin A1c; TG: Triglycerides; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; Hp: *Helicobacter pylori.*

understand the risk factors of the degree of DR lesions in the diabetic group, the degree of DR lesions was divided into NPDR and PDR groups for univariate and multivariate analyses (Table 6). In univariate analysis, there were statistically significant differences in age and values of BMI, SBP, FPG, HbA1c, and HDL-C (P<0.05). After excluding multicollinearity and confounding factors, only age and SBP were statistically significant, indicating that age and SBP were independent risk factors for the degree of DR lesions. For every 1-mm Hg increase in SBP, the risk of PDR was increased by 0.9% compared with NPDR (OR=1.009, P=0.0013).

Prevalence of Diabetes and DR in Different Age Groups All participants in the diabetic group were divided into five groups according to age (Figure 1). The detection rate of diabetes and DR increased gradually with an increase in age, and the detection rate of DR in people older than 50 years of age was higher than the average detection rate of diabetes (6.88%).

DISCUSSION

A foreign study[14] used 7-field 30° stereoscopic photography developed by ETDRS as the gold standard and found that single-field fundus photography had a higher reliability in screening for DR than a direct fundus examination after mydriasis, with a kappa value of 0.97, sensitivity of 78%, and specificity of 86%. Single-field non-dilated fundus photography is simple, noninvasive, and highly reliable for the physical examination population requiring large-scale primary

Table 4 Comparison of Hp infection data of different degrees in diabetic population

Parameters	Hp(-) (*n*=4767)	Hp(+) (*n*=1715)	Hp(++) (*n*=614)	Hp(+++) (*n*=11)	*P*
Gender (male/female)	3794/973	1430/285	427/187	5/6	<0.0001
Age (y)	54.044±10.061	53.965±9.836	55.558±9.555	56.909±9.954	0.0026
BMI (kg/m^2)	25.298±3.179[d]	25.668±3.272[d]	25.269±3.040[d]	23.454±2.14[a,b,c]	<0.0001
SBP (mm Hg)	128.124±16.85	128.376±16.90	127.905±17.23	123.545±16.03	0.7387
DBP (mm Hg)	77.679±10.97[d]	78.405±10.865[d]	77.143±10.644[d]	71±9.262[a,b,c]	0.0064
FPG (mmol/L)	8.276±2.695	8.458±2.718	8.541±2.934	7.295±1.243	0.0127
HbA1c (%)	7.241±1.357[d]	7.352±1.446[d]	7.456±2.357[d]	6.477±0.997[a,b,c]	0.0045
TG (mmol/L)	2.352±2.070	2.420±2.303	2.353±2.097	1.796±1.540	0.5482
TC (mmol/L)	5.029±1.121	5.018±1.116	5.085±1.124	4.740±0.899	0.4878
LDL-C (mmol/L)	2.975±0.921	2.973±0.899	3.021±0.906	2.779±0.740	0.5753
HDL-C (mmol/L)	1.236±0.349	1.201±0.327[d]	1.237±0.349	1.402±0.301[b]	0.0011

P<0.05 was considered statistically significant. For SNK pairwise comparison, [a]*P*<0.05 compared to Hp(-); [b]*P*<0.05 compared to Hp(+); [c]*P*<0.05 compared to Hp(++); [d]*P*<0.05 compared to Hp(+++). BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated hemoglobin A1c; TG: Triglycerides; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; Hp: *Helicobacter pylori*.

Table 5 Correlation analysis between the degree of DR lesion and Hp infection in diabetic groups

Hp	NDR (%)	NPDR (%)	PDR (%)	*ρ*	*P*
Hp positive	2182 (32.97)	157 (33.62)	1 (4.55)		
Hp negative	4436 (67.03)	310 (66.38)	21 (95.45)	-0.00339	0.7753
Total	6618	467	22		

ρ is the Spearman rank correlation coefficient=-0.00339, *P*=0.7753, indicating that the result was not statistically significant. NDR: Non-diabetic retinopathy; NPDR: Non-proliferative diabetic retinopathy; PDR: Proliferative diabetic retinopathy; Hp: *Helicobacter pylori*; DR: Diabetic retinopathy.

Table 6 Univariate and multivariate logistics analysis of the degree of DR lesions

Parameters	Single factor analysis		Multiple factor analysis	
	P	OR (95%CI)	*P*	OR (95%CI)
Gender (female)	0.9325	0.99 (0.788, 1.244)	0.1025	0.818 (0.643, 1.041)
Age (y)	<0.0001	1.038 (1.029, 1.049)	<0.0001	1.035 (1.024, 1.046)
BMI (kg/m^2)	0.0093	0.961 (0.933, 0.99)	0.0613	0.969 (0.938, 1.001)
SBP (mm Hg)	<0.0001	1.012 (1.007, 1.018)	0.0013	1.009 (1.004, 1.015)
DBP (mm Hg)	0.2702	0.995 (0.987, 1.004)	/	/
FPG (mmol/L)	<0.0001	1.073 (1.042, 1.106)	/	/
HbA1c (%)	0.0004	1.117 (1.05, 1.187)	/	/
TG (mmol/L)	0.5969	0.988 (0.944, 1.033)	0.6855	0.984 (0.911, 1.063)
TC (mmol/L)	0.9664	0.998 (0.92, 1.084)	/	/
LDL-C (mmol/L)	0.2707	0.945 (0.854, 1.045)	0.1756	0.858 (0.688, 1.071)
HDL-C (mmol/L)	0.0015	1.499 (1.168, 1.924)	/	/
Hp (positive/negative)	0.734	0.967 (0.794, 1.176)	0.7009	0.962 (0.788, 1.174)

P<0.05 was considered statistically significant. BMI: Body mass index; SBP: Systolic blood pressure; DBP: Diastolic blood pressure; FPG: Fasting plasma glucose; HbA1c: Glycated hemoglobin A1c; TG: Triglycerides; TC: Total cholesterol; LDL-C: Low-density lipoprotein cholesterol; HDL-C: High-density lipoprotein cholesterol; Hp: *Helicobacter pylori*; DR: Diabetic retinopathy; OR: Odds ratio; CI: Confidence interval.

screening for DR. The detection rate of DR in this study was 6.88%, which was significantly lower than the reported prevalence rate of DR globally (34.6%)[15] and lower than the standardized prevalence rate of DR in rural areas of China reported by the Dongguan Ophthalmology Department[16]. Our results were inconsistent with those of a similar article published in 2021 which analyzed the prevalence and risk factors of DR in patients with type 2 diabetes. The article reported that the prevalence of DR in patients with type 2 diabetes in Shanghai was 16.97%[17]. The low DR detection rate in this study may be related to ethnic differences[18] and different types of populations. This study included a population that underwent a routine physical examination, with higher economic and cultural levels than those in rural areas, and had

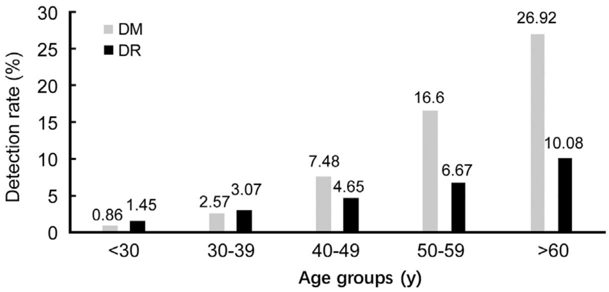

Figure 1 Detection rate of DM and DR in different age groups DM: Diabetes mellitus; DR: Diabetic retinopathy.

a higher understanding and management of diabetes and its complications, which may be the reason why the DR detection rate in the population undergoing a physical examination is lower than that in rural areas. The detection rate of DR in the diabetic population of a hospital in Beijing was 7%[19]. The possible reason for this finding is that the average age of the diabetic population in that study was 57.1±11.6y, which was not significantly different from the average age of the diabetic group in the present study (54.16±9.97y). Although the detection rate of DR herein was low, only 10.18% of participants were older than 60 years of age and 1.45% were younger than 30 years of age. Therefore, the incidence of DR tended to be lower, so DR screening should be performed as early as possible. To the best of our knowledge, this is the first study to include Hp as a risk factor for DR, and it was found that it was significantly correlated with DR, and the severity of DR was compared with the degree of Hp infection to explore the degree of linkage between them. There was no statistically significant difference between them.

Hp infection is common worldwide, with different infection rates in different regions[20]. Nigeria had the highest prevalence rate (87.7%), Switzerland had the lowest prevalence rate (18.9%), and China had a prevalence rate in the middle of those (55.8%). A cross-sectional study involving 13 397 healthy people who underwent a physical examination found that the positive infection rate of Hp was 28.2%[21], which was almost consistent with the results of this study. However, the diagnosis of Hp in this study was based on the ^{13}C urea breath test. Similarly, the Hp infection rate of healthy people in Anhui was 36% when the ^{13}C or ^{14}C urea breath test was used to determine Hp infection[22]. The immune colloidal gold method was used to evaluate the Chongqing region health check-up crowd, and the Hp infection rate was 24.58%[23]; the Hp infection rate was lower than the general Hp prevalence rate in China possibly due to the differences in the population and the different examination equipment or standards. The Hp infection rate has been reported to be closely related to socioeconomic status and family health conditions[24].

The detection rates of Hp, diabetes, and NPDR in the whole population were 28.1%, 32.97%, and 33.62%, respectively. There was only one case of PDR in the Hp-positive group in the entire study, which reduced the comparability of the correlation analysis between the degree of DR lesions and Hp infection. Future studies need to expand the sample size of the NPDR and PDR groups to further explore the correlation between Hp infection and the degree of DR lesions. Results of Spearman rank correlation analysis of Hp infection were not statistically significant. In regression analysis, Hp infection was an independent risk factor for DR. This finding is consistent with the results of a cross-sectional study of 80 patients[25], in which Hp infection positivity was significantly associated with DR (P<0.001), diabetic neuropathy (P<0.01), and diabetic nephropathy (P<0.001). Hp infection is a metabolic syndrome that causes insulin resistance[26], which can induce hyperglycemia. Hp also activates inflammatory factors and participates in the occurrence and development of diabetic complications[27]. In regression analysis of the degree of DR lesions, Hp infection was not associated with DR. Some studies also reported that Hp infection was not associated with diabetes and its complications[28], and no correlation between Hp infection and HbA1c was found[29]. However, most of these studies were cross-sectional retrospective analyses; thus, more prospective cohort studies are needed to confirm this.

The present study found that male sex, age, BMI, SBP, TG level, LDL-C level, and Hp infection were independent risk factors for DR. A cross-sectional study (n=1008)[30] conducted in Shijiazhuang City reported that age (P=0.049), male sex (P=0.048), high BMI (P<0.0001), hypertension (P=0.048), serum TC level (P=0.028), and serum triglyceride level (P=0.035) were associated with DR, which also suggested that aging, other comorbidities, and metabolic syndrome are associated with DR. Additionally, a study performed in Beijing[31] reported that older age, higher blood pressure, and higher LDL-C levels were independent risk factors for DR, a complication of diabetes. Some authors also believe that[32] TG and LDL-C levels are not independent risk factors for DR, whereas the TC level is an independent risk factor for DR[33]. Conversely, some studies have suggested that abnormal levels of all lipid types are associated with the risk of macular edema and progression to PDR[34]. In regression analysis of the degree of DR lesions, no correlation was found between lipid levels and DR in our study. The possible reason for this finding is that the study population was a physical examination population, rather than a population with chronic diseases, such as hypertension and hyperlipidemia; thus, the numbers of participants with dyslipidemia and the those with PDR were small.

Many studies have reported the influence of BMI on the risk of DR, but the results remain controversial. Some studies have reported[35] that any increase in BMI above the normal weight level will increase the risk of being diagnosed with DR. A Meta-analysis of 27 studies showed that overweight (OR=0.89, 95%CI: 0.75, 1.07; *P*=0.21) and obesity (OR=0.97, 95%CI: 0.73, 1.30; *P*=0.86) were not associated with an increased risk of DR[36]. In contrast, a cross-sectional study of 2533 patients[37] investigated the mediating factors of the relationship between BMI and DR in Chinese patients with type 2 diabetes, and found that the prevalence of DR in overweight patients was lower than that in normal weight individuals, which may be related to better β-cell function in overweight patients.

Single factor and multiple factor regression analysis showed that SBP and age are independent risk factors for DR lesion severity. Blood pressure, and age, and that disease course is an independent risk factor for DR[38-39], in DR patients with a long diabetes duration and older age, the prevalence of DR and degree of pathological changes also increase accordingly. The occurrence and development of DR are positively correlated with the duration of DM[40], and some scholars believe[41] that DR is the most common complication of DM, with its main risk factors being the course of DM, poor blood glucose control, and hypertension. In 150 patients with DM, Chen *et al*[42] found that blood glucose and lipid levels were the influencing factors of DR, while the course of disease was positively correlated with DR and its severity.

Unfortunately, due to insufficient retrospective data in this study, the course of diabetes was unknown, so the degree of association between the course of diabetes and DR could not be determined. The fundus examination in this study was a single 45° fundus photograph taken with the macula as the center, which may have caused errors in the interpretation of retinal conditions in patients with DM, especially in cases of mild NPDR. Therefore, non-invasive examinations such as optical coherence tomography/optical coherence tomography angiography should be included in future studies. In addition, in subsequent related scientific research, the correlation between DR and Hp infection in the community and patient populations should be further studied.

In conclusion, there was a significant correlation between DR and Hp infection in the physical examination population. Hp infection is a risk factor for DR, and there was no significant difference between Hp infection and DR of different pathological degrees.

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