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ARTICLE

A Model to Predict the Risk of Adverse Ocular Outcomes in Pregnant Women

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Abstract

Aims/Background Pregnancy can affect various bodily functions, including metabolism, cardiovascular function, and eyesight. Pathological ocular changes observed during pregnancy are linked to the development of pregnancy-specific conditions, such as preeclampsia/eclampsia and gestational diabetes. This study aims to analyze clinical data disease history and maternal characteristics collected during pregnancy, to determine ocular parameters and develop a risk prediction model for adverse ocular outcomes.

Methods We retrospectively analyzed the medical records of 760 pregnant women (1520 eyes) from September 2020 to September 2022 at The Third Affiliated Hospital of Guangzhou Medical University. We identified maternal variables that could influence adverse ocular outcomes, including maternal age, pregnancy-induced hypertension (PIH), gestational diabetes mellitus (GDM), eclampsia, pre-eclampsia, uterine disease, fetal abnormalities, *in vitro* fertilization with embryo transfer, hypoproteinemia, and major comorbidities during pregnancy. Univariate and multivariate logistic regression analyses were conducted to evaluate the effects of these independent predictors on adverse ocular outcomes. Additionally, receiver operating characteristic (ROC) curve analysis was performed to determine the cut-off probability with for optimal sensitivity and specificity.

Results Eclampsia, pre-eclampsia, GDM, a history of chronic hypertension, and hypoproteinemia were identified as independent predictors of adverse ocular outcomes during pregnancy ($p < 0.05$). Maternal age, PIH, intrauterine growth retardation (IUGR), obesity, and pregnancy with immunoglobulin A nephropathy were predictors of moderate and severe retinal arteriole sclerosis during pregnancy ($p < 0.05$). Additionally, hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome were predictors of retinal hemorrhage and exudate during pregnancy ($p < 0.05$). The area under the ROC curve for adverse ocular outcomes were 0.75 and 0.74, respectively.

Conclusion Our predictive model effectively forecasts adverse ocular outcomes during pregnancy, incorporating risk factors such as maternal age, eclampsia and pre-eclampsia, GDM, obesity, a history of chronic hypertension, hypoproteinemia, IUGR, pregnancy with immunoglobulin A nephropathy, and HELLP syndrome.

Key words: risk prediction model; adverse ocular outcome; pregnancy; maternal health

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Introduction

With the advancement of assisted reproductive technology, the incidence of complications in pregnant women is increasing. Pregnancy can affect various bodily functions, including metabolism, cardiovascular function, and eyesight (Marshall et al, 2021). As an end organ, the eyes may directly reflect changes in the

terminal microvasculature. Pregnancy impacts the eyes both physiologically and pathologically (Qin et al, 2020). Documented alterations include changes in corneal shape and sensation, as well as intraocular pressure (Strelow and Fleischman, 2020; Taradaj et al, 2018). Additionally, exacerbation of preexisting ocular conditions may occur. Examples include glaucoma (Strelow and Fleischman, 2020), diabetic chorioretinopathy (Rosenthal and Johnson, 2018), uveitis (Ting et al, 2024), and retinal changes in patients with pregnancy-induced hypertension (PIH) (Khong et al, 2021).

Many predictive models have been used to assess the associations between risk factors and adverse pregnancy outcomes (Jing et al, 2022; Li et al, 2018; Wu et al, 2021). Common independent predictors include pre-eclampsia, gestational diabetes mellitus (GDM), obesity, cardiac disease, and delivery method, among others (Kumar et al, 2023; Wu et al, 2021; Zhou et al, 2022). Adverse maternal and fetal outcomes can be evaluated by examining maternal disease history, lifestyle, disease onset, and biochemical markers, among other factors. For example, the full pre-eclampsia Integrated Estimate of RiSk (PIERS) model predicts pre-eclampsia within 48 hours and indicates that 59% of high-risk patients experience adverse outcomes within 7 days (von Dadelszen et al, 2011). This model includes predictors such as gestational age, chest pain or dyspnea, oxygen saturation, platelet count, and concentrations of creatinine and aspartate transaminase. By using this model, clinicians can improve maternal and fetal outcomes through timely clinical interventions for high-risk patients exhibiting these predictors. While predictive models in ophthalmology have often focused on glaucoma, age-related macular degeneration, and cataract surgery (Oskarsdottir et al, 2019; Trivedi et al, 2019), few studies have investigated ocular changes associated with systemic diseases.

In this study, we aim to identify independent predictors of adverse ocular outcomes during pregnancy and develop a risk prediction model to enable earlier intervention for pregnant women at risk. We conducted a retrospective analysis of common clinical data, disease history, and maternal characteristics to determine ocular parameters during pregnancy. This study offers a novel approach to evaluating and identifying maternal eye conditions, allowing for the implementation of early interventions.

Methods

Participants

This retrospective study analyzed data from pregnant women who attended The Third Affiliated Hospital of Guangzhou Medical University, Guangzhou, China, for ophthalmic consultation between September 2020 and September 2022. All patients were examined by an experienced physician and underwent a detailed ophthalmologic assessment, including slit-lamp biomicroscopy and non-mydriatic fundus photography. The study was approved by the institutional ethics committee of The Third Affiliated Hospital of Guangzhou Medical University (approval number [2023] No. 152) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants. An example of patient flowchart flow in this study is shown in Fig. 1.

Inclusion and Exclusion Criteria

Data from patients who delivered at our hospital, attended ophthalmic consultations, and consented to participate in the study were included. Patients with keratitis, cataracts, glaucoma, previous ocular surgery, ocular trauma, or preexisting retinopathy were excluded.

Parameter Selection for Adverse Ocular Outcomes

The grading system used to describe adverse ocular changes was based on a modified and simplified classification for hypertensive retinopathy (Downie et al, 2013), as follows:

- Grade 0: No detectable signs.
- Grade 1: Mild, moderate, or severe retinal arteriole sclerosis, arteriolar narrowing, arteriovenous nicking, and an arteriovenous ratio (AVR) of <0.67.
- Grade 2: Hemorrhage (blot-shaped, dot-shaped, or flame-shaped), microaneurysm, cotton wool spots, hard exudate, or a combination of these signs; retinal detachment; or any other condition that may affect the patient's vision.

Retinal Vessel Diameter Measurements

All pregnant women were assessed using a fundus camera (Kowa Fundus Camera VX-10α; Aichi, Japan). Two pairs of fundus photographs were obtained, focusing on the center of the optic disc and the macula. The retinal vessel diameters of the six largest retinal arteries and veins within a specified zone (0.5–1 disc diameter) from the optic disc margin were measured using a semiautomated system (Integrative Vessel Analysis (IVAN), Department of Ophthalmology Visual Science, University of Wisconsin, Madison, WI, USA). The grading of retinal vessels followed the Atherosclerosis Risk in Communities study protocol. The revised Parr-Hubbard-Knudtson formula was used to standardize and summarize the retinal arteriolar and venular calibers as the central retinal artery equivalent and the central retinal vein equivalent. Measurements were completed by two masked graders. If the difference between the two graders exceeded 10%, a third grader assessed the images, and the average of these three values was used for analysis.

Statistical Analyses

Statistical data analyses were conducted using SPSS software (version 23.0; IBM Corporation, Chicago, IL, USA). Categorical variables are described as frequencies and percentages. Univariate logistic regression analysis was performed to assess the effect of individual risk factors on various adverse ocular outcomes. Variables that were significant at $p < 0.05$ in the univariate analysis were included in the multivariate logistic regression analysis. Receiver operating characteristic (ROC) curve analysis was used to determine the cut-off probability with optimal sensitivity and specificity. Odds ratios (ORs) with 95% confidence intervals (CIs) were calculated. A p-value of <0.05 was considered statistically significant.

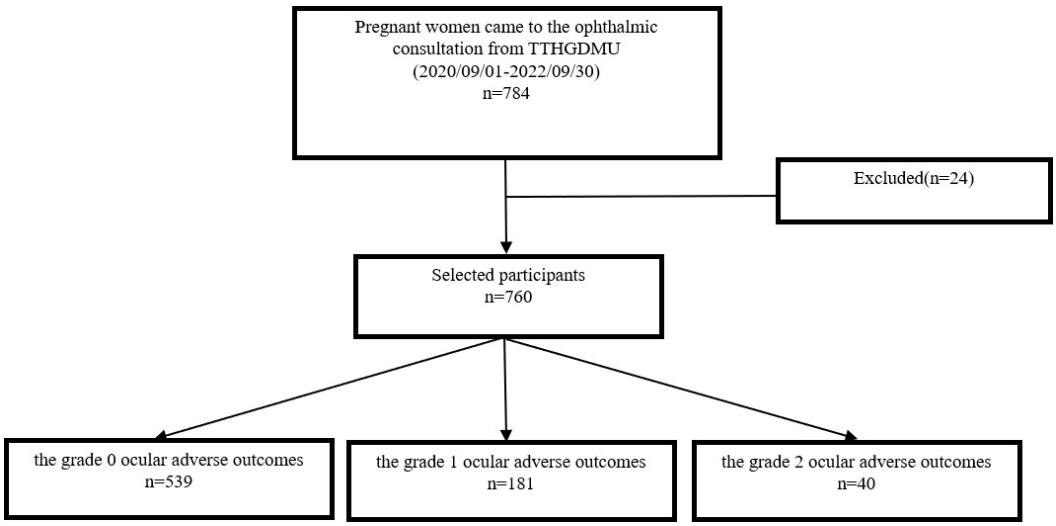

Fig. 1. Patient flowchart flow in the present study. The grade 0 of ocular adverse outcomes: no detectable signs; grade 1: mild, moderate, or severe retinal arteriole sclerosis, arteriolar narrowing, arteriovenous nicking, and arteriovenous ratio (AVR) of <0.67; grade 2: hemorrhage (blot-shaped, dot-shaped, or flame-shaped), microaneurysm, cotton wool spots, hard exudate, or a combination of these signs, or retinal detachment and any other condition that may affect the patient's vision. TTHGDMU, The Third Affiliated Hospital of Guangzhou Medical University.

Results

Descriptive Statistics

The patients' demographic characteristics are summarized in Table 1. A total of 760 women were enrolled in the study. The following complications were considered: PIH, eclampsia and pre-eclampsia, GDM, multiple pregnancy (MP), *in vitro* fertilization with embryo transfer (IVF-ET), stillbirth, and intrauterine growth retardation (IUGR) (Table 1).

The study included 760 pregnant women who attended ophthalmic consultations and delivered at our hospital (Fig. 1). The demographic characteristics of the participants and their fetuses are detailed in Table 1. Maternal age ranged from 19 to 50 years, with an average age of 33.4 ± 4.99 years. PIH was observed in 85 patients (11.18%); eclampsia and pre-eclampsia in 213 (28.03%); a history of chronic hypertension in 103 (13.55%); and hemolysis, elevated liver enzymes, and low platelets (HELLP) syndrome in 8 (1.05%). A total of 452 pregnant women (59.47%) developed GDM, and 48 (6.31%) were classified as obese. There were 97 patients (12.76%) with MP and 520 patients (68.42%) with repeated pregnancies. Regarding uterine disease, uterine myoma was observed in 77 patients (10.13%), uterine scarring in 201 (26.45%), cervical incompetence in 47 (6.18%), and endometriosis in 2 (0.26%). Of the 71 pregnant women with fetal abnormalities, 18 (2.37%) had stillbirth and 53 (6.97%) had IUGR.

Among the patients, 171 (22.5%) had a history of IVF-ET. Anemia, hypoproteinemia, hyperlipidemia, and infectious reproductive diseases were observed in 171 (22.5%), 44 (5.79%), 53 (6.97%), and 31 (4.08%) patients, respectively. Major comorbidities during pregnancy included thyroid disease in 82 patients (10.79%),

Table 1. Maternal baseline characteristics.

Parameter	Mean ± SD/number (%)
Age, years	33.40 ± 4.99
PIH	85 (11.18%)
Eclampsia and pre-eclampsia	213 (28.03%)
GDM	452 (59.47%)
Multiple pregnancy	97 (12.76%)
Myoma of uterus	77 (10.13%)
IVF-ET	171 (22.50%)
Stillbirth	18 (2.37%)
Repeated pregnancy	520 (68.42%)
History of chronic hypertension	103 (13.55%)
Pregnancy with thyroid disease	82 (10.79%)
Scarred uterus	201 (26.45%
Anemia	171 (22.50%)
Hypoproteinemia	44 (5.79%)
Pregnancy with infectious disease	68 (8.95%)
Cervical incompetence	47 (6.18%)
Pregnancy with antiphospholipid syndrome	35 (4.61%)
Hyperlipidemia	2 (0.26%)
IUGR	53 (6.97%)
Obesity	48 (6.31%)
Endometriosis	2 (0.26%)
Pregnancy with cardiac disease	24 (3.16%)
Infectious reproductive disease	31 (4.08%)
Pregnancy with systemic lupus erythematosus	14 (1.84%)
Pregnancy with rheumatoid arthritis	2 (0.26%)
Pregnancy with IgA nephropathy	7 (0.92%)
Intrahepatic cholestasis of pregnancy.	19 (2.50%)
HELLP syndrome	8 (1.05%)

GDM, gestational diabetes mellitus; HELLP, hemolysis, elevated liver enzymes, and low platelets; IgA, immunoglobulin A; IUGR, intrauterine growth retardation; IVF-ET, *in vitro* fertilization and embryo transfer; PIH, pregnancy-induced hypertension.

infectious disease in 68 (8.95%), antiphospholipid syndrome in 35 (4.61%), cardiac disease in 24 (3.16%), systemic lupus erythematosus in 14 (1.84%), rheumatoid arthritis in 2 (0.26%), immunoglobulin A (IgA) nephropathy in 7 (0.92%), and intrahepatic cholestasis of pregnancy in 19 (2.5%).

Comparison with the Incidence of Adverse Ocular Outcomes and the Occurrence of Risk Factors in Pregnant Women

The results of the univariate logistic regression analysis for the grade of adverse ocular outcomes and associated risk factors in pregnant women are shown in Tables 2,3. Significant associations were found for maternal age (odds ratio (OR) [95% CI]: 1.04 [1.00–1.08]), PIH (OR [95% CI]: 1.75 [1.07–2.88]), eclampsia and

Table 2. Univariate logistic regression analysis for grade 1 adverse ocular outcomes among risk factors in pregnant women.

Parameter	Incidence of grade 1 adverse ocular outcome, % (with complication vs. without complication)	β	SE	Wald χ^2	p value	OR (95% CI)
Age		0.0386	0.0175	4.8536	0.0276	1.04 (1.00–1.08)
PIH	23.87 vs. 35.44	0.5607	0.2528	4.9196	0.0266	1.75 (1.07–2.88)
Eclampsia and pre-eclampsia	19.47 vs. 40.84	1.0490	0.1836	32.6294	<0.0001	2.85 (1.99–4.09)
GDM	37.15 vs. 17.13	–1.0508	0.1766	35.4159	<0.0001	0.35 (0.25–0.49)
Multiple pregnancy	26.31 vs. 16.85	–0.5660	0.2972	3.6253	0.0569	0.57 (0.32–1.02)
Myoma of uterus	25.27 vs. 23.94	–0.0715	0.2924	0.0598	0.8069	0.93 (0.52–1.65)
IVF-ET	25.36 vs. 24.38	–0.0526	0.2082	0.0638	0.8006	0.95 (0.63–1.43)
Stillbirth	24.72 vs. 43.75	0.8633	0.5114	2.8495	0.0914	2.37 (0.87–6.46)
Repeated pregnancy	21.43 vs. 26.81	0.2952	0.1918	2.3687	0.1238	1.34 (0.92–1.96)
History of chronic hypertension	20.61 vs. 55.32	1.5623	0.2298	46.2260	<0.0001	4.77 (3.04–7.48)
Pregnancy with thyroid disease	25.31 vs. 23.68	–0.0880	0.2846	0.0955	0.7573	0.92 (0.52–1.60)
Scarred uterus	23.53 vs. 29.53	0.3091	0.1883	2.6954	0.1006	1.36 (0.94–1.97)
Anemia	24.51 vs. 27.33	0.1470	0.2023	0.5281	0.4674	1.16 (0.78–1.72)
Hypoproteinemia	23.94 vs. 46.15	1.0024	0.3335	9.0321	0.0027	2.72 (1.42–5.24)
Pregnancy with infectious disease	25.27 vs. 23.81	–0.0787	0.3091	0.0648	0.7991	0.92 (0.50–1.69)
Cervical incompetence	25.71 vs. 17.02	–0.5228	0.3980	1.7253	0.1890	0.59 (0.27–1.29)
Pregnancy with antiphospholipid syndrome	24.93 vs. 29.41	0.2271	0.3866	0.3450	0.5570	1.25 (0.59–2.68)
Hyperlipidemia	25.10 vs. 0.00	–12.4720	623.9000	0.0004	0.9841	0.00 (0.00, >999.99)
IUGR	24.26 vs. 37.50	0.6279	0.3114	4.0646	0.0438	1.87 (1.02–3.45)
Obesity	24.30 vs. 37.78	0.6375	0.3203	3.9615	0.0466	1.89 (1.01–3.54)
Endometriosis	25.21 vs. 0.00	–12.4740	622.9000	0.0004	0.9840	0.00 (0.00, >999.99)
Pregnancy with cardiac disease	24.79 vs. 36.36	0.5510	0.4518	1.4877	0.2226	1.74 (0.72–4.21)
Infectious reproductive disease	25.07 vs. 26.67	0.0832	0.4221	0.0388	0.8438	1.09 (0.48–2.49)
Pregnancy with systemic lupus erythematosus	25.07 vs. 28.57	0.1786	0.5979	0.0892	0.7652	1.20 (0.37–3.86)
Pregnancy with rheumatoid arthritis	25.21 vs. 0.00	–12.4740	622.9000	0.0004	0.9840	0.00 (0.00, >999.99)
Pregnancy with IgA nephropathy	24.65 vs. 83.33	2.7256	1.0984	6.1570	0.0131	15.27 (1.77–131.40)
Intrahepatic cholestasis of pregnancy	25.32 vs. 17.65	–0.4580	0.6419	0.5091	0.4755	0.63 (0.18–2.23)
HELLP syndrome	24.79 vs. 60.00	1.5153	0.9170	2.7307	0.0984	4.55 (0.75–27.45)

Incidence data are presented as yes vs. no. CI, confidence interval; GDM, gestational diabetes mellitus; HELLP, hemolysis, elevated liver enzymes, and low platelets; IgA, immunoglobulin A; IUGR, intrauterine growth retardation; IVF-ET, *in vitro* fertilization and embryo transfer; OR, odds ratio; PIH, pregnancy-induced hypertension.

Table 3. Univariate logistic regression analysis for grade 2 adverse ocular outcomes among the risk factors in pregnant women.

Parameter	Incidence of grade 2 adverse ocular outcome, % (with complication vs. without complication)	β	SE	Wald χ^2	p value	OR (95% CI)
Age		0.0117	0.0337	0.1200	0.7291	1.01 (0.95–1.08)
PIH	6.69 vs. 8.93	0.3131	0.5001	0.3919	0.5313	1.37 (0.51–3.64)
Eclampsia and pre-eclampsia	4.05 vs. 16.30	1.5277	0.3350	20.8003	<0.0001	4.61 (2.39–8.88)
GDM	9.95 vs. 5.29	–0.6820	0.3291	4.2945	0.0382	0.51 (0.27–0.96)
Multiple pregnancy	6.63 vs. 8.64	0.2877	0.4345	0.4383	0.5079	1.33 (0.57–3.12)
Myoma of uterus	6.55 vs. 10.00	0.4606	0.4655	0.9791	0.3224	1.58 (0.64–3.95)
IVF-ET	6.49 vs. 8.33	0.2704	0.3688	0.5376	0.4634	1.31 (0.64–2.70)
Stillbirth	6.69 vs. 18.18	1.1312	0.7996	2.0016	0.1571	3.10 (0.65–14.86)
Repeated pregnancy	8.33 vs. 6.20	–0.3186	0.3356	0.9014	0.3424	0.73 (0.38–1.40)
History of chronic hypertension	5.87 vs. 17.65	1.2342	0.4113	9.0026	0.0027	3.44 (1.53–7.69)
Pregnancy with thyroid disease	6.60 vs. 9.38	0.3808	0.4641	0.6733	0.4119	1.46 (0.59–3.63)
Scarred uterus	7.36 vs. 5.56	–0.2998	0.4075	0.5413	0.4619	0.74 (0.33–1.65)
Anemia	6.64 vs. 7.87	0.1843	0.3798	0.2354	0.6276	1.20 (0.57–2.53)
Hypoproteinemia	6.33 vs. 19.23	1.2595	0.5274	5.7042	0.0169	3.52 (1.25–9.91)
Pregnancy with infectious disease	6.65 vs. 9.43	0.3793	0.5014	0.5723	0.4494	1.46 (0.55–3.90)
Cervical incompetence	7.41 vs. 0.00	–13.1890	413.9000	0.0010	0.9746	0.00 (0.00, >999.99)
Pregnancy with antiphospholipid syndrome	7.04 vs. 4.00	–0.5974	1.0340	0.3338	0.5634	0.55 (0.07–4.18)
Hyperlipidemia	6.93 vs. 0.00	–12.1180	1108.5000	0.0001	0.9913	0.00 (0.00, >999.99)
IUGR	6.43 vs. 14.29	0.8858	0.5136	2.9742	0.0846	2.42 (0.89–6.64)
Obesity	6.75 vs. 9.68	0.3919	0.6309	0.3858	0.5345	1.48 (0.43–5.10)
Endometriosis	6.93 vs. 0.00	–12.1180	1108.5000	0.0001	0.9913	0.00 (0.00, >999.99)
Pregnancy with cardiac disease	6.75 vs. 12.50	0.6800	0.7743	0.7712	0.3799	1.97 (0.43–9.00)
Infectious reproductive disease	7.01 vs. 4.35	–0.5066	1.0359	0.2391	0.6248	0.60 (0.08–4.59)
Pregnancy with systemic lupus erythematosus	7.03 vs. 0.00	–13.1330	817.4000	0.0003	0.9872	0.00 (0.00, >999.99)
Pregnancy with rheumatoid arthritis	6.93 vs. 0.00	–12.1180	1108.5000	0.0001	0.9913	0.00 (0.00, >999.99)
Pregnancy with IgA nephropathy	6.92 vs. 0.00	–11.1160	950.9000	0.0001	0.9907	0.00 (0.00, >999.99)
Intrahepatic cholestasis of pregnancy	6.75 vs. 12.50	0.6800	0.7743	0.7712	0.3799	1.97 (0.43–9.00)
HELLP syndrome	6.45 vs. 60.00	3.0801	0.9285	11.0041	0.0009	21.76 (3.53–134.30)

Incidence data are presented as yes vs. no. CI, confidence interval; GDM, gestational diabetes mellitus; HELLP, hemolysis, elevated liver enzymes, and low platelets; IgA, immunoglobulin A; IUGR, intrauterine growth retardation; IVF-ET, *in vitro* fertilization with embryo transfer; OR, odds ratio; PIH, pregnancy-induced hypertension.

pre-eclampsia (OR [95% CI]: 2.85 [1.99–4.09]), GDM (OR [95% CI]: 0.35 [0.25–0.49]), a history of chronic hypertension (OR [95% CI]: 4.77 [3.04–7.48]), hypoproteinemia (OR [95% CI]: 2.72 [1.42–5.24]), IUGR (OR [95% CI]: 1.87 [1.02–3.45]), obesity (OR [95% CI]: 1.89 [1.01–3.54]), and pregnancy with IgA nephropathy (OR [95% CI]: 15.27 [1.77–131.4]) with the incidence of grade 1 adverse ocular outcomes (all $p < 0.05$).

Significant differences for grade 2 adverse ocular outcomes were associated with eclampsia and pre-eclampsia (OR [95% CI]: 4.61 [2.39–8.88]), GDM (OR [95% CI]: 0.51 [0.27–0.96]), a history of chronic hypertension (OR [95% CI]: 3.44 [1.53–7.69]), hypoproteinemia (OR [95% CI]: 3.52 [1.25–9.91]), and HELLP syndrome (OR [95% CI]: 21.76 [3.53–134.3]) (all $p < 0.05$). However, no significant differences were observed for IVF-ET, MP, repeated pregnancy, uterine scarring, uterine myoma, cervical incompetence, endometriosis, fetal abnormalities, and certain comorbidities in either the grade 1 or grade 2 adverse ocular outcomes groups (all $p > 0.05$).

Multivariate Logistic Regression of the Prediction Model

Multivariate logistic regression was employed to analyze the correlations between various risk factors and adverse ocular outcomes in pregnant women (Tables 4,5). The analysis identified several predictors of grade 1 adverse ocular outcomes during pregnancy. Maternal age was associated with a decreased risk (OR [95% CI]: 0.953 [0.916–0.991], $p = 0.0154$). PIH emerged as a risk factor with an increased odds ratio (OR [95% CI]: 1.334 [1.015–1.752], $p = 0.0387$). Eclampsia and pre-eclampsia were also significant predictors (OR [95% CI]: 1.451 [1.18–1.784], $p = 0.0004$). Conversely, GDM was associated with a decreased risk (OR [95% CI]: 0.661 [0.538–0.81], $p < 0.0001$), as was a history of chronic hypertension (OR [95% CI]: 2.021 [1.581-2.582], $p < 0.0001$). Other factors such as hypoproteinemia (OR [95% CI]: 1.216 [0.842–1.758], $p = 0.2972$), IUGR (OR [95% CI]: 1.15 [0.82–1.611], $p = 0.4182$), obesity (OR [95% CI]: 1.255 [0.882–1.786], $p = 0.206$), and pregnancy with IgA nephropathy (OR [95% CI]: 3.231 [1.038–10.056], $p = 0.0429$) were also evaluated.

After calculation, the final model for grade 1 adverse ocular outcome prediction among pregnant women was as follows: $\text{Ln}(p \div (1 - p)) = 0.2279 - 0.0483 \times \text{maternal age} + 0.288 \times 1(\text{PIH}) + 0.3721 \times 1(\text{eclampsia and pre-eclampsia}) - 0.4146 \times 1(\text{GDM}) + 0.7035 \times 1(\text{history of chronic hypertension}) + 0.1958 \times 1(\text{hypoproteinemia}) + 0.1394 \times 1(\text{IUGR}) + 0.2274 \times 1(\text{obesity}) + 1.1729 \times 1(\text{pregnancy with IgA nephropathy})$.

For the grade 2 adverse ocular outcome group, the multivariate logistic regression analysis identified several predictors. Maternal age was not significantly associated with grade 2 outcomes (OR [95% CI]: 0.978 [0.911–1.049], $p = 0.5341$). However, eclampsia and pre-eclampsia were significant predictors (OR [95% CI]: 1.957 [1.36–2.815], $p = 0.0003$). GDM was not a significant predictor for grade 2 outcomes (OR [95% CI]: 0.962 [0.664–1.394], $p = 0.8366$). A history of chronic hypertension was associated with an increased risk (OR [95% CI]: 1.621 [1.046–2.513], $p = 0.0306$). Hypoproteinemia did not significantly predict grade 2 out-

Table 4. Multivariate logistic regression analysis for grade 1 adverse ocular outcomes among the risk factors in pregnant women.

Parameter	β	SE	Wald χ^2	p value	OR (95% CI)
Age	–0.0483	0.0199	5.8722	0.0154	0.953 (0.916–0.991)
PIH	0.2880	0.1393	4.2757	0.0387	1.334 (1.015–1.752)
Eclampsia and pre-eclampsia	0.3721	0.1054	12.4527	0.0004	1.451 (1.180–1.784)
GDM	–0.4146	0.1043	15.8091	<0.0001	0.661 (0.538–0.810)
History of chronic hypertension	0.7035	0.1251	31.6101	<0.0001	2.021 (1.581–2.582)
Hypoproteinemia	0.1958	0.1879	1.0865	0.2972	1.216 (0.842–1.758)
IUGR	0.1394	0.1722	0.6553	0.4182	1.150 (0.820–1.611)
Obesity	0.2274	0.1798	1.5993	0.2060	1.255 (0.882–1.786)
Pregnancy with IgA nephropathy	1.1729	0.5792	4.1008	0.0429	3.231 (1.038–10.056)

CI, confidence interval; GDM, gestational diabetes mellitus; IgA, immunoglobulin A; IUGR, intrauterine growth retardation; OR, odds ratio; PIH, pregnancy-induced hypertension.

Table 5. Multivariate logistic regression analysis for grade 2 adverse ocular outcomes among the risk factors in pregnant women.

Parameter	β	SE	Wald χ^2	p value	OR (95% CI)
Age	–0.0224	0.0360	0.3866	0.5341	0.978 (0.911–1.049)
Eclampsia and pre-eclampsia	0.6712	0.1856	13.0827	0.0003	1.957 (1.360–2.815)
GDM	–0.0390	0.1892	0.0425	0.8366	0.962 (0.664–1.394)
History of chronic hypertension	0.4833	0.2236	4.6726	0.0306	1.621 (1.046–2.513)
Hypoproteinemia	0.3272	0.2902	1.2714	0.2595	1.387 (0.785–2.450)
HELLP syndrome	1.2646	0.5226	5.8548	0.0155	3.542 (1.272–9.864)

CI, confidence interval; GDM, gestational diabetes mellitus; HELLP, hemolysis, elevated liver enzymes, and low platelets; OR, odds ratio.

comes (OR [95% CI]: 1.387 [0.785–2.45], $p = 0.2595$). HELLP syndrome was a significant predictor (OR [95% CI]: 3.542 [1.272–9.864], $p = 0.0155$).

The final model for grade 2 adverse ocular outcome prediction among pregnant women was as follows: $\text{Ln}(p \div (1-p)) = 1.3273 - 0.0224 \times \text{maternal age} + 0.6712 \times 1(\text{PIH}) - 0.039 \times 1(\text{GDM}) + 0.4833 \times 1(\text{history of chronic hypertension}) + 0.3272 \times 1(\text{hypoproteinemia}) + 1.2646 \times 1(\text{HELLP syndrome})$.

ROC Curve Analysis

The ROC curve analysis, based on multivariate logistic regression for different adverse ocular outcomes in pregnant women, was performed using the available study variables. For the grade 1 adverse ocular outcomes group, the area under the curve (AUC) was 0.7517 (95% CI: 0.7100–0.7933, SE = 0.02127). For the grade 2 adverse ocular outcomes group, the AUC was 0.7431 (95% CI: 0.6565–0.8297, SE = 0.04418) (Figs. 2,3).

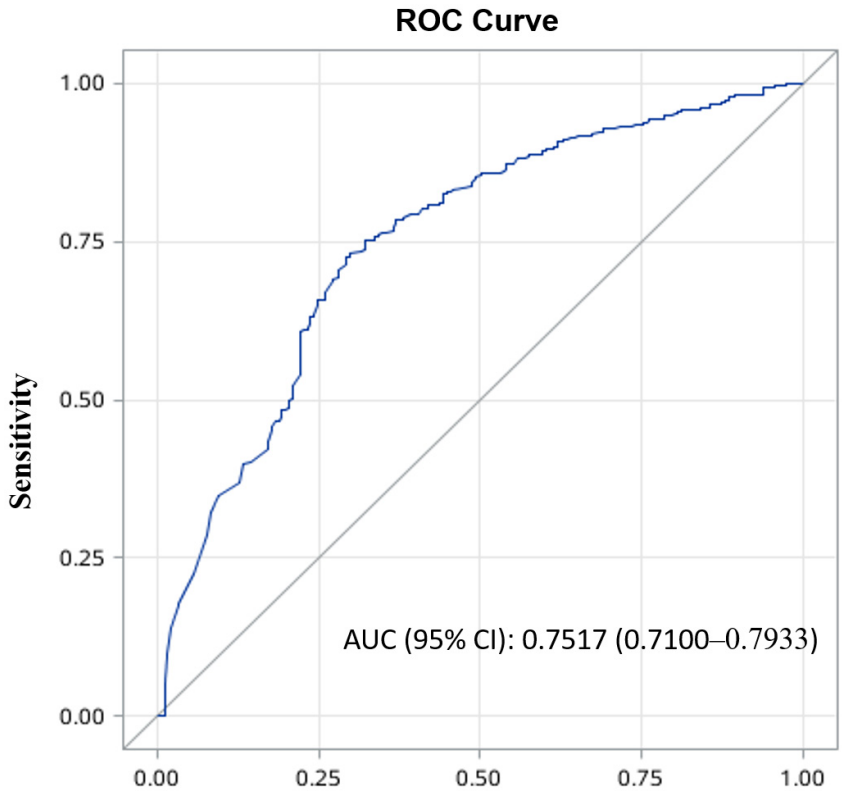

Fig. 2. ROC curve for predicting grade 1 adverse ocular outcomes by risk factors during pregnancy. The area under the ROC curve was 0.7517 (95% CI: 0.7100–0.7933) in the grade 1 adverse ocular outcomes group. ROC, receiver operating characteristic; AUC, area under the curve.

Discussion

To our knowledge, this is the first study to identify risk factors of adverse ocular outcomes during pregnancy. We found that eclampsia and pre-eclampsia, GDM, history of chronic hypertension, and hypoproteinemia were independent predictors of both grade 1 and grade 2 adverse ocular outcomes during pregnancy. Additionally, maternal age, PIH, IUGR, obesity, and pregnancy with IgA nephropathy were predictors of moderate and severe retinal arteriole sclerosis. Furthermore, HELLP syndrome emerged as a risk factor for retinal hemorrhage, exudate, and other vision-disrupting conditions during pregnancy. The predictive models proposed in this study demonstrated reasonable accuracy and sensitivity, as indicated by the area under the ROC curve values.

Pregnancy complications such as eclampsia and pre-eclampsia can lead to pregnancy-specific ocular diseases, including cortical blindness (Khong et al, 2021). Vision is affected in approximately 25% of pregnancies with pre-eclampsia and 50% of pregnancies with eclampsia (Qin et al, 2020). The most common ocular findings in these conditions include retinal arteriole constriction (Soullane et al, 2024), which aligns with our study's correlation of eclampsia and pre-eclampsia with grade 1 adverse ocular outcomes. Additionally, as eclampsia and pre-eclampsia worsen, complications such as retinal edema, hemorrhage, exudate, and cotton wool spots may occur, consistent with our findings for grade 2 adverse ocular outcomes.

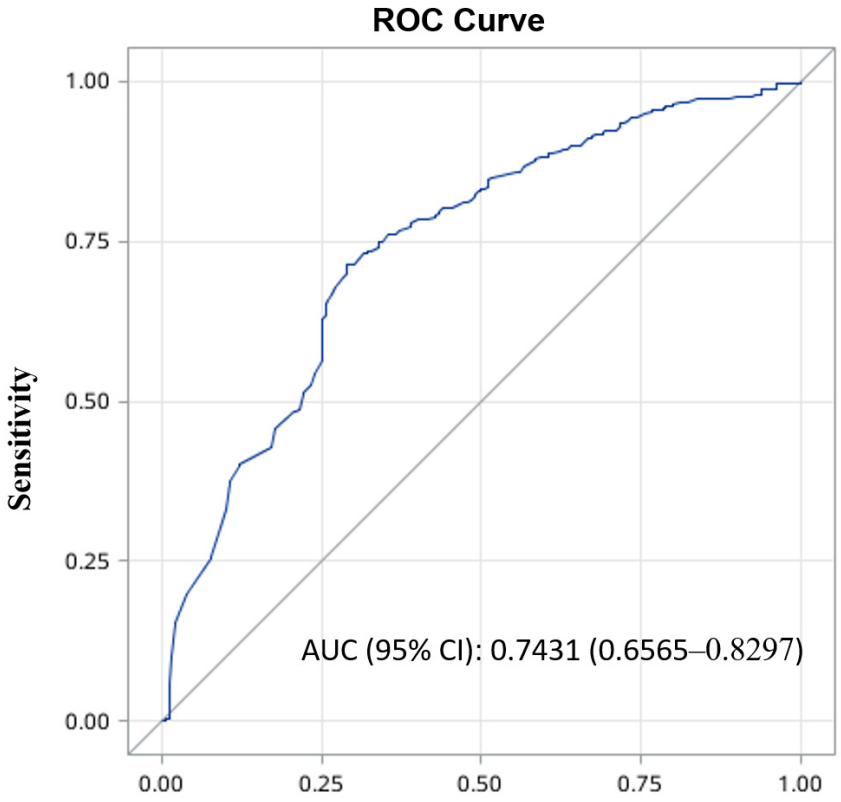

Fig. 3. ROC curve for predicting grade 2 adverse ocular outcomes by risk factor during pregnancy. The area under the ROC curve was 0.7431 (95% CI: 0.6565–0.8297) in the grade 1 adverse ocular outcomes group. ROC, receiver operating characteristic; AUC, area under the curve.

Diabetic retinopathy can also be exacerbated during pregnancy (Huang et al, 2024). Our study found that GDM affects both grade 1 and grade 2 adverse ocular outcomes. This result can be explained in two ways: First, hyperglycemia during pregnancy might increase retinal capillary basement membrane thickness and gliosis due to oxidative stress, the polyol pathway, and advanced glycation end-products (Chandrasekaran et al, 2021). Second, GDM did not significantly correlate with grade 2 ocular adverse outcomes in multivariate logistic regression analysis, indicating that while GDM is a risk factor, it might not be the primary risk indicator for severe adverse ocular outcomes among various confounding factors.

There is a study has highlighted that women of advanced maternal age face a higher risk of various maternal and fetal complications compared to younger women, such as ectopic pregnancy, spontaneous abortion, GDM, pre-eclampsia, and cesarean delivery (Pinheiro et al, 2019). However, research specifically evaluating ocular changes associated with advanced maternal age has been lacking. In our study, maternal age emerged as a significant predictor of grade 1 adverse ocular outcomes. Previous researches have indicated that aging is associated with impairments in uterine and systemic arteries during pregnancy, likely due to increased vascular oxidative stress and altered nitric oxide synthesis (Care et al, 2015; Kao et al, 2016). Excessive nitric oxide and dysregulation of oxidative stress can contribute to retinal arteriole narrowing (Gericke and Buonfiglio, 2024).

Obesity during pregnancy is a common comorbidity that is associated with numerous complications for both the mother and fetus, including increased risks of GDM, PIH, pre-eclampsia, and venous embolism (Catalano and Shankar, 2017; Lin et al, 2022; Zehravi et al, 2021). In our study, obesity was identified as a significant predictor of adverse ocular outcomes during pregnancy. Previous research by Köchli et al (2022) has demonstrated that obesity in young children can lead to retinal arteriole narrowing and retinal venular widening. This is thought to be associated with oxidative stress and complement activation within the retinal environment, which impacts the retinal vasculature (Natoli et al, 2018). Additionally, our study found that IUGR was significantly associated with moderate and severe retinal arteriole sclerosis during pregnancy. While much research has focused on the adverse fetal outcomes associated with IUGR, such as abnormal fetal blood flow and its impact on retinal vascular morphology later in life (Yang et al, 2023), there has been limited investigation into how IUGR affects the maternal microvasculature. Therefore, further studies are needed to explore this aspect more thoroughly.

Pregnancy with IgA nephropathy has garnered significant attention due to its association with high risks of adverse pregnancy outcomes (Liu et al, 2016). In patients with IgA nephropathy, proteinuria during pregnancy is a notable risk factor for pre-eclampsia, and severe proteinuria often leads to hypoproteinemia (Cheung and Barratt, 2019). The exacerbation of IgA nephropathy, along with hypoproteinemia, can reduce intravascular volume and impair vascular endothelial function, contributing to hypoxia and increased oxidative stress (Liu et al, 2016). These conditions likely cause changes in the retinal vasculature, resulting in adverse ocular outcomes during pregnancy. Furthermore, HELLP syndrome, a severe manifestation of pre-eclampsia/eclampsia, can lead to serious ocular complications such as retinal vascular occlusion, serous retinal detachment, and acute visual loss (Teodoru et al, 2023). Our study corroborates that HELLP syndrome is an independent risk factor for grade 2 adverse ocular outcomes, which are more likely to impair vision compared to grade 1 adverse ocular outcomes.

This study has several limitations that should be acknowledged. Firstly, the research was constrained to patients who attended ophthalmic consultations, which resulted in a relatively small sample size. To strengthen the findings, future studies with larger sample sizes are necessary to validate the proposed risk model. Secondly, the correlations of GDM, obesity, and IUGR with adverse ocular outcomes need further exploration through prospective studies. Additionally, a follow-up study is warranted, as data collection for these patients is ongoing. Finally, due to the absence of relevant study types, the prediction model data in this study lacked independent validation.

Conclusion

In summary, our model demonstrated high sensitivity and specificity in predicting the occurrence of adverse ocular outcomes during pregnancy, incorporating risk factors such as maternal age, eclampsia and pre-eclampsia, GDM, obesity, history of chronic hypertension, hypoproteinemia, IUGR, pregnancy with IgA

nephropathy, and HELLP syndrome. We identified several new risk factors associated with adverse ocular outcomes during pregnancy. To validate and further understand these findings, additional prospective studies are needed. This research offers a novel approach for identifying and evaluating maternal ocular conditions, potentially facilitating early interventions and improving management of pregnancy-related ocular complications.

Key Points

- In our study, we found that the following factors were associated with an increased risk of adverse ocular outcomes during pregnancy: maternal age, eclampsia and pre-eclampsia, gestational diabetes mellitus, obesity, history of chronic hypertension, hypoproteinemia, intrauterine growth retardation, pregnancy with immunoglobulin A nephropathy, and HELLP syndrome.
- The model proposed in this study demonstrated effectiveness in predicting grade 1 and grade 2 adverse ocular outcomes during pregnancy, with area under the receiver operating characteristic curve values of 0.7517 (95% CI: 0.7100–0.7933) and 0.7431 (95% CI: 0.6565–0.8297), respectively.
- The prediction model proposed in this study can be utilized to identify pregnant women who are at high risk of adverse ocular outcomes.
- This study provides a novel approach to identifying and evaluating maternal ocular conditions, facilitating early interventions for adverse ocular outcomes during pregnancy.

Availability of Data and Materials

Data and materials are available on request from the corresponding authors.

Author Contributions

XTL and SYW designed the study. XTL, YYW, HQZ, SYW performed the literature research, data acquisition, data analysis, and manuscript editing. XTL, SYW conducted the clinical studies. XTL drafted the manuscript. XTL and SYW reviewed the manuscript. All authors contributed to important editorial changes in the manuscript. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

The study was approved by the institutional ethics committee of The Third Affiliated Hospital of Guangzhou Medical University (approval number [2023] No. 152) and was conducted in accordance with the Declaration of Helsinki. Written informed consent was obtained from all participants.

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Conflict of Interest

The authors declare no conflict of interest.

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