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Pregnancy-Induced Changes in Ocular Biomechanics Are Related to Maternal Hormone Levels in Healthy Chinese Pregnant Women

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Abstract

Background: To explore the changes in ocular biomechanics during pregnancy and the postpartum period and their association with maternal hormone level changes. **Methods:** In a prospective cohort study, 24 eyes of 12 pregnant women were enrolled and monitored throughout pregnancy and after delivery (6 weeks). Intraocular pressure (IOP), central corneal thickness (CCT), corneal endothelium cell (CEC), axial length (AL), corneal curvature (K1, K2), anterior chamber depth (ACD), central subfield thickness (CST), macular volume (MV), cube average thickness (CAT), retinal nerve fibre layer (RNFL), tear meniscus height (TMH), and breaking up time (BUT) were measured throughout pregnancy, and blood plasma levels of maternal hormones were determined at the same time points. **Results:** A gradual decrease in IOP values was observed as gestation progressed, and there was a statistically significant difference in IOP between the 3rd trimester and the 1st and 2nd trimester and postpartum ($p = 0.002$, $p = 0.006$, $p = 0.050$). There was a significant difference between the 1st and 2nd trimesters in terms of MV ($p = 0.023$). The difference in RNFL in the 3rd trimester and postpartum was significant ($p = 0.011$). The levels of the β-hCG showed a significant correlation with K2, ACD, and TMH only in the 2nd trimester ($r = 0.588$, $p = 0.045$; $r = -0.740$, $p = 0.006$; $r = 0.642$, $p = 0.024$). Regarding luteinizing hormone, there was a negative correlation with MV in the 1st and 2nd trimesters ($r = -0.598$, $p = 0.040$; $r = -0.672$, $p = 0.017$) and CAT in the 1st and 2nd

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trimesters (r = −0.599, p = 0.040; r = −0.655, p = 0.021). Luteinizing hormone levels were correlated with ACD (r = −0.702, p = 0.011) in the 2nd trimester and K2 (r = 0.585, p = 0.046) in the 3rd trimester. A correlation was found between follicle-stimulating hormone levels and CEC, MV and CAT in the 1st trimester (r = −0.677, p = 0.016; r = −0.602, p = 0.039; r = −0.584, p = 0.046) and AL in the 3rd trimester (r = −0.618, p = 0.032). The correlation between oestradiol and CST in the 1st trimester (r = −0.621, p = 0.031) and RNFL (r = 0.594, p = 0.041) in the postpartum. A statistically significant correlation between progesterone and MV (r = 0.583, p = 0.047) and TMH (r = 0.762, p = 0.004) was observed in the 1st trimester. No significant intergroup correlation was observed postpartum (p > 0.05). **Conclusion:** Ophthalmological parameters showed physiological changes induced by hormone levels in pregnancy and returned to baseline levels after delivery.

Keywords

Pregnancy, Hormones, Ocular Biomechanics, Hormone-Related Differences

1. Background

Due to fluctuations in hormones during pregnancy, a series of metabolic, immunologic, haematologic, and cardiovascular changes occur, as the preprint mentioned [1]. The changing levels of hormones during pregnancy are well documented. Beta human chorionic gonadotropin (β-hCG) levels increase 10 - 14 days after conception and proliferate rapidly until they peak in the eighth week of pregnancy [2]. Oestradiol and progesterone levels peak in the third of trimester pregnancy [3].

Hormone receptors have been demonstrated in the human cornea [4]; thus, the biological functions of corneal cells may be influenced through direct interaction with specific hormones during this period. Many past studies have reported pregnancy-induced changes in the eyes, including changes in the central corneal thickness [5], intraocular pressure [6], biomechanics in the cornea [7], tear production changes [6], etc., and some existing ocular diseases are exacerbated or new pathology develops in pregnant women, such as diabetic retinopathy [8], and central serous chorioretinopathy [9]. Due to individual variability, the results of ocular changes induced by pregnancy vary. There are a few previous studies demonstrating the effect of pregnancy and the associated changes in maternal hormone levels on simultaneously measured anterior and posterior ocular segment parameters in the same population throughout pregnancy.

Therefore, we attempted to evaluate the changes in the biomechanical properties of the anterior and posterior ocular segment parameters during pregnancy in the same female population and the potential associations of these changes with hormone levels. Knowledge of these associations may help in the prevention and early management of ocular disorders during pregnancy.

2. Methods and Materials

2.1. Study Population

The research protocol was approved by the First Affiliated Hospital of Jinan University Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each participant before enrolment in the study.

The study included 24 eyes of 12 healthy singleton pregnant women who presented to the physiological pregnancy clinic and met the following inclusion criteria: women with uncomplicated term pregnancy admitted for delivery, women who were willing to participate in the study, and women who were not related and of Han Chinese ethnicity. None of the participants had a history of systemic diseases, such as hypertension, diabetes, or any collagen diseases. Furthermore, the participants had not undergone procedures for eye diseases, including high myopia, best-corrected visual acuity < 20/20 (Snellen chart), an IOP of more than 21 mmHg, or previous ocular surgery.

2.2. Ocular Examination

All ocular examinations were performed by the same experienced technician, and laboratory tests were performed by the same examiner. A routine ophthalmological examination was performed for each participant to confirm that there was no ophthalmological pathology. Participants were evaluated at appointments at the following times: the first trimester, second trimester, and third trimester of pregnancy and 6 weeks after delivery.

Intraocular pressure (IOP) was measured in both eyes (right eye first) using a noncontact tonometer (TX-20 model) (Canon, Tokyo, Japan) in auto mode at the same time of the day (before 10:00 AM to avoid the influence of diurnal variations). The anterior corneal parameters, including horizontal keratometry (K1), vertical keratometry (K2), anterior chamber depth (ACD), and axial length (AL), were measured by IOL Master (Zeiss, Germany). Central corneal thickness (CCT) and corneal endothelial cells (CECs) were assessed with a specular microscope (SP-2000P), and the tear meniscus height (TMH) and break-up time (BUT) data were obtained using an ocular surface analyser. An optical coherence tomography scanner (Zeiss Cirrus) was used to analyse macular volume (MV) by scanning the optic nerve, central subfield thickness (CST) and cube average thickness (CAT), and the thickness of the retinal nerve fibre layer (RNFL) was circumferentially measured along the optic nerve papilla using six concentric circular patterns.

Three measurements were taken for each eye, and the average value was included in the analysis to avoid inter-eye correlation and to increase the sensitivity to systemic changes.

2.3. Hormonal Levels

At each visit, we collected 4.0 ml of venous blood into vacutainer tubes (Kangjie

Medical Instrument Co. Ltd. Jiangsu, China) to measure the levels of hormones, including oestradiol, progesterone, luteinizing hormone, and follicle-stimulating hormone. Beta human chorionic gonadotropin (β-hCG) levels were not tested postpartum, and human prolactin (hPL) levels were measured only postpartum owing to the fluctuation of this hormone during pregnancy.

2.4. Statistical Analysis

All statistical analyses were performed using SPSS (version 22.0; IBM, New York, USA). The Kolmogorov-Smirnov test was used to demonstrate the normal distribution of data for all groups. The data are presented as the mean ± standard deviation (SD). A comparison of the ophthalmological parameters during pregnancy was performed using repeated-measures analysis of variance (repeated-measures ANOVA) with Bonferroni correction for multiple comparisons. The linear correlation between the ocular parameters and hormone levels was explored using Pearson's correlation (if the data were normally distributed) and Spearman's correlation (for non-normally distributed data). The significance level $p < 0.05$ was adopted.

3. Results

3.1. Demographic Data of the Study Participants

The mean age of the 12 pregnant women was 33.36 ± 3.90 (27 - 37) years. More than half of the pregnant women (7/12) had refractive errors, which were associated with their years of education.

3.2. Ocular Parameters in Different Trimesters of Pregnancy

The parameter value change differences between groups are shown in **Figure 1** and **Figure 2**. The comparison of the following study parameters between groups is shown in **Table 1**: IOP, K1, K2, AL, ACD, CCT, CEC, TMH, BUT, MV, CST, CAT, and RNFL. The results were pairwise compared at 4 time points for repeated-measures ANOVA. Bold font is used to indicate parameters with statistically significant differences. A statistically significant difference was found in IOP in the third trimester compared with the first and second trimester and postpartum measurements ($p < 0.05$). The IOP was found to be lowest in the third trimester (12.99 ± 2.01 mmHg). The MV in the second trimester was significantly higher than that in the first trimester ($p = 0.023$), but there was no significant difference in MV between the third trimester and postpartum.

In the quantitative assessments during the first, second, and third trimesters of pregnancy and at 6 weeks postpartum, no statistically significant differences were found regarding the mean K1, K2, AL, ACD, CCT, CEC, TMH, BUT, CST and CAT values. There was no statistically significant difference in the other parameters between measurement periods ($p > 0.05$ for all time points) (**Table 1**).

Table 1. Clinical data (presented as the mean ± SD) of the pregnant women (n = 12).

Variable	1st Trimester	2nd Trimester	3rd Trimester	Postpartum	p (1 vs 2)	p (1 vs 3)	p (1 vs 4)	p (2 vs 3)	P (2 vs 4)	p (3 vs 4)
CEC	2593.55 ± 249.24	2628.18 ± 244.58	2615.35 ± 238.12	2605.43 ± 228.96	1.000	1.000	1.000	1.000	1.000	1.000
CCT (mm)	0.54 ± 0.03	0.54 ± 0.03	0.54 ± 0.02	0.54 ± 0.04	0.287	1.000	1.000	1.000	1.000	1.000
AL (mm)	24.15 ± 1.34	24.16 ± 1.35	24.17 ± 1.34	24.12 ± 1.31	1.000	1.000	0.677	0.969	0.703	0.228
K1 (D)	43.30 ± 1.38	43.34 ± 1.37	43.37 ± 1.46	43.29 ± 1.41	1.000	0.796	1.000	1.000	1.000	0.653
K2 (D)	44.29 ± 1.27	44.27 ± 1.29	44.33 ± 1.30	44.36 ± 1.34	1.000	1.000	1.000	1.000	1.000	1.000
ACD (mm)	3.38 ± 0.30	3.40 ± 0.30	3.42 ± 0.31	3.38 ± 0.30	0.789	0.255	1.000	1.000	1.000	0.459
CST (um)	236.38 ± 19.77	237.04 ± 22.54	238.67 ± 21.44	236.50 ± 20.20	1.000	1.000	0.149	0.492	1.000	0.697
MV (mm^2)	9.77 ± 0.22	9.858 ± 0.254	9.871 ± 0.230	9.804 ± 0.291	**0.023**	0.091	1.000	1.000	0.428	0.885
CAT (um)	272.71 ± 6.26	273.83 ± 7.21	274.17 ± 6.60	272.79 ± 6.68	1.000	1.000	1.000	1.000	1.000	1.000
RNFL (um)	100.38 ± 6.57	101.46 ± 6.97	102.08 ± 7.58	100.04 ± 7.58	1.000	0.084	1.000	1.000	0.630	**0.011**
TMH (mm)	0.23 ± 0.04	0.24 ± 0.06	0.25 ± 0.04	0.23 ± 0.05	1.000	0.274	1.000	1.000	1.000	0.357
BUT (s)	9.16 ± 7.34	9.81 ± 4.13	8.73 ± 4.70	8.64 ± 5.48	1.000	1.000	1.000	1.000	1.000	1.000
IOP (mmHg)	14.30 ± 1.90	13.83 ± 2.19	12.99 ± 2.01	13.59 ± 1.89	0.909	**0.002**	0.052	**0.006**	1.000	**0.050**

One-way analysis of variance for repeated measures. Bold values indicate significance at the $p < 0.05$ level. Abbreviations: CEC, corneal endothelial cell; CCT, central corneal thickness; AL, axial length; K1, flat keratometry; K2, steep keratometry; ACD, anterior chamber depth; CST, central subfield thickness; MV, macular volume; CAT, cube average thickness; RNFL: retinal nerve fibre layer; TMH: tear meniscus height; BUT, break-up time; IOP, intraocular pressure. 1 vs. 2 means comparison between the 1st trimester and the 2nd trimester; 1 vs. 3 means comparison between the 1st trimester and the 3rd trimester; 1 vs. 4 means comparison between the 1st trimester and postpartum; applied for the latter.

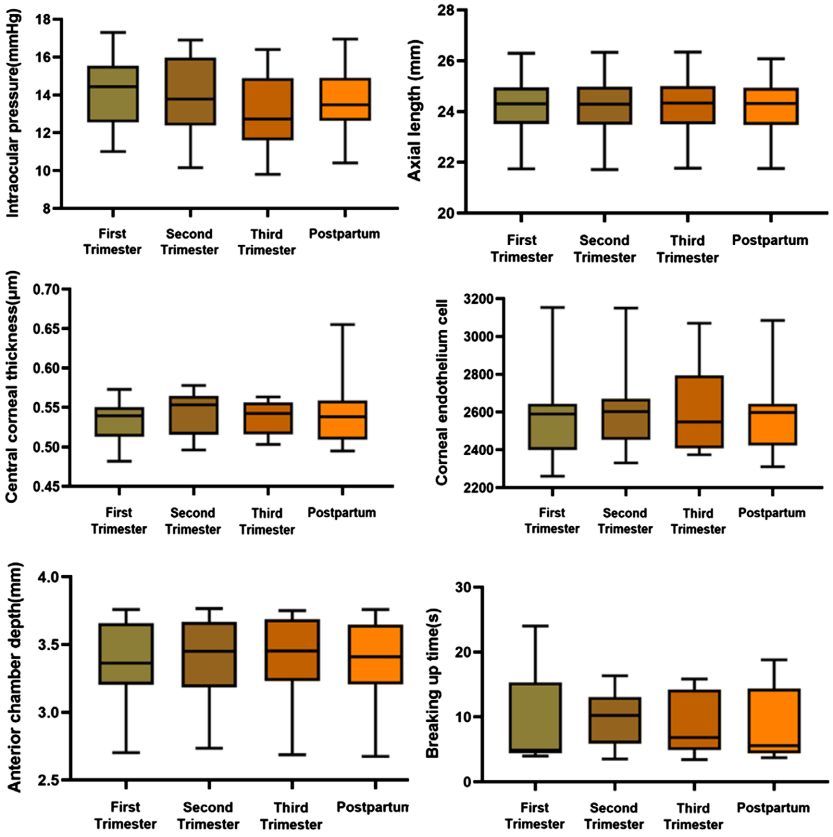

Figure 1. Mean ± SD study parameters (IOP, AL, CCT, CEC, ACD and BUT) according to trimester.

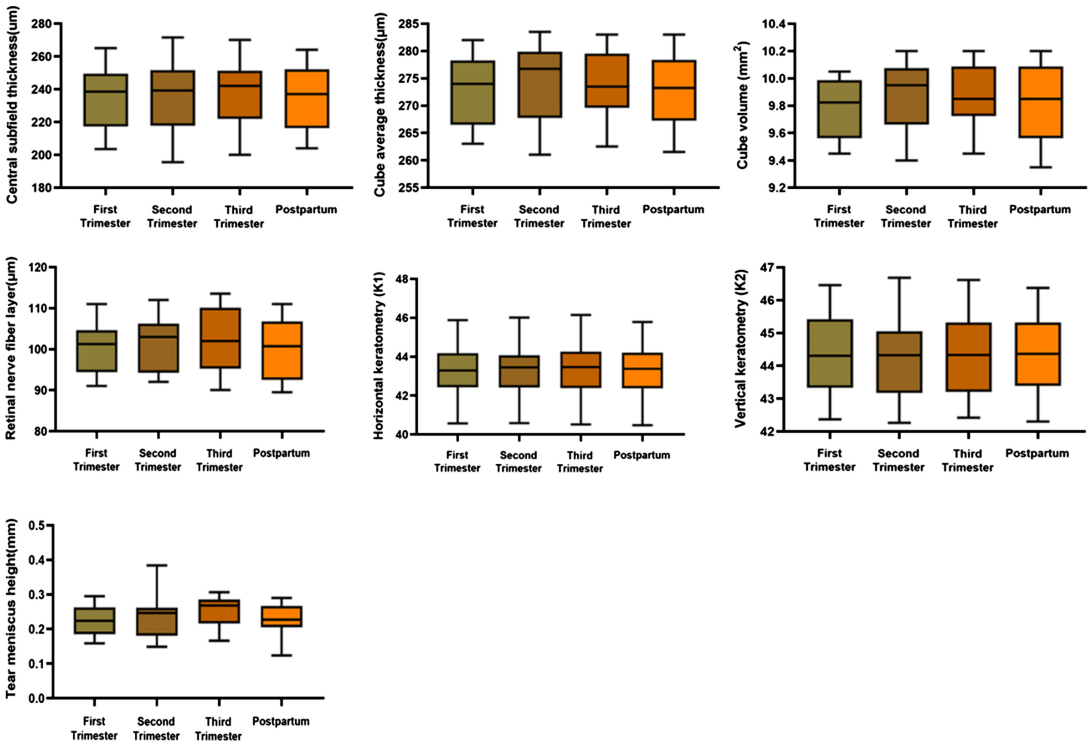

Figure 2. Mean ± SD study parameters (CST, CAT, CV, RNFL, K1, K2 and TMH) according to trimester.

3.3. Correlations between Hormone Levels

The specific concentrations of oestrogen and progesterone in the third trimester could not be evaluated because their levels exceed the threshold values of the measurement instrument. Thus, we did not perform a correlation analysis on those data.

The partial correlations between biomechanical parameters and hormone levels are listed in Tables 2-7. We analysed the correlation between the levels of different hormones in different trimesters and different parameters. β-hCG levels peaked in the first trimester, but there was a significant positive correlation between β-hCG levels and K2, ACD, and TMH only in the second trimester (rk2 = 0.588, p = 0.045; rACD = −0.740, p = 0.006; rTMH = 0.642, p = 0.024). In studying the correlation between ophthalmological parameters and luteinizing hormone levels, we found a significantly negative correlation with MV (r = −0.598, p = 0.040 in the first trimester; r = −0.672, p = 0.017) and CAT (r = −0.598, p = 0.040 in the first trimester; r = −0.672, p = 0.040 in the second trimester). Luteinizing hormone levels were correlated with ACD (r = −0.702, p = 0.011) in the 2nd trimester and K2 (r = 0.585, p = 0.046) in the 3rd trimester. A negative correlation was found between follicle stimulating hormone levels and CEC, MV and CAT in the first trimester (r = −0.677, p = 0.016; r = −0.602, p = 0.039; r = −0.584, p = 0.046; respectively) and AL in the third trimester (r = −0.618, p = 0.032). Interestingly, we found that oestradiol levels were correlated

Table 2. Correlations between β-hCG levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester	
	r	p	r	p	r	p
CEC	−0.493	0.103	−0.029	0.929	−0.089	0.783
CCT (mm)	−0.342	0.276	0.265	0.405	−0.300	0.344
AL (mm)	−0.039	0.905	−0.407	0.189	−0.445	0.147
K1 (D)	0.119	0.712	0.469	0.124	0.449	0.143
K2 (D)	0.062	0.847	0.588*	**0.045**	0.397	0.201
ACD (mm)	−0.245	0.442	−0.740**	**0.006**	−0.233	0.466
CST (um)	−0.155	0.631	−0.131	0.684	−0.229	0.475
MV (mm^2)	−0.490	0.106	−0.089	0.784	−0.245	0.442
CAT (um)	−0.493	0.103	−0.081	0.803	−0.268	0.400
RNFL (um)	−0.311	0.325	−0.150	0.642	−0.152	0.638
TMH (mm)	−0.220	0.493	0.642*	**0.024**	−0.113	0.727
BUT (s)	0.069	0.832	0.421	0.173	−0.017	0.958
IOP (mmHg)	0.361	0.249	0.154	0.633	−0.058	0.859

Bold values indicate significance at the $p < 0.05$ level.

Table 3. Correlations between luteinizing hormone levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester		Postpartum	
	r	p	r	p	r	p	r	p
CEC	−0.615*	**0.033**	−0.040	0.901	0.324	0.304	−0.500	0.098
CCT (mm)	−0.016	0.961	0.394	0.205	−0.299	0.345	−0.124	0.701
AL (mm)	−0.180	0.575	−0.233	0.467	−0.300	0.344	0.100	0.757
K1 (D)	0.444	0.148	0.359	0.252	0.516	0.086	0.357	0.255
K2 (D)	0.295	0.352	0.366	0.242	0.585*	**0.046**	0.214	0.503
ACD (mm)	0.004	0.990	−0.702*	**0.011**	0.010	0.976	0.103	0.750
CST (um)	−0.116	0.720	−0.386	0.216	−0.011	0.974	−0.150	0.641
MV (mm^2)	−0.598*	**0.040**	−0.672*	**0.017**	−0.035	0.913	−0.441	0.151
CAT (um)	−0.599*	**0.040**	−0.655*	**0.021**	−0.011	0.973	−0.467	0.126
RNFL (um)	−0.125	0.699	0.124	0.700	−0.063	0.847	−0.246	0.441
TMH (mm)	0.011	0.973	0.293	0.356	0.013	0.969	0.559	0.059
BUT (s)	0.076	0.813	−0.309	0.328	0.166	0.606	0.112	0.728
IOP (mmHg)	0.122	0.705	0.291	0.359	−0.453	0.139	−0.051	0.875

Bold values indicate significance at the $p < 0.05$ level.

Table 4. Correlations between follicle-stimulating hormone levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester		Postpartum	
	r	p	r	p	r	p	r	p
CEC	−0.677*	**0.016**	−0.019	0.954	0.119	0.712	−0.500	0.998
CCT (mm)	0.086	0.790	0.334	0.288	0.002	0.995	−0.124	0.439
AL (mm)	−0.056	0.863	0.030	0.926	−0.618*	**0.032**	0.100	0.097
K1 (D)	0.459	0.134	0.084	0.796	0.540	0.070	0.357	0.013
K2 (D)	0.334	0.289	0.041	0.898	0.564	0.056	0.214	0.021
ACD (mm)	0.212	0.508	−0.062	0.848	−0.456	0.136	0.103	0.955
CST (um)	0.104	0.748	0.141	0.663	−0.244	0.445	−0.150	0.561
MV (mm^2)	−0.602*	**0.039**	−0.267	0.401	−0.131	0.686	−0.441	0.879
CAT (um)	−0.584*	**0.046**	−0.305	0.335	−0.075	0.817	−0.467	0.933
RNFL (um)	−0.154	0.633	−0.417	0.177	0.263	0.409	−0.246	0.962
TMH (mm)	−0.121	0.708	−0.236	0.460	−0.161	0.616	0.559	0.881
BUT (s)	−0.191	0.552	0.317	0.315	0.147	0.648	0.112	0.224
IOP (mmHg)	−0.163	0.614	−0.016	0.961	−0.082	0.800	−0.051	0.474

Bold values indicate significance at the $p < 0.05$ level.

Table 5. Correlations between oestradiol levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester		Postpartum	
	r	p	r	p	r	p	r	p
CEC	0.468	0.125	0.045	0.889	-	-	0.369	0.238
CCT (mm)	0.260	0.415	−0.485	0.110	-	-	0.326	0.301
AL (mm)	−0.283	0.373	−0.100	0.758	-	-	−0.284	0.371
K1 (D)	−0.084	0.795	0.000	0.999	-	-	0.151	0.639
K2 (D)	−0.028	0.930	0.007	0.983	-	-	0.326	0.301
ACD (mm)	−0.533	0.074	0.194	0.546	-	-	−0.471	0.122
CST (um)	−0.621*	**0.031**	−0.087	0.789	-	-	−0.385	0.217
MV (mm^2)	−0.032	0.922	0.321	0.309	-	-	−0.088	0.785
CAT (um)	−0.039	0.904	0.361	0.249	-	-	0.091	0.779
RNFL (um)	0.452	0.140	0.396	0.203	-	-	0.594*	**0.041**
TMH (mm)	0.318	0.314	0.144	0.656	-	-	−0.097	0.765
BUT (s)	0.243	0.447	−0.252	0.430	-	-	0.200	0.533
IOP (mmHg)	0.327	0.300	−0.103	0.750	-	-	−0.061	0.851

Bold values indicate significance at the $p < 0.05$ level.

Table 6. Correlations between progesterone levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester		Postpartum	
	r	p	r	p	r	p	r	p
CEC	0.318	0.315	−0.061	0.850	-	-	−0.370	0.237
CCT (mm)	−0.299	0.344	−0.269	0.397	-	-	−0.115	0.721
AL (mm)	0.055	0.865	−0.047	0.885	-	-	0.159	0.622
K1 (D)	−0.190	0.554	0.129	0.689	-	-	0.117	0.717
K2 (D)	−0.093	0.775	0.039	0.905	-	-	0.174	0.589
ACD (mm)	0.290	0.361	0.363	0.246	-	-	−0.050	0.877
CST (um)	0.205	0.524	−0.071	0.826	-	-	0.094	0.770
MV (mm^2)	0.583*	**0.047**	0.310	0.326	-	-	0.075	0.817
CAT (um)	0.352	0.262	0.305	0.335	-	-	0.090	0.782
RNFL (um)	0.056	0.862	0.136	0.672	-	-	−0.422	0.171
TMH (mm)	0.762**	**0.004**	0.115	0.723	-	-	0.473	0.120
BUT (s)	0.347	0.270	0.471	0.122	-	-	0.427	0.166
IOP (mmHg)	−0.216	0.501	−0.053	0.870	-	-	−0.097	0.764

Bold values indicate significance at the $p < 0.05$ level.

Table 7. Correlations between human prolactin levels and biomechanical parameters during pregnancy.

Parameter	1st Trimester		2nd Trimester		3rd Trimester		Postpartum	
	r	p	r	p	r	p	r	p
CEC	-	-	-	-	-	-	−0.198	0.536
CCT (mm)	-	-	-	-	-	-	0.549	0.064
AL (mm)	-	-	-	-	-	-	0.280	0.378
K1 (D)	-	-	-	-	-	-	−0.163	0.612
K2 (D)	-	-	-	-	-	-	−0.225	0.482
ACD (mm)	-	-	-	-	-	-	−0.095	0.769
CST (um)	-	-	-	-	-	-	−0.222	0.488
MV (mm^2)	-	-	-	-	-	-	−0.396	0.202
CAT (um)	-	-	-	-	-	-	−0.342	0.276
RNFL (um)	-	-	-	-	-	-	0.212	0.508
TMH (mm)	-	-	-	-	-	-	−0.003	0.992
BUT (s)	-	-	-	-	-	-	−0.137	0.671
IOP (mmHg)	-	-	-	-	-	-	0.166	0.607

Bold values indicate significance at the $p < 0.05$ level.

only with the ocular parameters CST in the first trimester ($r = -0.621$, $p = 0.031$) and RNFL ($r = 0.594$, $p = 0.041$) postpartum. In addition, our work showed a statistically significant correlation between progesterone levels and MV ($r = 0.583$, $p = 0.047$) and TMH ($r = 0.762$, $p = 0.004$) in the first trimester. In the postpartum period, there were no significant correlations between the ocular parameters evaluated and prolactin levels (all $p > 0.05$).

4. Discussion

Physiological changes are induced by hormones released from the placenta in almost all tissues and organ systems, and the visual system is no exception. Despite numerous previous studies, no precise mechanism to explain the changes in some tissues and organs during pregnancy has been determined [10]. Pregnancy-induced ocular changes have been reported by many authors, but this study differs from earlier reports in those changes in ocular parameters, including anterior and posterior parameters, were observed during each trimester of pregnancy and in the postpartum period, and hormone levels were measured at these same time points in the same population.

In our study, IOP decreased throughout the trimesters, particularly during the third trimester, and returned to normal levels postpartum, which confirmed the observations of many studies and has been well documented in the literature [11] [12] [13]. Although the exact mechanism responsible for IOP reduction

during pregnancy is not well known, several possible factors are generally agreed upon. First, an increase in the levels of the hormones oestrogen, progesterone, and β-hCG could lead to an expansion in aqueous outflow and a reduction in systemic vascular resistance, leading to diminished episcleral venous pressure [14]. Another hypothesis is that excess progesterone acts as a glucocorticoid antagonist to block the ocular hypertensive effect of endogenous steroids [15]. Although, Spoerl *et al.* [16] reported that connective tissue loosening, indicated by parameters such as increased CCT, could reduce the stiffness of the corneoscleral wall and lead to a mistakenly low IOP measurement based on stress-strain curves. There were no significant differences in the CCT measurements during the three trimesters and postpartum in our study, which was consistent with the study conducted by the Sen team [17]. Finally, the expanded tissue flexibility of aqueous outflow could lead to an increase in ACD, although there was no significant difference in ACD during the three trimesters in our study [12]. However, there are no further studies regarding the plasticity mechanisms in the anterior chamber.

At present, there is still no explicit evidence in the literature concerning the influence of pregnancy on CEC. Örnek *et al.* [18] first reported that endothelial cell density was decreased in the first trimester and increased in the second and third trimesters, but the difference was not significant ($p > 0.05$), and the hexagonal cell ratio was decreased significantly in the first trimester ($p < 0.05$). However, an increasing number of researchers have pointed out that this study did not exclude patients who used contact lenses, which could lead to incorrect conclusions.

There was no general conclusion on the changes in corneal curvature in pregnancy. It is well known that the biomechanical stability of the cornea and the surrounding soft tissue pressure on the cornea may affect corneal curvature, which was confirmed in other studies [10] [19]. In contrast, other studies [7] [12] found no significant alterations in K1 and K2 values related to pregnancy. Similarly, our study showed no statistically significant differences in K1 and K2 values during pregnancy and after delivery.

In line with Ataş *et al.* [20], we found that the thickness of the RNFL was significantly higher in pregnant women in their 3rd trimester ($p = 0.011$). However, we did not find any difference in CST or CAT, in contrast with the results of Ataş *et al.* [20]. And Sayin *et al.* [21]. A prospective cross-sectional study carried out by Sait Alim [22] demonstrated that the mean RNFL thickness was higher in the twin pregnancy group than in the singleton and healthy nonpregnant groups. However, in a comparative study of 39 pregnant and 50 nonpregnant women, Liu, CC *et al.* [23] found that the retinal thickness of patients with high myopia during the third trimester of pregnancy was thinner than that of nonpregnant women with age-matched high myopia. Teberik, K *et al.* [24] reported that the average thickness of the RNFL in the different sectors was significantly higher in women with polycystic ovary syndrome than in healthy women. Therefore, the increase in the axial length in this study may result from the con-

comitant increase in the RNFL. Some theories suggest that elevated hormonal levels may cause fluid retention in all organs during pregnancy, which can be responsible for increased RNFL, especially in the third trimester [25]. However, no low reflection indicative of fluid retention was found in the OCT images obtained in this study.

In this study, we found that there was no uniform agreement between the dynamic changes in ocular parameters and their correlation with hormone levels. This finding thus convinced us that pregnancy is a very complex process involving many physiological changes and that these physiological changes in ocular parameters in each period were not determined by one specific factor alone. It was also possible that this finding was related to the fact that we excluded the influence of heterogeneity through our selection of study participants. The interactions between hormone levels and ocular changes would be as meaningful as they are complex, and more research should be designed in the future.

The current study has some limitations. Further studies with larger study populations and longer follow-up durations should be performed. Another limitation is the lack of specific values for oestradiol and progesterone levels in the third trimester. Furthermore, tests of ocular blood flow should be designed to investigate how these hormones (and which hormones) regulate physiological or pathogenic processes.

5. Conclusion

In this study, we revealed physiological fluctuations in ophthalmic conditions, in which the magnitude of the differences in various parameters was not clinically significant, and these conditions returned to normal levels after delivery. However, our study did not identify significant ocular changes related to fluctuations in hormone levels during and after pregnancy.

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Authors' Contributions

JT Zhou designed the studies and collected the data. FY Chen performed the statistical analysis and drafted the manuscript. XJ He participated in technical support. XX Han and Qing Zhou critically revised the intellectual content and approved the final version to be published. All authors reviewed the manuscript.

Availability of Data and Materials

The dataset used and/or analyzed during the current study is available from the corresponding author on reasonable request.

Ethics Approval and Consent to Participate

The research protocol was approved by the First Affiliated Hospital of Jinan University Ethics Committee and adhered to the tenets of the Declaration of Helsinki. Written informed consent was obtained from each subject before enrolment in the study.

Conflicts of Interest

The authors have no proprietary or commercial interest in any materials discussed in this article.

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Abbreviations

CEC, Corneal Endothelial Cell; CCT, Central Corneal Thickness; AL, Axial Length; K1, flat Keratometry; K2, steep Keratometry; ACD, Anterior Chamber Depth; CST, Central Subfield Thickness; MV, Macular Volume; CAT, Cube Average Thickness; RNFL: Retinal Nerve Fibre Layer; TMH: Tear Meniscus Height; BUT, Breakup Time; IOP, Intraocular Pressure; β-hCG, beta-human Chorionic Gonadotropin; hPL, human Prolactin.