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Central Retinal Artery Doppler Resistance Index (RI) and Pulsatility Index (PI) Study in Assessment of Diabetic Retinopathy

Conflict of interest: nothing to declare.
Authors' contribution: Huda Danon – conceptualization, data curation, investigation, methodology, project administration, resources, software, visualization, writing (original draft), review & editing; Firas Albaghdadi, Imad Sachit – conceptualization, data curation, supervision, validation, visualization, writing (original draft), review & editing.

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Abstract

Introduction. Diabetic retinopathy (DR) is one of commonest DM microvascular complications, and a leading reason of blindness. The DR progression is ranging from mild non-proliferative diabetic retinopathy (NPDR) abnormalities, to moderate and severe NPDR, to proliferative diabetic retinopathy (PDR) and macular edema. Ocular ultrasound (OUS) is a widely used tool for evaluating a variety of eye illnesses, when ophthalmoscopy is not possible due to opacity of the lens and in peri-orbital edema.
Purpose. The study aimed to estimate the ocular blood flow indices in patients with diabetic retinopathy, and to evaluate the blood flow parameters in the central retinal artery in patients with PDR and NPDR and to compare the findings with a control group of healthy subjects.
Materials and methods. A prospective study conducted in Al-Haboubi Teaching Hospital. Totally, 96 individuals enrolled, 25 patients diagnosed with proliferative DR, 25 patients with non-proliferative DR, 23 diabetic patients without DR and 23 healthy individuals. Radiological images of the eyes performed in all subjects using a Color Doppler and gray scale sonography.
Results. ANOVA test revealed that RI (max), RI (mean), PI (max) and PI (mean) were significantly difference among all groups. The areas under curve (AUC) of RI (max), RI (mean), PI (max), and PI (mean) were 0.823, 0.965, 0.707, and 0.874, respectively. RI of central retinal artery (CRA) had high sensitivity and specificity, at various cut off values.
Conclusions. Older age, long duration of DM and high level of HbA1c are greatly impact Doppler US indices. The highest means peak of RI, and PI reported is in the PDR indicated the progress of DR. The highest areas under curve (AUC) for RI (mean), RI (max), and PI (mean) indicate that RI (max), and PI (mean) are most better indices for diagnose CRA retinopathy.
Keywords: central retinal artery, doppler study, resistance index, pulsatility index, diabetic retinopathy

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Исследование индекса доплеровского сопротивления центральной артерии сетчатки (RI) и индекса пульсации (PI) при оценке диабетической ретинопатии

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Резюме

Введение. Диабетическая ретинопатия (ДР) является одним из наиболее распространенных микрососудистых осложнений сахарного диабета (СД) и основной причиной слепоты. Прогрессирование ДР варьируется от легких непролиферативных нарушений диабетической ретинопатии (ННДР) до умеренных и тяжелых ННДР, пролиферативной диабетической ретинопатии (ПДР) и отека макулы. Ультразвуковое исследование глаза является широко используемым инструментом для оценки различных заболеваний органа зрения, когда офтальмоскопия невозможна из-за непрозрачности хрусталика или при периорбитальном отеке.
Цель. Оценка показателей глазного кровотока у пациентов с диабетической ретинопатией и параметров кровотока в центральной артерии сетчатки у пациентов с ПДР и ННДР и сравнение результатов с контрольной группой здоровых лиц.
Материалы и методы. Проспективное исследование проведено в учебной больнице Аль-Хабуби, всего в него были включены 96 человек: 25 пациентов с пролиферативной ДР, 25 пациентов с непролиферативной ДР, 23 пациента с диабетом без ДР и 23 практически здоровых человека. Рентгенологические изображения глаз были сделаны у всех испытуемых с использованием цветного доплера и серой шкалы сонографии.
Результаты. Тест ANOVA показал, что RI (макс.), RI (среднее), PI (макс.) и PI (среднее) значительно различались между всеми группами. Площади под кривой (AUC) RI (макс.), RI (среднее), PI (макс.) и PI (среднее) составили 0,823, 0,965, 0,707 и 0,874 соответственно. RI центральной артерии сетчатки имел высокую чувствительность и специфичность при различных пороговых значениях.
Выводы. Пожилой возраст, большая продолжительность СД и высокий уровень HbA1c оказывают значительное влияние на индексы доплеровского УЗИ. Самый высокий средний пик RI и PI при ПДР указывает на прогрессирование ДР. Самые высокие площади под кривой (AUC) для RI (среднее), RI (макс.) и PI (среднее) указывают на то, что RI (макс.) и PI (среднее) являются лучшими индексами для диагностики ретинопатии центральной артерии сетчатки.

Ключевые слова: центральная ретинальная артерия, доплеровское исследование, индекс резистентности, индекс пульсации, диабетическая ретинопатия

■ INTRODUCTION

Diabetic retinopathy (DR) is one of commonest DM microvascular complications, a leading reason of blindness and it occurring because of the long-term effects of DM, it causes vision-threatening damage to the retina, and causing blindness [1–3].

The DR progression is ranging from mild non-proliferative diabetic retinopathy (NPDR) abnormalities (raised vascular permeability), to moderate and severe NPDR (vascular closure), to proliferative diabetic retinopathy (PDR) (new vessels growth on retina and posterior substance of vitreous) and macular edema [4]. The DR prevalence influenced by many factors which are DM duration, DM type, blood sugar poor control, hypertension, dyslipidemia and raise urinary albumin-to-creatinine ratio [5]. Uncontrolled DM led to ocular disorders as glaucoma, cataracts, ocular surface disorders, non-arteritic anterior ischemic optic-neuropathy, recurrent stye, diabetic papillopathy and DR [6].

Ocular ultrasound (OUS) is a widely used tool for evaluating a variety of eye illnesses, when ophthalmoscopy is not possible due to opacity of the lens and in peri-orbital edema. An US examination is an accessible, easy, quick, non-invasive, and dynamic technique. Doppler US (DUS) examination of the ophthalmic vessels has become a very useful for detection of various vascular eye diseases. DUS allow for examining ocular blood flow even in the presence of dense ocular opacities that cover a posterior segment direct view of the eye. In addition, compared to angiography with fluorescein, DUS allow for assessing ocular blood flow in a non-invasive manner [7–9].

These are diagnostic adjunctive roles in persistent fetal vasculature, intrabulbar tumors, arterial occlusion, ocular ischemic syndrome and carotid cavernous fistula; as prognostication and follow-up in Glaucoma, thyroid eye diseases, DR, vascular malformations and Mucormycosis; and age-related macular degeneration, CRVO, central serous chorio-retinopathy, Sickle cell disease, Behcet disease and orbital cysticercosis [10].

■ MATERIALS AND METHODS

Study design and setting

A combine retrospective-prospective study conducted in Department of Surgery, Al-Haboubi Teaching Hospital. Totally, 96 individuals enrolled, 25 patients diagnosed with proliferative DR, 25 patients with non-proliferative DR, 23 diabetic patients without DR and 23 healthy individuals, during the period from 12th June 2024 to 2nd February 2025. The study sample consisted of 44 males and 51 females, with their age mean (median) was 50.23±10.49 (49) years.

Inclusion Criteria

- Patients with DR (PDR and NPDR).
- Diabetic cases without retinopathy.
- Both genders.
- Age between 25–75 years.

Exclusion Criteria

- Inflammatory and infectious eye diseases.
- Orbital benign or malignant lesions.
- Ophthalmic surgeries and trauma.
- Laser photocoagulation therapy.
- Anomalies.
- Glaucoma.
- Eye traumas.

Data collection

These were included age of subject, gender, side of eye involve with retinopathy, minimum, maximum, median and mean of RI and PI. In addition, type of DR, duration of DM and the level of HbA1c.

Blood flow Doppler indices [11–13].

Resistance index (RI), i. e., ratio of the difference between systolic and diastolic velocities to the systolic velocity of blood flow (normal = 0.69).

Pulsatility index (PI), defined as the difference between the peak systolic flow and minimum diastolic flow velocity, divided by the mean velocity documented throughout the cardiac cycle (normal = 1.05).

DR assessment

The diagnosis of DR done by expert ophthalmologists. The dilated fundoscopy using the bio-microscopic indirect ophthalmoscope to diagnosed DR according to the definition by the presence of microaneurysms, hemorrhage, and hard exudates, according to retinopathy level 2–3 in the Airlie House classification [13].

Ethical considerations

Written informed consent was obtained from the patients for participating in this study. The study conforms to the 1995 Helsinki declaration and was approved by The Medical Ethical Committee of College of medicine, University of Thi-Qar (No. 7/54/142 in 27/02/2025).

Statistical analysis

Statistical package for social science (SPSS statistics for windows, version 26.0, Chicago: SPSS, Inc.) software version 24 was used. Results were described in the form of frequencies and percentage distribution for qualitative data and mean and SD for quantitative data. One-way ANOVA followed by post-hoc comparison was used to estimated differences in quantitative variables within three or more groups. Paired samples T-test was used to estimated differences in quantitative variables within two groups. The area under a receiver operating characteristic (ROC) curve was used to evaluated the diagnostic performance. The sensitivity, specificity, PPV, NPP, accuracy index was calculated. A one-sided P value of 0.05 or less was considered statistically significant [14, 15].

■ RESULTS

Among control group, the mean age was 44.5±10.43 years with median of 43.5 years. Among gender, results observed 10 (45.5%) were male, and 12 (54.5%) of patients were

female. In DM without retinopathy group, the mean age was 51.3±10.43 years with median of 50 years. Among gender, findings observed 12 (52.2%) were male, and 11 (47.8%) of patients were female. The mean (median) duration of DM was 8.9 (9) years, besides, more individuals reported diabetic more than ten years. The mean (median) concentration of HbA1C was 5.7 (5.7) mmol/mol. In PDR group, the mean age was 46.12±5.7 years with median of 47 years. Among gender, results observed 9 (36%) were male, and 16 (64%) were female. Both sides of eye involved documented in 19 (76%) cases. Left side only in five and one case right eye involved. The mean (median) duration of DM was 12.08 (9) years, besides, more individuals reported diabetic below than ten years. The mean (median) concentration of HbA1C was 9.4 (9) mmol/mol. In NPDR, the mean age was 58.72±9.04 years with median of 58 years. Among gender, results observed 13 (52%) were male, and 12 (48%) were female. Left side involved was most frequent (13, 52%) of cases. The mean (median) duration of DM was 9.08 (10) years, besides, more individuals reported diabetic more than ten years. The mean (median) concentration of HbA1C was 8.14 (8.2) mmol/mol (Table 1).

Table 1
General characters

Group	Character		No.	%
Control	Age (years) Mean±SD (Median) = 44.5±10.43 (43.5)	20–30 31–40 41–50 >50	3 5 8 16	13.6 22.7 36.4 27.3
	Gender	M	10	45.5
		F	12	54.5
DM without retinopathy	Age (years) Mean±SD (Median) = 51.3±10.43 (50)	30–40	5	21.7
		41–50	8	34.8
		>50	10	43.5
	Gender	M	12	52.2
		F	11	47.8
	DM duration (years) Mean±SD (Median) = 8.9±1.7 (9)	<10	12	52.2
		≥10	11	47.8
	$HbA1_C$ (mmol/mol) Mean±SD (Median) = 5.7±0.5 (5.7)	≤5.7	12	52.2
		>5.7	11	47.8
PDR	Age (years) Mean±SD (Median) = 46.12±5.7 (47)	30–40	4	16
		41–50	18	72
		>50	3	12
	Gender	M	9	36
		F	16	64
	Side	Right	1	4
		Left	5	20
		Both	19	76
	DM duration (years) Mean±SD (Median) = 12.08±5.5 (9)	<10	14	56
		≥10	11	44
	$HbA1_C$ (mmol/mol) Mean±SD (Median) = 9.4±0.47 (9)	≤5.7	0	0
		>5.7	25	100

End of table 1

NPDR	Age (years) Mean±SD (Median) = 58.72±9.04 (58)	40–50	8	32
		51–60	6	24
		>60	11	44
	Gender	M	13	52
		F	12	48
	Side	Right	5	20
		Left	13	52
		Both	7	28
	DM duration (years) Mean±SD (Median)= 9.08±4.39 (10)	<10	10	40
		≥10	15	60
	$HbA1_c$ (mmol/mol) Mean±SD (Median) = 8.14±1.52 (8.2)	≤5.7	0	0
		>5.7	25	100

Doppler US indices mean±SD (median) including RI (max), RI (mean), PI (max), and PI (mean) were recorded as following: in control group [0.62±0.01 (0.62), 0.61±0.02 (0.62), 1.17±0.37 (1.06), and 1.13±0.29 (1.01), respectively], in DM without retinopathy [0.67±0.04 (0.69), 0.66±0.02 (0.65), 1.24±0.22 (1.17), and 1.13±0.23 (1.08), respectively], in PDR [0.74±0.03 (0.74), 0.75±0.03 (0.76), 1.81±1.07 (1.24), and 1.29±0.11 (1.31), respectively], in NPDR [0.73±0.04 (0.73), 0.65±0.07 (0.62), 1.25±0.14 (1.24), 1.07±0.15 (1.06), respectively] (Table 2).

Doppler parameters for assessment of DR in central retinal artery by Post Hoc Tukey and ANOVA analysis was listed in Table (3). ANOVA test revealed that RI (max), RI (mean), PI (max) and PI (mean) were significantly difference among all groups (F=78.83; p<0.0001, F=41.37; p<0.0001, F=6.18; p=0.0007 and F=3.93; p=0.011), respectively. The Tukey tests

Table 2
Control group Doppler US parameters

Group	* Parameter (cm/sec)	Mean±SD	Median	Max	Min
Control	1	0.62±0.01	0.62	0.65	0.61
	2	0.61±0.02	0.62	0.63	0.57
	3	1.17±0.37	1.06	2.06	0.93
	4	1.13±0.29	1.01	1.83	0.94
DM without retinopathy	1	0.67±0.04	0.69	0.71	0.62
	2	0.66±0.02	0.65	0.65	0.63
	3	1.24±0.22	1.17	1.69	1.01
	4	1.13±0.23	1.08	1.82	1.00
PDR	1	0.74±0.03	0.74	0.78	0.7
	2	0.75±0.03	0.76	0.79	0.7
	3	1.81±1.07	1.24	3.9	1.14
	4	1.29±0.11	1.31	1.45	1.09
NPDR	1	0.73±0.04	0.73	0.79	0.65
	2	0.65±0.07	0.62	0.74	0.56
	3	1.25±0.14	1.24	1.5	0.93
	4	1.07±0.15	1.06	1.27	0.85

Notes: * 1 – RI (max); 2 – RI (mean); 3 – PI (max); 4 – PI (mean).

showed that RI (max) in control group was smaller described than No DR (p<0.0001), PDR (p<0.0001) and NPDR (p<0.0001). The RI (max) No DR was greater significantly than PDR (p<0.0001). The RI (max) PDR was greater significantly than NPDR (p<0.0001). The Tukey tests showed that RI (mean) in control group was smaller described than No DR (p=0.028), PDR (p<0.0001) and NPDR (p=0.003). The RI (mean) No DR was greater significantly than PDR (p<0.0001). The RI (mean) PDR was greater significantly than NPDR (p<0.0001). The Tukey tests showed that PI (max) in control group was smaller than PDR (p=0.002). The PI (max) of No DR was smaller significantly than PDR (p=0.008). The PI (max) of PDR was greater significantly than NPDR (p=0.007). In post hoc analysis, the PI (mean) of No DR was smaller significantly than PDR (p=0.007).

Depend on Doppler parameters of CRA and by using receiver operating characteristics (ROC) curve analysis, sensitivity and specificity, the accuracy was assessed. The ROC curve analysis showed the accuracy of Doppler parameters of CRA in differentiating controls

Table 3
Doppler parameters analysis by Post Hoc Tukey and ANOVA

Parameter (cm/sec)	Control (n=22)	No DR (n=23)	PDR (n=25)	NPDR (n=25)	ANOVA test	P-value	Post Hoc Tukey
RI (max)	0.62	0.73	0.74	0.67	78.83	<0.0001	G1:G2 G1:G3 G1:G4 G2:G4 G3:G4
RI (mean)	0.61	0.64	0.75	0.66	41.37	<0.0001	G1:G2 G1:G3 G1:G4 G2:G3 G3:G4
PI (max)	1.16	1.25	1.81	1.23	6.18	0.0007	G1:G3 G2:G3 G3:G4
PI (mean)	1.12	1.08	1.28	1.13	3.93	0.011	G2:G3

Table 4
Accuracy of Doppler indices in PDR and NPDR

PDR					
Parameter (cm/sec)	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
RI (max)	77.8	70	60.9	84	72.9
RI (mean)	83.3	88.9	90.9	80	85.7
PI (max)	82.6	76	76	82.6	79.2
PI (mean)	77.3	72	70.8	78.2	74.5
NPDR					
Parameter (cm/sec)	**Sensitivity**	**Specificity**	**PPV**	**NPV**	**Accuracy**
RI (max)	82.6	88	86.4	84.6	85.4
RI (mean)	80	92	90.9	82.1	86
PI (max)	77.3	80	77.3	80	78.7
PI (mean)	84.2	72	69.6	85.7	77.3

from DR. The areas under curve (AUC) of RI (max), RI (mean), PI (max), and PI (mean) were 0.823, 0.965, 0.707, and 0.874, respectively. RI of CRA had high sensitivity and specificity, at various cut off values, as shown in Table 4. In the PDR, the most sensitive parameter was RI (mean) 83.3%, most specific 88.9%, and most accurate 90.9%. In the NPDR, the most sensitive parameter was PI (mean) 84.2%, most specific was RI (mean) 92% and also the most accurate 90.9%.

■ DISCUSSION

In control group, the Doppler indices median including RI (max), RI (mean), PI (max), and PI (mean) were recorded as following: 0.62, 0.62, 1.06, and 1.01, respectively; of DM without DR are: 0.69, 0.65, 1.17, and 1.08, respectively; in PDR: 0.74, 0.76, 1.24, and 1.31, respectively and in NPDR: 0.73, 0.62, 1.24, .06), respectively. In Sarkar et al. [16] study, and Somfai et al. [17], they reported a dropping in RI. Other study by Wang et al. [18] study, groups: healthy, DM without DR, NPDR and PDR. The RI among PDR was the highest mean and the lowest mean among healthy subjects ($P \leq 0.001$). The PI values were greatest among their DM. Nadeem and co-authors concluded a significant change occur in ocular-retro-bulbar blood flows in DR, which discover by Doppler US. These Doppler indices could serve as diagnostic screening to determine the hemodynamic differences. There are significant differences between DR and non-diabetic ophthalmic Doppler indices. A predictive power can be identified when monitoring with Doppler US may have to those at greatest risk to develop PDR [19].

Aharwal and colleagues [20] investigated three indices only (PSV, EDV and RI) on 100 eyes (50 persons) of 30 males and 20 females. The mean DM duration was 8.4±1.2 years. The mean RI in DM without DR was 0.92±0.05. In comparison with the findings in this study, it has lower RI. These could be explained by large population of this study and the range of values measurement. These variation in results might be attributed to DM, which lead to microcirculation disturbances in the endothelial dysfunction leading to perfusion dysfunctions, which seen at US doppler as a significant drop coronary vulnerable plaque in CRA occlusion (CRAO), ocular ischemic syndrome (OIS) and thrombosis of veins [21]. The CRA flow is antegrade, with rounded systolic peak, low resistance and diastolic continuous flow [20].

In the current study, the Doppler indices of CRA assessment by Post Hoc Tukey and ANOVA analysis revealed that RI (max), RI (mean), PI (max) and PI (mean) were significantly difference among all groups ($p<0.0001$, $p<0.0001$, $p=0.0007$ and $p=0.011$), respectively. These findings dissimilar with what obtained by Pauk-Domańska et al. [12] study. They found among cases with DM, there were statistically significant differences in blood flow indices in the CRA (an elevate in RI) compared to the control group ($p<0.05$). In the control group, the value was significantly higher. The value of RI in DR group was significantly higher than in the control group ($p<0.0001$). The reasons behind that were the differences in parameters of blood flow were found between the DM groups without changes of fundus and the groups of subjects with mild NPDR or severe PDR resulting in disorientation of RI [12, 20].

Chronic DM disturb the body auto-regulatory mechanisms, leading to the onset of DR by altering the blood vessels diameter, dropping the perfusion pressure and inductions changes of resistance of peripheries [12, 22].

Depend on accuracy parameters of CRA Doppler indices the ROC curve analysis showed the areas under curve (AUC) of RI (max), RI (mean), PI (max), and PI (mean), which was highest for RI (mean), RI (max), and PI (mean). RI of CRA had high sensitivity and specificity. Khatri et al. [23] studied 107 DM cases (40–70 years), they divided sample to 4 groups: control (n=26), No DR (n=26), PDR (n=26) and NPDR (n=29). However, they study only one index which was RI as a significant raise in RI (P<0.001) with severity of DR. The ROC analysis showed diagnostic accuracy of RI (AUC = 0.84–0.99) among control and DM. RI had high sensitivity and specificity. Wang et al., reported that the sensitivity, specificity, PPV, NPV and accuracy of RI and PI, in PDR might reached to 100%. They mentioned that color Doppler was a more efficient screening method for DR [18]. RI has been considered as a marker of vascular resistance; it is elevated with raising resistance [24]. CRA RI is found to be a useful marker for early detection and follow-up of DR [25].

In another study, PI blood flow is found to be more in cases with no DR as well as PDR as compared to controls. Hemodynamic circulation is found to playing a causative role in the DR pathogenesis [26].

Pauk-Domańska et al. [12] concluded that blood flow indices alterations in CRA reflecting a vascular dysfunction precede the onset of visible signs of DR. Thus, they might serve as hemodynamic disorders sensitive markers in DM without fundus injuries, and they are more prominent in DR. The level of HbA1c, besides, decrease vascular flow velocities of CRA by Doppler indication of uncontrolled DM.

■ CONCLUSIONS

The Doppler indices of control group slightly more than in DM without DR group. The highest means peak of RI, and PI reported is in the PDR indicated the progress of DR. The highest AUC for RI (mean), RI (max), and PI (mean) indicate that RI (max), and PI (mean) are most better indices for diagnose CRA retinopathy. RI of CRA has a high sensitivity and specificity.

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