Predictive factors for adherence to intravitreal anti-vascular endothelial growth factor therapy in Palestinian patients with diabetic retinopathy, retinal vein occlusion, and age-related macular degeneration: a retrospective cohort study

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Abstract

Background The burden of retinal vascular and degenerative diseases on patients and healthcare systems can be significant if patients do not complete scheduled intravitreal injections. This study aimed to identify the factors that influence adherence with follow-up injections in patients with diabetic retinopathy, age-related macular degeneration, and retinal vein occlusion receiving intravitreal injections of anti-vascular endothelial growth factor treatment.

Methods This study utilized data from patients who received intravitreal anti-vascular endothelial growth factor injections between 2022 and 2023 at An-Najah National University Hospital. Patient information, such as demographic information, number of injections administered, and details of follow-up visits, was obtained from the hospital's electronic records. When electronic records lacked certain information, patients or their relatives were contacted to provide the missing data. Data entry and analysis were performed using chi-square tests and the Statistical Package for Social Sciences. A *p*-value ≤ 0.05 indicated statistical significance.

Results A total of 107 patients, 43 (40.2%) were adherent, while 64 (59.8%) were non-adherent. Sex was significantly associated with adherence (*P* = 0.035), with females more likely to adhere. Planned number of injections correlated with adherence (*P* = 0.004), as those receiving fewer injections were more adherent. Cost problems negatively impacted adherence (*P* = 0.016), with non-adherent patients more frequently reporting financial barriers. Positive patient expectations for vision improvement were strongly associated with adherence (*P* = 0.003). Mobility problems influenced adherence (*P* = 0.049), as those without mobility issues adhered more. Physical assistance from relatives significantly improved adherence (*P* = 0.036). Factors not significantly influencing adherence included comorbidities, education level, and insurance status.

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Conclusion Our study revealed that 60% of patients did not adhere to intravitreal anti-vascular endothelial growth factor treatment injections. Factors influencing adherence included the planned number of injections, cost problems, indication for injections, sex, need for physical assistance, and mobility problems. It is crucial to increase awareness of these factors to prevent complications such as blindness. Raising awareness could lead to improved adherence rates, better treatment outcomes, and positive impacts on patient and community health.

Keywords Retinopathy, Patient adherence, Intravitreal anti-vascular endothelial growth factor injections, Anti-VEGF

Background

Retinal vascular and degenerative diseases are characterized by pathological alterations caused by factors such as oxidative stress and circulatory system damage. These conditions include diabetic retinopathy (DR), age-related macular degeneration (AMD), and retinal vein occlusion (RVO), which are the leading causes of ophthalmic morbidity worldwide [1]. The AMD incidence is 0.44% globally, varies across ethnic groups, and increases with age [2]. In 2015, the global incidence of RVO in people aged 30–89 years was 0.77% [3]. The global prevalence of DR and diabetic macular edema (DME), from 2015 to 2019 was 27.0% [4]. According to the American Academy of Ophthalmology, in 2016, the global prevalence of DR was 77.3% for Type I DM and 25.1% for Type II DM. It is predicted that up to 84.5% of diabetic patients who have had DM for more than 20 years will develop DR [5]. According to the survey conducted between July 2018 and April 2019, the overall prevalence of diabetes in the West Bank and Gaza was 33.2% [6]. Retinal neovascularization is driven by hypoxia, ischemia, and inflammation, disrupting the vascular endothelial growth factor (VEGF) and pigment epithelium-derived factor (PEDF) balance [7]. Intravitreal anti-VEGF drugs inhibit proangiogenic factors with varying selectivity and potencies. Ranibizumab and bevacizumab target all VEGF-A isoforms, while aflibercept also blocks VEGF-B and placental growth factor [8]. The purpose of anti-VEGF treatments is to counteract pathological neovascularization and disease progression and in the best case, to achieve recovery [9]. Visual outcomes depend on injection frequency, making adherence crucial for successful therapy. Addressing barriers to adherence is essential, especially for younger patients with progressive retinal diseases [10]. Anti-VEGF adherence is affected by visit frequency, travel logistics, waiting time, appointment access, caregiver support, financial burden, and patient perception of treatment effectiveness [11]. Improved doctor-patient relationship communication and patient education together with new therapies offering convenience, long-acting effectiveness, and better tolerability may improve treatment adherence [11]. This study addresses the gap in understanding the specific barriers to adherence to anti-VEGF therapy in Palestinian patients with retinal vascular diseases (RVDs), a topic that remains underexplored in existing literature. The aim is to identify factors affecting adherence, including socioeconomic challenges, healthcare system limitations, and patient perceptions of treatment. The study will assess the extent of adherence, evaluate its impact on treatment outcomes, and propose strategies to improve adherence rates. Focusing on the Palestinian context, it offers valuable insights into the unique barriers faced by patients in this region, contributing to a deeper understanding of adherence challenges. While numerous studies have investigated adherence to intravitreal anti-VEGF therapy in high-resource settings, our research provides valuable insight into adherence patterns within the unique healthcare context of Palestine. This study adds to the literature by highlighting region-specific barriers such as economic constraints, transportation difficulties, and the impact of political instability, all of which may significantly affect adherence. Unlike studies from more developed healthcare systems, our findings reflect real-world challenges faced by patients in low-resource settings, offering a critical perspective that can inform more equitable and context-sensitive strategies to improve treatment adherence globally and so provide recommendations for healthcare improvements and policy interventions to reduce sight-threatening complications like blindness.

Methodology

This study examined factors that affect adherence to anti-VEGF injections and evaluated the results based on single-center and retrospective data. We reviewed the medical records of patients with retinal vascular and degenerative diseases which included DR, AMD, and RVO, who were receiving anti-VEGF injections from January 2022 to August 2023 at An-Najah National University Hospital.

The ethics committee and the Institutional Review Board of An-Najah National University (Med. Sept. 2023/5) approved this study which followed the tenets of the Declaration of Helsinki. Patients were eligible if they initiated anti-VEGF (bevacizumab, ranibizumab, or aflibercept) injections elsewhere in Palestine including in private centers or governmental hospitals, for any indication of treatment related to retinal vascular and

Abualhasan *et al. BMC Ophthalmology*　　(2025) 25:268

Page 3 of 8

degenerative disease during the period from January 2022 to August 2023 and if the required documentation was available in our tertiary hospital's system. The Exclusion criterion included patients who lacked the required documentation despite trying to collect information from the patients by phone. A total of 200 patients were initially reviewed for inclusion in the study. Of these, 107 met the eligibility criteria and were successfully included in the final analysis. The remaining patients were excluded due to loss of follow-up, inability to establish contact, or failure to meet all inclusion criteria. Patients were considered adherent if they received their planned number of injections on time and maintained follow-up for 3 months. Patients who failed these two conditions were considered non-adherent for the sake of this analysis. Participants'privacy and data confidentiality were ensured, and informed consent was obtained from all patients. Patient data were obtained from hospital electronic records. The following data were obtained for this study: age, sex, indication for injection (DR, AMD, or RVO), history of other comorbidities, name and number of injections, details of follow-up, and insurance status. Patients or relatives were called to obtain additional data that were not found in the electronic records such as physical assistance, mobility problems; traffic difficulties when patients needed to reach the care center to take their planned anti-VEGF injections), education; levels of education, expectations of patients; about the improvement of vision after initiating anti-VEGF injections, counseling; the patient complete understanding about injection importance, cost problems; refer to patients who lack insurance or sufficient financial resources to afford necessary medical treatments, and comorbidities; such as DM II or HTN with 1 or more other chronic diseases. The Statistical Package for Social Sciences (SPSS) version 21 software was used for data entry and analysis. Continuous data are presented as the mean ± SD or median (1 st quartile, 3rd quartile), as appropriate. A frequency table and appropriate charts were used to describe categorical data. To assess the associations between different groups, univariate inference was conducted using the appropriate significance test (chi-square test). The correlations between individual variables were tested by the Pearson correlation coefficient. The goodness of fit of the regression was assessed.

Using the adjusted R-squared test with a *P*-value ≤ 0.05. A *p*-value ≤ 0.05 was considered to indicate statistical significance.

While we understand the value of controlling for multiple factors to determine their independent significance, we believe that univariate analysis is more appropriate for this particular study. Our analysis aimed to first identify the individual contributions of each factor without the potential complexity of interactions between variables. So, we focused on univariate analysis to provide a clearer and more straightforward understanding of each factor's direct relationship with the outcome. Additionally, introducing multivariable analysis may introduce complexities that are beyond the scope of our current study, especially considering the small sample size. We appreciate this comment and will certainly consider a multivariable approach in subsequent studies with larger datasets, a more refined research design, and a larger sample size.

Results
A total of 107 patients were included in the study, with 54 (50.5%) males and an overall mean age of 61.9 ± 10.9 years. Among the participants, 96 (89.7%) had DR, 7 (6.5%) had RVO, and 4 (3.7%) had AMD. Regarding treatment adherence, 43 (40.2%) patients were adherent, while 64 (59.8%) were non-adherent.

The patient population had diverse comorbidities: 48 (44.9%) had a history of diabetes, 11 (10.2%) had hypertension, and 48 (44.9%) had multiple comorbidities. Anti-VEGF treatments included ranibizumab for 10 (9.3%) patients, bevacizumab for 57 (53.3%), and aflibercept for 40 (37.4%). In terms of insurance, 36 (33.6%) patients had insurance, while 71 (66.4%) were uninsured.

Concerning social support, 75 (70.1%) patients received assistance from relatives or others, whereas 32 (29.9%) did not. Educational backgrounds varied, with 23 (21.5%) having elementary school education, 33 (30.8%) having secondary education, 10 (9.3%) holding a diploma, 40 (37.4%) with a bachelor's degree, and 1 (0.9%) holding a master's degree. Financial challenges were reported by 50 (47.2%) patients, while 56 (52.8%) did not face such difficulties.

Finally, 72 (67.3%) patients had positive expectations for their vision after receiving their planned injections, while 35 (32.7%) expressed concerns regarding their vision outcomes (Tables 1 and 2).

A notable relationship was found between sex and adherence (*P*= 0.035). Among non-adherent patients, 36 (56.2%) were male and 28 (43.8%) were female, while among adherent patients, 18 (41.9%) were male and 25 (58.1%) were female.

Adherence also showed a strong correlation with the planned number of injections (*P*= 0.004). Among non-adherent patients, 12 (18.8%) received less than three injections, 23 (35.9%) received three injections, and 29 (45.3%) received more than three injections. In contrast, among adherent patients, 19 (44.2%) received less than three injections, 16 (37.2%) received three injections, and 8 (18.6%) received more than three injections.

Cost problems were significantly linked to adherence (*P*= 0.016). Among non-adherent patients, 36 (56.3%)

Abualhasan *et al. BMC Ophthalmology*   (2025) 25:268

Page 4 of 8

Table 1 Demographic characteristics

Variables		Frequency (n = 107)	Percentage (%)
Gender	Male	54	50.5
	Female	53	49.5
Age	less than 65	61	57
	65 or more	46	43
Education	Elementary	23	21.5
	Secondary	33	30.8
	Bachelor	40	37.4
	Diploma	10	9.3
	Master	1	0.9
Comorbidities	DM	48	44.9
	HTN	11	10.2
	Multiple	48	44.9

Table 2 Suspected factors that could affect adherence

Variables		Frequency (n = 107)	Percentage (%)
Physical assistance	NO	32	29.9
	YES	75	70.1
Mobility problems	NO	65	60.7
	YES	42	39.3
Counseling	Uncounseled	16	15
	Counseled	91	85
Patients Expectations	Good	72	67.3
	Bad	35	32.7
Cost Problems	NO	56	52.3
	YES	50	46.7
Indication of injections	DR	96	89.7
	AMD	4	3.7
	RVO	7	6.5
Insurance state	Insured	36	33.6
	Noninsured	71	66.4
Number of injections	Less than 3	31	29
	3	39	36.4
	More than 3	37	34.6

reported cost problems, while 28 (43.8%) did not. Among adherent patients, 14 (32.6%) experienced cost problems, and 29 (67.4%) did not.

Expectations of patients after injections were strongly associated with adherence ($P = 0.003$). Among non-adherent patients, 36 (56.3%) had positive expectations about vision improvement, while 28 (43.8%) had negative expectations. In contrast, among adherent patients, 36 (83.7%) had positive expectations, and 7 (16.3%) had negative expectations.

Mobility problems were found to be closely linked to adherence ($P = 0.049$). Among non-adherent patients, 34 (53.1%) had no mobility problems, while 30 (46.9%) experienced mobility problems. Among adherent patients, 31 (72.1%) had no mobility problems, and 12 (27.9%) had mobility challenges.

Lastly, physical assistance from relatives was a key factor influencing adherence ($P = 0.036$). Among non-adherent patients, 24 (37.5%) received no physical assistance, while 40 (62.5%) had support. Among adherent patients, 35 (81.4%) received physical assistance, and 8 (18.6%) did not (Table 3).

Discussion

The World Health Organization (WHO) defines adherence to long-term therapy as "the extent to which a person's behavior- such as taking medication, following a diet, and/or implementing lifestyle changes- aligns with the recommendations provided by a healthcare professional"[12]. In the context of anti-VEGF therapies, adherence to intravitreal anti-VEGF therapy refers to how closely a patient's injection schedule aligns with the regimen prescribed by their physician. It includes regular attendance and consistency in the timing and frequency of injections. Definitions of non-adherence had even greater variation in terminology used including extent of irregular attendance by exceeding a 4-week follow-up by more than 2 weeks, more than 60 days between visits, unintended treatment gaps of more than 8 weeks, at least one missed appointment, skipped injections, delayed or dropped appointments in the first year, any deviation from the European guideline of 3 monthly doses followed by once every 2 months for 12 months, treatment gaps over 6 months, delayed follow-ups longer than 4 weeks, or missing any of the 3 monthly loading doses [13].

This retrospective cohort study evaluated adherence among patients with DR, RVO, and AMD and demonstrated that sex, number of planned injections, cost problems, mobility problems, and physical assistance had an impact on adherence with anti-VEGF therapy. The majority of adherent patients were females and the majority of non-adherent patients were males. Regardless of the insurance status, cost problems affect both adherent and non-adherent patients, most adherent patients had no cost problems and most non-adherent patients had cost problems. The majority of adherent patients had no mobility problems when they reached their care centers while taking their injections, but regarding non-adherent patients, mobility problems didn't significantly affect them. Physical assistance significantly affected adherent patients, and most adherent patients received physical assistance. However, there was no significant association with non-adherent patients, which could be

Abualhasan *et al. BMC Ophthalmology*   (2025) 25:268

Page 5 of 8

Table 3 Association between adherence and all variables

Variables		Adherent		*P*-Value
		NO	**YES**	
Gender	Male	36 (56.2%)	18 (41.9%)	0.035
	Female	28 (43.8%)	25 (58.1%)	
Age	Less than 65	40 (62.5%)	21(48.8%)	0.162
	65 or more	24 (37.5%)	22 (51.2%)	
Education	Elementary	11 (17.2%)	12 (27.9%)	0.169
	Secondary	25 (39.1%)	8 (18.6%)	
	Bachelor	21 (32.8%)	19 (44.2%)	
	Diploma	6 (9.4%)	4 (9.3%)	
	Master	1 (1.6%)	0 (0%)	
Insurance state	Insured	18 (28.1%)	18 (41.9%)	0.140
	Noninsured	46 (71.9%)	25 (58.1%)	
Indication of injection	DR	60 (93.8%)	36 (83.7%)	0.035
	AMD	3 (4.7%)	1 (2.3%)	
	RVO	1 (1.6%)	6 (14%)	
Other comorbidities	DM	30 (46.8%)	18 (41.9%)	0.816
	HTN	6 (9.4%)	5 (11.6%)	
	Multiple comorbidities	28 (43.8%)	20 (46.5%)	
Patients expectations	Good	36 (56.3%)	36 (83.7%)	0.003
	Bad	28 (43.8%)	7 (16.3%)	
Physical assistance	NO	24 (37.5%)	8 (18.6%)	0.036
	YES	40 (62.5%)	35 (81.4%)	
Counseling	Uncounseled	11 (17.2%)	5 (11.6%)	0.429
	Counseled	53 (82.8%)	38 (88.4%)	
Cost Problems	NO	28 (43.8%)	29 (67.4%)	0.016
	YES	36 (56.3%)	14 (32.6%)	
MOBILITY PROBLEMS	NO	34 (53.1%)	31 (72.1%)	0.049
	YES	30 (46.9%)	12 (27.9%)	
Name of injection	Lucentis	8 (12.5%)	2 (4.7%)	0.353
	Avastin	34 (53.1%)	23 (53.5%)	
	Eylea	22 (34.4%)	18 (41.9%)	
Planned number of Injections	Less than 3	12 (18.8%)	19 (44.2%)	0.004
	3	23 (35.9%)	16 (37.2%)	
	More than 3	29 (45.3%)	8 (18.6%)	
Total (%)		64 (59.8%)	43 (40.2%)	

attributed to sociocultural value in our community. The results also demonstrated that the non-adherence rate increased significantly when the number of planned injections was more than three and the adherence rate decreased. In a previous study (approximately 30%) of the patients, treatment was discontinued after one or two injections (i.e., incomplete loading dose), which could have led to no improvement in vision and ultimately led to discontinuation or the seeking of treatment by another doctor [14]. According to the counseling and insurance status, it's surprising that the majority of non-adherence patients were counseled (82%), and about insurance

status, (71.9%) were non-adherent. in addition, the variables that didn't affect adherence were age, education, name of injections, and comorbidities. In contrast to our significant study variables that affected adherence, a systematic review study published in 2023 revealed that the most prevalent reasons for discontinuation or attendance irregularity were dissatisfaction with treatment results (29.9%), financial burden (19.0%), old age/comorbidities (15.5%), difficulty booking appointments (8.5%) and travel distance (7.9%) [13]. In our study, the percentage of adherence was)40.2%) and (59.8%) was the percentage of non-adherence patients. The level of

Abualhasan *et al. BMC Ophthalmology* (2025) 25:268

Page 6 of 8

non-adherence to intravitreal injection visits was high yet varied depending on the definition applied [13]. Overall non-adherence was measured as high as (95.6%) based on a definition utilized by Cohen et al. [15]. In contrast, (15.0%) of patients were defined as non-compliant by Abu-Yaghi et al. [16]. A recent report from the U.S. that included 2302 patients with proliferative diabetic retinopathy DR and 9007 patients with AMD, showed that approximately (22%) and (28%), respectively, of patients were lost to follow-up [17]. Another study from Germany, which included 708 patients with AMD, DME, and RVO, reported that (32%), (44%), and (25%) of patients, respectively, were non-adherent [18]. Similarly, a study from Germany showed that (46%) of patients with DR and (22%) of patients with AMD had at least one therapy break-off [19]. A study from Turkey, which evaluated 314 patients, also reported approximately (40%) non-adherence [20]. In contrast, in our study, the non-adherence percentage (58.2%) was higher than the percentages reported in the studies listed above. The variations in adherence rates among studies may be attributed to differences in the social and financial circumstances of the patient populations. These variations may be influenced by constraints within our country, particularly related to occupational policies, which affect regular follow-up.

Controlling angiogenesis with anti-VEGF therapy, which is now the standard treatment modality, prevents further deterioration by inhibiting the growth of new vessels and thus stabilizing vision. However, since the underlying pathology continues, anti-VEGF injections need to be continued repeatedly to control angiogenesis. Because clinical practice requires patients to continue attending monthly follow-ups, treatment adherence rates may vary depending on factors that push the limits of patients'adherence to treatment and the patient's level of awareness in terms of the disease and its treatment. While anti-VEGF therapy is promising for these patients, the need for repeated intraocular injections makes it difficult to successfully implement. This affects the efficacy and outcomes of treatment.

In the treatment of retinal vascular diseases, specific criteria guide the use of anti-VEGF therapy. For patients with DR and DME, treatment is indicated when there is significant visual impairment, with diagnosis confirmed through patient history, visual acuity testing, fundus examination, and OCT imaging. In cases of RVO with cystoid macular edema (CME), anti-VEGF therapy is recommended to prevent vision loss, with similar diagnostic procedures including OCT to assess macular edema. For wet AMD with choroid neovascularization (CNV), anti-VEGF injections are the standard of care to stabilize vision. Accurate diagnosis for all these conditions relies on a thorough clinical evaluation, including visual acuity, fundus examination, and OCT imaging to guide treatment decisions effectively.

During the initial visit, the patient underwent a thorough examination, including a detailed medical history, physical examination, visual acuity assessment, and a comprehensive fundus exam. The patient was then scheduled for their first injection within the following week.

Our treatment plan was to start with 3 loading doses and then do OCT. If there is morphological and functional improvement (depending on OCT findings and visual acuity), we shift to treat and extend (T&E) methods. The T&E regimen starts with a loading phase of injections until the patient's condition stabilizes. After that, the follow-up interval is gradually extended, with an injection administered at each visit. The goal is to determine the longest interval between injections that still maintains disease stability.

The average number of anti-VEGF injections per patient was approximately 2 for a single eye. None of the patients included in our study received steroid injections.

Adherence to anti-VEGF therapy in our region is influenced by a complex interplay of logistical, socioeconomic, and political challenges. Uncontrolled borders, a shortage of medical and financial resources, overcrowded cities and refugee camps, poverty, food insecurity, and the ongoing financial crisis all contribute to the difficulty patients face in accessing consistent care. Unlike studies from geographically vast areas where transportation is a primary barrier, our patients encounter different obstacles. Limited social support makes it difficult for family members to accompany elderly patients, especially when work commitments restrict their availability. Financial hardship forces many to delay or forgo treatment, while ongoing political conflict and regional instability further disrupt healthcare access, leading to missed or irregular treatment sessions.

Potential treatment-related complications or adverse effects may influence non-adherence, as patients might fear potential side effects or complications from the treatment. Additionally, some patients may not fully understand the purpose of the treatment, how it works, or the expected outcomes, leading to confusion and a lack of adherence.

While exploring a correlation between CRT and compliance is an interesting topic, it falls beyond the scope of our current study. However, we recognize its potential importance and will certainly consider investigating this correlation in future research.

We acknowledge the following limitations in our study. The first limitation of this study is the relatively small sample size, with only 107 patients included over 20 months. Despite the high and increasing prevalence

Abualhasan *et al. BMC Ophthalmology*   (2025) 25:268

Page 7 of 8

of AMD, RVO, and DME, several challenges limited our ability to include a larger number of patients. These challenges included difficulties in reaching and communicating with patients, as well as the lack of an electronic system in some hospitals, which made patient tracking and follow-up more difficult. As a result, these factors contributed to the smaller-than-expected sample size and posed significant obstacles during the study. The imbalance in disease distribution, with diabetic retinopathy (DR) being the most prevalent condition, can largely be attributed to the high prevalence of DR in Palestine, which is reported to be around 48.0%. This significant prevalence of DR likely explains why it constitutes the majority of cases in our study, and consequently, our findings may be more reflective of DR patient compliance. This point was added to the limitations of this study [21].

Second, this was a retrospective study and may have a bias because there was no control over the treatment regimen, and patients may have also received other medications. Third, the reasons for the loss of follow-up were not available for all patients, and every effort was made to contact patients for additional reasons; however, for a few patients, whom we were not able to contact the patient, either the number of patients changed or the patients did not respond to the call, was excluded from the study. The fourth one was a single-center study, so our sample represents a small percentage of the total patients in Palestine who received monthly anti-VEGF injections; hence, we warn the readers to carefully generalize these results. The main strength of this study is that it is almost the first study in Palestine on adherence to anti-VEGF therapy. Finally, we recommend the need for more flexible treatment regimens that reduce the burden of treatment, in line with patients'ability and willingness to attend regular anti-VEGF appointments. A better understanding of the comorbidities that present a high risk of non-adherence with treatment is needed to accurately identify at-risk individuals; this emphasizes the need for future researchers to introduce additional subcategories to allow for more specific data collection regarding the relationship between specific comorbidities and non-adherence to therapy. This recommendation raises awareness about the need for sufficient resource allocation to prevent unnecessary treatment delays in a growing patient pool and to prevent vision loss.

Conclusion

In summary, the present study revealed that approximately 60% of the participants of this study did not adhere to their anti-VEGF therapy. The most common reasons for non-adherence were the planned number of injections, cost problems, indication for injections, sex, lack of physical assistance, and mobility problems. It is important to recognize and address these structural barriers, such as financial constraints, mobility limitations, and patient expectations, which may significantly impact adherence. Understanding these factors can help healthcare providers implement tailored interventions and support systems, ultimately improving patient adherence and enhancing health outcomes. This approach can contribute to more effective treatment strategies and better long-term results for patients.

Abbreviations

Anti-VEGF	Anti-Vascular Endothelial Growth Factor
RVD	Retinal vascular disease
DM	Diabetes mellitus
HTN	Hypertension
DR	Diabetic retinopathy
RVO	Retinal vein occlusion
AMD	Age-related macular degeneration
OCT	Optical coherence tomography

Declarations

Ethics approval and consent to participate
Informed consent was obtained from all subjects. This study was performed under the guidelines of the Declaration of Helsinki and was approved by the institutional review board of An-Najah National University.
Your study title is "Predictive Factors for Adherence to Intravitreal anti-vascular Endothelial Growth Factor Therapy in Palestinian Patients with diabetic retinopathy, Retinal Vein Occlusion, and age-related macular Degeneration: A retrospective cohort study," was reviewed by the An-Najah National University IRB committee and was approved on 3rd Sept 2023 (Med. Sept. 2023/5).

Consent for publication
Informed consent for publication was obtained from every individual whose data are included in this manuscript.

Abualhasan *et al. BMC Ophthalmology*   (2025) 25:268

Page 8 of 8

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