Letter to the Editor

Treatment options for diabetic retinopathy in pregnancy

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KEYWORDS
gestational diabetes mellitus, diabetic retinopathies, hyperglycemias, blood flow, intravitreal injection, VEGFs, laser therapies

Dear Editor,

We read with great interest the recent review by Rashidian titled "Pregnancy and diabetic retinopathy" [1]. The article provides a comprehensive overview of the proposed pathophysiological mechanisms underlying the development and progression of diabetic retinopathy (DR) during pregnancy, while offering practical clinical care recommendations [1]. Given the rising prevalence of diabetes mellitus (DM) among women of reproductive age, this topic is highly relevant [2, 3]. We believe that some aspects of the treatment approach during pregnancy deserve further discussion and clarification based on the emerging clinical evidence.

Pregnancy is a risk factor for both the development and progression of DR [4]. Approximately 1 in 12 pregnant individuals with preexisting DM and no baseline retinopathy are expected to develop some form of DR during pregnancy. Moreover, patients with pre-existing retinopathy may experience disease worsening during this period. Notably, DR affects nearly 50% of pregnant women with type 1 DM and approximately one in seven women with type 2 DM [5]. This highlights the importance of understanding and optimizing DR management during pregnancy to preserve maternal vision and promote favorable fetal outcomes.

Preconception care is crucial in optimizing maternal health and reducing the risk of complications for both the mother and developing fetus. Ophthalmic examination before conception is strongly recommended in clinical guidelines to accurately assess DR severity [6]. If severe non-proliferative DR, proliferative DR, or diabetic macular edema (DME) is identified, laser photocoagulation is generally advised prior to pregnancy, in alignment with the standard recommendations for the general diabetic population. Women with proliferative DR in early pregnancy and treated with laser photocoagulation are more likely to experience disease progression than those diagnosed and treated prior to conception [7]. Current guidelines do not provide specific recommendations for the use of intravitreal injections to treat DME before pregnancy [8].

Laser photocoagulation (focal/grid or panretinal) is widely regarded as a safe and effective treatment for DR in pregnant women. It remains a key component of DR management during pregnancy. Rathinavelu et al. [9] recently reported successful laser photocoagulation of DR in pregnant women, without treatment-related complications [9]. Current guidelines acknowledge that panretinal photocoagulation may be needed earlier in pregnant patients—especially when DR advances to severe non-proliferative stages or worse—rather than delaying treatment in hopes of spontaneous regression, which could result in poorer outcomes [8, 9].

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How to cite this article: Kayabasi M, Karti O, Saatci AO. Treatment options for diabetic retinopathy in pregnancy. Med Hypothesis Discov Innov Optom. 2025 Summer; 6(2):83-85. DOI: https://doi.org/10.51329/mehdioptometry226

Received: 28 December 2024; Accepted: 20 June 2025

DME is the most common cause of vision loss related to DR; however, few studies have specifically examined DME during pregnancy. The reported prevalence of pregnancy-related DME ranges from 8.9% to 12.5% [4]. Pregnant women with mild to moderate DME can be managed with close observation, focusing on achieving and maintaining optimal glycemic control [10]. Nonetheless, these patients require more intensive monitoring than the non-pregnant population because of the potential for rapid disease progression during pregnancy [8]. If macular edema does not improve after a period of observation, focal/grid laser photocoagulation is recommended as the first-line treatment during pregnancy [11]. Alternative laser treatments, such as subthreshold micropulse or Endpoint Management laser therapy, may also be considered in cases involving the fovea, in which conventional laser treatment could threaten central vision [12].

Intravitreal administration of anti-vascular endothelial growth factor (anti-VEGF) agents is currently the most effective therapy for DME [13]. However, the use of anti-VEGF therapy during pregnancy is generally reserved for exceptional cases because of the limited long-term safety data, potential teratogenic effects, and classification of these agents as Category C drugs by the United States Food and Drug Administration [5]. Spontaneous abortion and preeclampsia have been reported following intravitreal bevacizumab injections [7]. If anti-VEGF treatment is deemed necessary—usually after other therapeutic options have proven ineffective or inappropriate—treatment delay is recommended until the later stages of pregnancy, particularly the third trimester. This approach aims to minimize fetal exposure during the critical periods of organogenesis and early development [8].

The successful use of intravitreal bevacizumab, ranibizumab, and aflibercept for various retinal disorders, including DR, in pregnant women has also been documented [9, 14]. The selection of an anti-VEGF agent during pregnancy is largely influenced by the systemic half-life of the drug. Among anti-VEGF agents, systemic exposure is reported to be highest with bevacizumab and lowest with ranibizumab [15]. Bevacizumab, aflibercept, and ranibizumab rapidly enter the systemic circulation; however, ranibizumab is cleared more quickly, whereas bevacizumab and aflibercept demonstrate prolonged systemic exposure. Furthermore, bevacizumab and aflibercept significantly suppress plasma VEGF levels for an extended period following intravitreal injection, raising concerns of prolonged systemic exposure [14]. In contrast, ranibizumab has limited systemic absorption and a shorter systemic half-life [16]. Moreover, the successful use of intravitreal ranibizumab during pregnancy—without maternal or fetal complications—has been documented, suggesting that it may be more suitable for pregnant women or those planning to conceive shortly after treatment [17].

Evidence on the use of intravitreal corticosteroid injections during pregnancy remains scarce, primarily because of the ethical challenges inherent in conducting large-scale clinical trials in pregnant populations [8]. Although systemic and topical corticosteroids have been associated with a range of fetal developmental abnormalities, the current data suggest that intravitreal administration leads to minimal systemic absorption, potentially reducing fetal exposure [18]. The successful use of intravitreal triamcinolone and dexamethasone for the treatment of DR during pregnancy has been documented in case reports and case series [7, 19]. Given the limited data on safety and efficacy, intravitreal corticosteroids during pregnancy should be selected on a case-by-case basis, ideally administered during the second or third trimester, and only after careful evaluation of the potential therapeutic benefits against known or theoretical risks [20]. A concise comparison of available treatments is provided in Table 1.

In conclusion, the management of DR during pregnancy requires a multidisciplinary, individualized approach that carefully balances the preservation of maternal retinal health and minimizing fetal risk. Laser photocoagulation remains the primary and safest treatment modality, whereas adjunctive intravitreal pharmacological therapies should be cautiously considered when clinically warranted. Larger prospective studies are crucial for optimizing treatment strategies and elucidating the safety profiles of intravitreal agents in this unique patient population.

Table 1. Treatment modalities [5, 7-11, 13, 18, 19] for diabetic retinopathy in pregnancy

Treatment Modality	Safety in pregnancy	Indications	Notes
Panretinal photocoagulation	Safe	PDR Severe NPDR	Standard of care
Focal / grid laser	Safe	Center-sparing DME	Preferred first-line for DME
Intravitreal anti-VEGFs	Limited data, use with caution	Center-involving DME Resistant PDR	Prefer ranibizumab in the third trimester
Intravitreal steroids	Limited data, use with caution	Refractory DME Contraindications to anti-VEGFs	Low systemic absorption
Observation	Safe for mild NPDR and DME	Early-stage disease	Requires close follow-up

Abbreviations: PDR, proliferative diabetic retinopathy; NPDR, non-proliferative diabetic retinopathy; DME, diabetic macular edema; VEGF, vascular endothelial growth factor.

ETHICAL DECLARATIONS

Ethical approval: Not required.

Conflict of interests: None.

FUNDING

None.

ACKNOWLEDGMENTS

None.

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