



An Enhanced Generative AI Model for Detecting Diabetic Retinopathy Anomalies Using Fundus Images: A Comprehensive Review

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Abstract

Diabetic retinopathy (DR) is a leading cause of preventable blindness among working-age adults, driven by chronic hyperglycemia and the global rise in diabetes prevalence. Although early detection and treatment can prevent up to 90% of vision loss cases, limited access to ophthalmologists, poor screening adherence, and the manual burden of retinal image analysis remain major challenges [2], [9], [13]. To address these issues, artificial intelligence (AI), particularly deep learning (DL) and generative AI, has emerged as a scalable and cost-effective solution for DR screening. Advances in computer vision have enabled automated analysis of retinal fundus and optical coherence tomography (OCT) images with diagnostic performance approaching that of expert clinicians. Convolutional neural networks (CNNs) dominate DR detection and grading due to their ability to learn hierarchical features directly from image data, supported by public benchmarks such as the APTOS 2019 dataset [1]. However, challenges including class imbalance, image quality variability, and limited annotated data continue to affect model robustness. This review presents a systematic overview of DL and generative AI methods for DR detection, classification, and lesion analysis using both fundus imaging and OCT modalities [5], [17], [24]. It highlights the importance of preprocessing and augmentation techniques such as CLAHE, color normalization, and GAN-based image synthesis to enhance performance and mitigate dataset imbalance [6], [8], [14], [15]. The paper also discusses weakly supervised and semi-supervised learning strategies that reduce annotation costs while maintaining accuracy [3], [19], [20]. Further emphasis is placed on lightweight model design, knowledge distillation for deployment in resource-limited settings [4], and explainable AI techniques to improve clinical trust and interpretability [28], [29]. The review concludes that while AI has significantly advanced automated DR screening, future research must prioritize robustness, explainability, and ethical deployment to enable reliable large-scale clinical integration [17], [26].

Keywords: Diabetic retinopathy, deep learning, generative AI, fundus imaging, OCT

1. Introduction

Diabetic retinopathy (DR) is one of the most common microvascular complications of diabetes mellitus and remains a leading cause of preventable blindness among working-age adults worldwide. Persistent hyperglycemia damages retinal blood vessels, leading to progressive structural and functional impairment of the retina, which, if left undetected or untreated, can culminate in irreversible vision loss. According to clinical guidelines and epidemiological evidence, early detection and timely intervention significantly reduce the risk of severe visual impairment [2]. However, despite well-established screening recommendations, adherence to regular dilated eye examinations remains suboptimal due to

factors such as limited access to ophthalmic care, high screening costs, and the growing global burden of diabetes [9], [13]. Traditional DR diagnosis relies on manual examination of retinal fundus images or optical coherence tomography (OCT) scans by trained ophthalmologists. While effective, this approach is labor-intensive, subjective, and difficult to scale for large populations. Teleophthalmology initiatives have attempted to bridge this gap by enabling remote screening, yet they still depend heavily on expert interpretation [11]. The increasing availability of large-scale retinal imaging datasets and advances in artificial intelligence (AI), particularly deep learning (DL), have catalyzed a

paradigm shift toward automated DR detection and classification systems. Publicly available datasets such as the APTOS 2019 Diabetic Retinopathy Dataset have played a pivotal role in benchmarking and accelerating research in this domain [1]. Over the past decade, convolutional neural networks (CNNs) and their variants have demonstrated remarkable performance in DR screening tasks, including binary detection, multi-class severity grading, and lesion segmentation. Comprehensive surveys highlight that architectures such as ResNet, EfficientNet, and ensemble models outperform traditional machine learning methods by learning hierarchical and discriminative retinal features directly from images [5], [17], [24]. Recent studies further report improvements through attention mechanisms, multi-scale feature extraction, and hybrid frameworks combining classification and segmentation [8], [31]. In addition to fundus photography, OCT and OCT angiography have emerged as valuable imaging modalities for capturing microstructural and vascular changes in diabetic eyes, prompting the development of DL models tailored for OCT-based DR analysis [10], [30]. Despite these advances, several challenges persist. High-quality labeled medical data are scarce and expensive to obtain, often requiring expert annotation. To address this limitation, researchers have explored semi-supervised, weakly supervised, and unsupervised learning strategies, including clustering-based labeling and anomaly detection methods [3], [18], [19], [20]. Data imbalance across DR severity classes and variability in image quality further complicate model training and generalization. Techniques such as data augmentation, elastic distortion, and generative adversarial networks (GANs) have been widely investigated to enhance data diversity and robustness [12], [15], [6]. Another emerging research direction is the use of generative AI and knowledge distillation to build lightweight, energy-efficient, and deployable models suitable for real-world clinical settings [4], [6]. These approaches are particularly relevant for resource-constrained environments where computational efficiency and scalability are critical. Moreover, explainable AI (XAI) has gained increasing attention to improve model transparency, trust, and clinical acceptance,

aligning automated decision-making with regulatory and ethical requirements [26]. Given the rapid evolution of AI-driven solutions for DR, a structured and up-to-date literature review is essential to synthesize existing knowledge, identify methodological trends, and highlight open research challenges. This paper presents a comprehensive review of state-of-the-art deep learning, generative, and weakly supervised approaches for diabetic retinopathy detection and analysis using retinal imaging. By systematically examining datasets, algorithms, evaluation metrics, and deployment considerations, this review aims to provide researchers and clinicians with a consolidated understanding of current progress and future directions in automated DR screening systems.

1.1. Year-wise Research Trend Analysis

The rapid advancement of artificial intelligence in diabetic retinopathy (DR) detection is reflected in the increasing number of published review and research articles over recent years. A chronological analysis of literature from 2020 to 2025 demonstrates a significant upward trend, particularly after 2023, indicating growing academic and clinical interest in deep learning, generative AI, and explainable AI applications in ophthalmology. The sharp increase in publications during 2024 and 2025 highlights the accelerated integration of generative models, multimodal learning approaches, and deployment-oriented AI systems. This trend underscores the necessity for a comprehensive and structured review to consolidate current methodologies and identify emerging research directions.

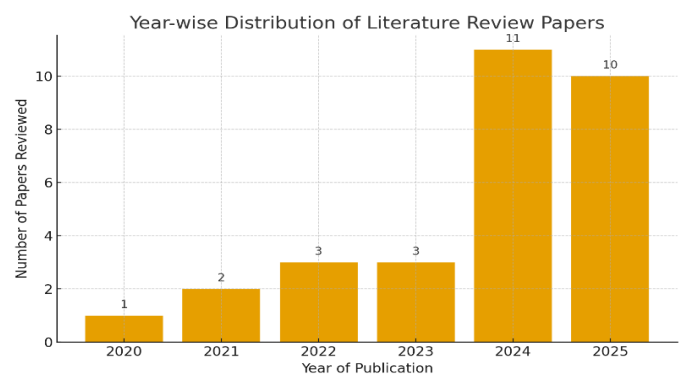


Figure 1 Year-wise Distribution of Literature Review Papers (2020–2025)

Figure 1 illustrates the increasing number of published review papers related to AI-based diabetic retinopathy detection between 2020 and 2025, showing substantial growth particularly in 2024 and 2025.

2. Proposed Conceptual Framework

The proposed conceptual framework integrates deep learning, transfer learning, generative AI, and explainable AI into a unified architecture for robust diabetic retinopathy (DR) detection. Initially, convolutional neural networks (CNNs) perform hierarchical feature extraction from fundus images to identify low-level textures and high-level pathological patterns such as microaneurysms and exudates. Transfer learning leverages pre-trained models to improve convergence speed and enhance performance, particularly in scenarios with limited annotated retinal datasets. Generative AI components, including GAN-based augmentation and anomaly synthesis, address class imbalance and enrich underrepresented DR severity categories. Furthermore, explainable AI (XAI) techniques such as Grad-CAM and attention heatmaps provide visual justifications for model predictions, thereby increasing transparency and clinical trust. The integration of these modules results in an enhanced generative AI-driven diagnostic system that is accurate, scalable, interpretable, and suitable for deployment in real-world ophthalmic screening environments. Shown in Figure 2 Conceptual Framework [1 – 6]

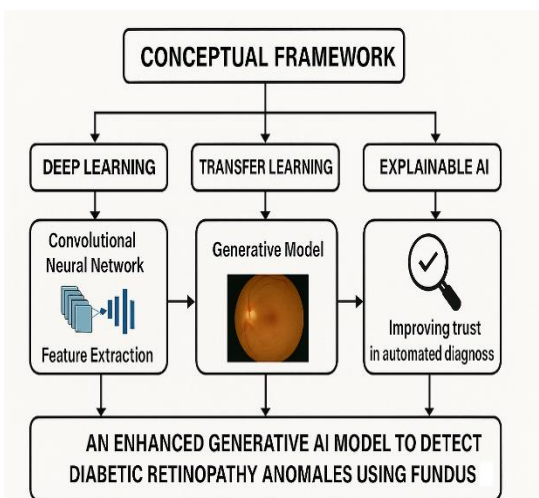


Figure 2 Conceptual Framework

3. Clinical Background of Diabetic Retinopathy

3.1. Pathophysiology and Stages

Diabetic retinopathy is a microvascular complication characterized by damage to retinal blood vessels due to prolonged hyperglycemia. The disease progresses through well-defined stages: mild, moderate, and severe non-proliferative DR (NPDR), followed by proliferative DR (PDR). Key pathological features include microaneurysms, hemorrhages, hard exudates, cotton wool spots, neovascularization, and macular edema [2].

3.2. Imaging Modalities

Color fundus photography remains the most widely used imaging modality for DR screening due to its non-invasive nature and cost-effectiveness. However, optical coherence tomography (OCT) and OCT angiography (OCTA) provide high-resolution cross-sectional views of retinal layers and microvasculature, enabling more detailed analysis of retinal abnormalities [10]. Recent studies have leveraged OCT-based biomarkers for early DR detection using DL techniques [19], [20].

4. Publicly Available Datasets

High-quality annotated datasets are critical for training and evaluating DL models. Several publicly available datasets have significantly contributed to DR research.

4.1. APTOS 2019 Dataset

The APTOS 2019 Diabetic Retinopathy Dataset is one of the most widely used benchmarks for DR classification [1]. It contains thousands of fundus images labeled into five DR severity levels. Despite its utility, the dataset exhibits class imbalance and variability in image quality, posing challenges for model generalization.

4.2. Teleophthalmology Datasets

Early initiatives such as TeleOphta demonstrated the feasibility of automated DR screening in teleophthalmology settings using machine learning and image processing techniques [11]. These datasets laid the foundation for modern DL-based approaches.

4.3. Challenges in Annotation

Manual annotation of medical images is costly and time-consuming, requiring expert ophthalmologists. Semi-supervised and weakly supervised approaches have been proposed to reduce dependency on pixel-



level annotations, particularly in OCT-based analysis [3], [19], [30].

5. Image Preprocessing and Data Augmentation

5.1. Preprocessing Techniques

Preprocessing plays a vital role in enhancing image quality and improving model performance. Common techniques include contrast-limited adaptive histogram equalization (CLAHE), noise reduction, color normalization, and resizing [8], [14]. Retinal image quality assessment networks have also been proposed to filter low-quality images prior to classification [14].

5.2. Data Augmentation

To mitigate overfitting and class imbalance, data augmentation techniques such as rotation, flipping, scaling, and elastic distortion are widely employed [12]. Elastic distortion has been shown to improve robustness by simulating realistic anatomical variations [18].

5.3. GAN-Based Augmentation

Generative adversarial networks (GANs) have gained popularity for synthesizing realistic retinal images, particularly for underrepresented DR classes. Studies have demonstrated that GAN-generated samples can significantly improve classification performance [6], [15].

6. Deep Learning Architectures for DR Detection

6.1. Convolutional Neural Networks

CNNs form the backbone of most DR detection systems. Architectures such as VGG, ResNet, DenseNet, and Inception have been extensively evaluated for fundus image classification [5], [17], [31]. ResNet-based models, in particular, have shown superior performance due to their ability to mitigate vanishing gradient issues.

6.2. Transfer Learning

Given limited labeled data, transfer learning from large-scale datasets such as ImageNet has become a standard practice. Fine-tuned pre-trained models have consistently outperformed models trained from scratch [24].

6.3. Ensemble and Hybrid Models

Ensemble approaches combining multiple CNN architectures or integrating handcrafted features have been proposed to improve robustness and

generalization [21]. Hybrid systems leveraging segmentation and classification networks have also been explored [16].

7. Weakly Supervised and Semi-Supervised Learning

7.1. Motivation

Pixel-level annotations for retinal lesions are expensive and impractical at scale. Weakly supervised learning aims to localize and classify lesions using only image-level labels.

7.2. Weakly Supervised OCT Analysis

Recent works have introduced weakly supervised networks for biomarker localization and anomaly segmentation in OCT images [19], [20], [30]. These methods employ attention mechanisms and reconstruction-based learning to identify pathological regions without explicit annotations.

7.3. Semi-Supervised Labeling

Semi-supervised approaches leverage unlabeled data through clustering and pseudo-labeling strategies. Such techniques have been successfully applied in medical imaging to generate reliable ground truth with minimal expert intervention [3].

8. Generative AI and Knowledge Distillation

8.1. Generative Adversarial Networks

Beyond data augmentation, GANs have been utilized for image enhancement, lesion synthesis, and anomaly detection. Generative AI-based DR detection frameworks have shown improved sensitivity for early-stage DR [6].

8.2. Knowledge Distillation

Teacher-student frameworks enable the transfer of knowledge from large, complex models to lightweight models suitable for deployment on edge devices. Knowledge distillation has been explored to reduce computational cost while maintaining high accuracy [4].

9. Explainable AI in DR Diagnosis

9.1. Importance of Interpretability

Clinical adoption of AI systems requires transparency and trust. Explainable AI (XAI) techniques provide visual and quantitative explanations for model predictions, aiding clinical validation.

9.2. Visualization Techniques

Class activation maps (CAMs), Grad-CAM, and attention-based heatmaps are commonly used to

highlight pathological regions influencing model decisions [28], [29]. Such techniques are essential for ensuring that models focus on clinically relevant features.

9.3. Clinical Integration Challenges

Despite promising results, integrating AI systems into real-world clinical workflows requires careful consideration of usability, reliability, and regulatory compliance [26].

10. Performance Evaluation Metrics

Performance evaluation metrics play a vital role in assessing the effectiveness and clinical reliability of automated diabetic retinopathy (DR) detection systems. Since DR screening directly impacts early diagnosis and prevention of vision loss, the selected metrics must capture both predictive accuracy and clinical sensitivity [2], [5]. Most studies evaluating deep learning-based DR systems rely on benchmark datasets such as the APTOS 2019 dataset, which facilitates standardized comparison across different models and methodologies [1]. For classification tasks, widely used metrics include accuracy, sensitivity (recall), specificity, precision, F1-score, and area under the receiver operating characteristic curve (AUC-ROC). Accuracy provides an overall measure of correct predictions; however, due to the imbalanced nature of DR datasets, it may not adequately reflect true clinical performance [17]. Sensitivity is particularly critical in screening applications, as missing a DR-positive case may delay treatment and lead to irreversible vision loss [2]. Specificity complements sensitivity by reducing false-positive referrals, which is essential in large-scale teleophthalmology systems [11]. The F1-score balances precision and recall, while AUC-ROC is commonly used to evaluate the discriminative ability of models independent of classification thresholds [5], [24]. For segmentation and lesion localization tasks, pixel-level metrics such as the Dice similarity coefficient (DSC) and Intersection over Union (IoU) are predominantly used. These metrics quantify the spatial overlap between predicted lesion regions and ground-truth annotations, making them suitable for evaluating the segmentation of retinal abnormalities such as microaneurysms and exudates [16]. In weakly supervised and OCT-based approaches, Dice and IoU

remain standard evaluation measures despite limited annotation availability [19], [30]. In unsupervised and anomaly detection frameworks, evaluation is often performed using reconstruction error-based metrics and AUC scores, which measure how effectively abnormal retinal structures deviate from learned normal patterns [18]. Additionally, recent studies emphasize the importance of computational efficiency metrics, including inference time and model complexity, to support real-world deployment in resource-constrained clinical environments [26]. Overall, a comprehensive evaluation strategy combining classification, segmentation, and efficiency metrics is essential for the reliable translation of AI-based DR systems into clinical practice [5], [17].

11. Challenges and Open Issues

11.1. Data Imbalance and Bias

Class imbalance remains a major challenge, particularly for severe DR stages. Biased datasets may lead to reduced generalizability across populations [17].

11.2. Generalization and Robustness

Variability in imaging devices, acquisition protocols, and patient demographics affects model robustness. Domain adaptation and multi-center training are potential solutions.

11.3. Ethical and Regulatory Considerations

The deployment of AI in healthcare raises ethical concerns related to data privacy, accountability, and fairness. Regulatory frameworks must evolve to ensure safe and effective use of AI-based diagnostic tools [26].

12. Future Research Directions

Future research should focus on:

- Multimodal learning combining fundus, OCT, and clinical data.
- Self-supervised and foundation models for retinal imaging.
- Real-time and edge-deployable AI systems.
- Clinician-in-the-loop learning paradigms.
- Standardized benchmarks for fair comparison.

Conclusion

This review has presented a comprehensive overview



of deep learning and generative AI techniques for diabetic retinopathy detection and analysis. Advances in CNN architectures, weakly supervised learning, and generative models have significantly improved automated DR screening performance. However, challenges related to data quality, interpretability, and clinical deployment remain. Continued interdisciplinary collaboration between engineers, clinicians, and policymakers is essential to translate these technological advancements into real-world clinical impact.

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