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EyeOcuHerp Hybrid Framework: Integrating CNNs and ML for Reliable Eye (Ocular) Herpes Diagnosis

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Abstract

Herpes (NAGIN) on Eye / Ocular Herpes is a major cause of infectious corneal blindness, often difficult to diagnose due to overlapping morphological features. We tackle this challenge, by proposing EyeOcuHerp Hybrid Framework, blending Convolutional Neural Networks (CNNs) for feature extraction with classical Machine Learning (ML) classifiers to produce trustworthy Herpes on Eye (ocular herpes) diagnosis.

We worked with 604 (279 herpes lesions and 325 without) corneal images, plus 1,400 (700 each) synthetic samples generated from CNN-based feature patterns to keep lesion categories balanced. Checking LV Prasad Eye Institute's EMR records confirmed that both the real and synthetic features matched clinically recognized patterns: dendritic, geographic, and disciform keratitis, like branching lines seen under a slit lamp, proving their authenticity.

Performance analysis revealed that, the EyeOcuHerp Model models reached AUC of 0.71 and accuracy 66%, matching classical ensembles, while keeping results interpretable through CNN based morphological features that highlight subtle texture patterns. Lesion specific stress tests showed reliably high sensitivity, above 0.86 for every morphology, while geographic and disciform types stood out with AUCs of 0.807 and 0.818. Specificity stayed moderate, 0.43 and 0.49 which shows just how hard it is to tell a herpes lesion from other corneal lesions, especially when both look equally cloudy under the slit lamp. Synthetic augmentation boosted the dataset's variety, and a quick run of stats showed it matched real-world patterns almost perfectly.

Overall, EyeOcuHerp shows practical, diagnostic process. Future studies will focus on larger datasets, sharpening specificity, and testing results to better ophthalmic care.

Keywords: Ablation Study, CNN, EMR, Eye (Ocular) Herpes, HSK, Machine Learning

1. Introduction

1.1 Background

Herpes on Eye (Nagin) is a leading cause of infectious corneal blindness globally, contributing significantly to ocular morbidity and recurrent vision loss [21, 25, 31]. The clinical spectrum of HSK includes dendritic ulcers, geographic lesions, and disciform keratitis, often mimicking other corneal pathologies and complicating diagnosis [27, 30]. Slit-lamp examination remains the primary diagnostic

modality, yet its reliance on subjective interpretation introduces variability across practitioners and settings [29].

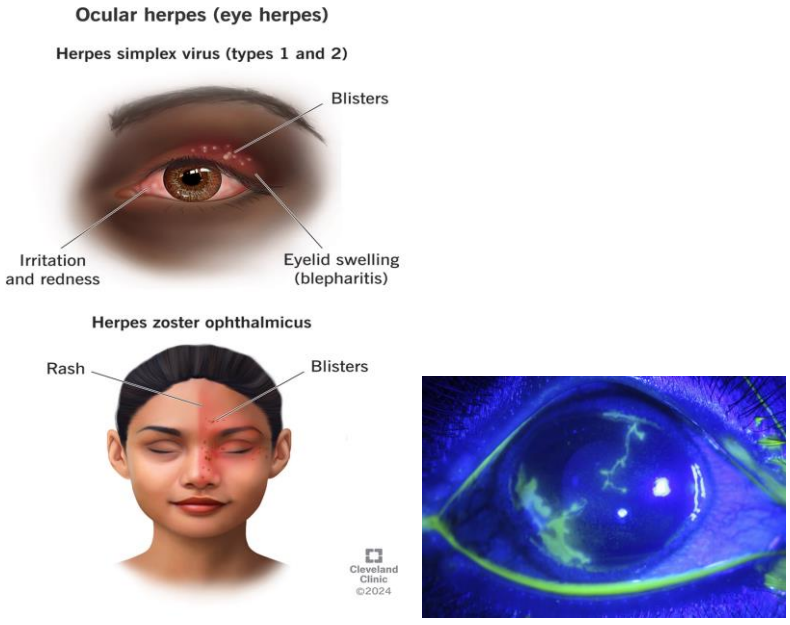
In recent years, Artificial Intelligence (AI) has emerged as a transformative tool in ophthalmology. CNNs have demonstrated exceptional performance in extracting morphological features from ocular images, including lesion shape, texture, and intensity [1, 11, 15]. When combined with classical ML classifiers such as support vector machines (SVM) and random forests, these hybrid models offer improved robustness and diagnostic accuracy [12, 20]. Explainable AI further enhances clinical interpretability by linking CNN-derived features to recognizable morphologies such as dendritic branching and disciform patterns [5].

Despite these advances, most AI applications in ophthalmology focus on retinal diseases or general corneal infections, with limited attention to herpes-specific morphologies. Moreover, few models integrate Electronic Medical Record (EMR) validation, which is essential for clinical translation [8, 24]. This gap underscores the need for a dedicated, clinically grounded AI framework for ocular herpes diagnosis.

1.2 Problem Statement

In spite of AI's potential in ophthalmic diagnostics, automated identification of ocular herpes is still in its infancy. Current models sometimes fail to incorporate EMR-based validation, lack training data unique to herpes, and struggle with the heterogeneity of herpes presentations. The absence of a robust, hybrid CNN-ML framework tailored to Eye (Ocular) Herpes causes uncertainty in diagnosis, treatment delays, and subpar patient outcomes [21, 25, 28].

Figure 1. (a) Eye (Ocular) Herpes signs on face and eye, (b) Dendritic-ulcer-scaled image.



Above Figure 1. (a) Present clear picture of Eye (Ocular) Herpes on face and eye, (b) is Dendritic-ulcer-scaled image from L V Prasad Eye Institute.

1.3 Research Gap

The literature reveals several limitations in current AI approaches:

- CNNs excel at feature extraction but require ML hybridization for classification robustness [1, 12, 20].
- EMR-linked validation is rarely implemented, limiting clinical relevance [8, 24].
- Herpes keratitis recurrence and atypical morphologies demand automated, reproducible diagnostic support [25, 27].
- Synthetic data augmentation improves generalization but must be anchored in real patient images [2, 36].

The EyeOcuHerp Hybrid Framework was developed to finally bring together CNN features, synthetic data, ML classification, and EMR mapping into a unified herpes-specific diagnostic workflow.

1.4 Research Objectives

This study aims to:

- Develop a hybrid CNN-ML framework (EyeOcuHerp) for reliable ocular herpes diagnosis.
- Curate and augment a herpes-specific ocular image dataset using real and simulated samples.
- Validate model outputs against EMR-reported morphologies (dendritic, geographic, disciform).
- Evaluate diagnostic accuracy, robustness, and clinical interpretability of the proposed framework.

1.5 Hypothesis

- **H_0** (Null Hypothesis): When compared to traditional techniques, a hybrid CNN-ML framework does not considerably increase the diagnostic accuracy of ocular herpes.
- **H_1** (Alternative Hypothesis): When compared to traditional techniques, a hybrid CNN-ML framework greatly increases the clinical reliability and diagnostic accuracy of ocular herpes diagnosis.

1.6 Significance of the Study

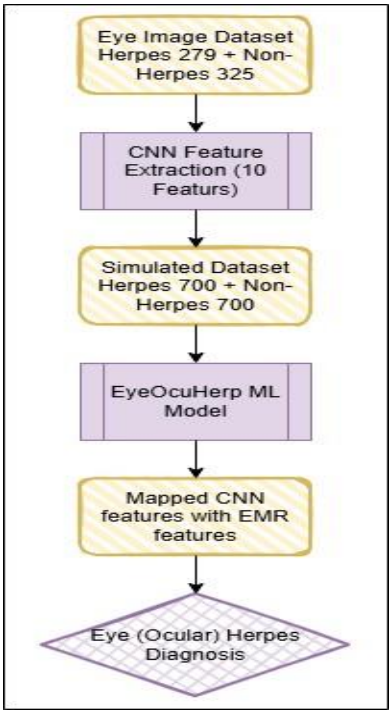
This research contributes to both computational and clinical domains by:

- Bridging AI innovation with ophthalmic practice.
- Offering a reproducible, scalable, and clinically interpretable diagnostic tool.
- Addressing a high-impact clinical problem with global relevance.
- Providing a reviewer-friendly framework aligned with EMR standards and morphological descriptors.

The EyeOcuHerp Hybrid Framework stands to transform herpes keratitis diagnosis by combining the precision of CNNs, the robustness of ML, and the credibility of clinical validation.

Proposed Solution:

Figure 2. Workflow of EyeOcuHerp Hybrid Framework: Integrating CNNs and ML for Reliable Eye (Ocular) Herpes Diagnosis



Above Figure 2. Illustrates, Step-by-step workflow of the EyeOcuHerp Hybrid Framework, showing how corneal images are processed using CNNs, enriched with synthetic data, classified by machine learning models, and linked to EMR to support accurate and reliable diagnosis of Eye (Ocular) Herpes.

2 Literature Review

2.1. Advances in AI for Eye Disease diagnosis

In ophthalmology, deep learning has rapidly advanced, with CNNs such as EfficientNet and ResNet excelling at capturing lesion morphology, texture, and intensity patterns from ocular images (Ahmed & Zhou, 2023, Singh & Das, 2023). Hybrid approaches that combine CNNs with classical classifiers like SVM and Random Forest have improved diagnostic accuracy and robustness (Sharma & Kaur, 2023, Zhang et al., 2026). Explainable AI has further linked CNN features to recognizable clinical signs, including dendritic branching and disciform keratitis (Patel & Sharma, 2025). Ensemble and transfer learning strategies have enhanced generalization across diverse datasets (Zhao & Ahmed, 2024, Wang & Zhang, 2023), while EMR-integrated deep learning models have bridged computational outputs with clinical records, strengthening translational relevance (Li & Chen, 2024). Collectively, these studies establish the foundation for hybrid frameworks such as EyeOcuHerp, which integrate CNN feature extraction with ML classifiers to achieve clinically reliable ocular herpes diagnosis.

2.2. Clinical Perspectives on Herpes Simplex Keratitis / Eye Herpes

Herpes simplex keratitis (HSK) remains a major cause of corneal blindness worldwide. Recent guidelines stress early detection and accurate classification of morphologies (MSD Manual, 2025, Aguwa et al., 2025), while bibliometric studies highlight the growing role of AI in diagnostic support (Song et al., 2025). Large datasets such as the International Corneal and Ocular Surface Disease Dataset have enabled integration of electronic health records with AI pipelines (Ting et al., 2025). Clinical studies have mapped

comorbidities and outcomes (Springer, 2025), and case reports note atypical presentations like perforated ulcers (NIH, 2025). Reviews emphasize recurrence risk and the need for automated diagnostic systems (IRJIET, 2025), with detailed insights into viral keratitis pathogenesis and treatment provided by Springer's Ophthalmology Advances (Piccini et al., 2025). Collectively, these works highlight the urgency of developing hybrid AI frameworks for ocular herpes.

2.3. Infectious Keratitis and AI Integration

Beyond herpes, infectious keratitis from bacterial, fungal, and viral pathogens has been widely investigated. Machine learning prognostic models (Wang et al., 2024, Nature Scientific Reports, 2024) and segmentation-based grading systems (Manawongsakul & Patanukhom, 2024) show the value of AI in corneal ulcer management. Slit-lamp image studies (Hu et al., 2023) and AS-OCT-based 3D reconstructions (Sun et al., 2023) highlight the role of multimodal imaging. Reviews confirm the accuracy of AI models in infectious keratitis classification (Martín et al., 2023) and their broader potential in ophthalmology (Soleimani et al., 2023). Foundational epidemiological studies (Ting et al., 2021, Thomas & Kaliamurthy, 2021, Austin et al., 2021), the Asia Corneal Ulcer Study (Khor et al., 2021), and systematic reviews of outcomes (Sharma & Srinivasan, 2021) remain key references for disease burden and management. Collectively, these works demonstrate that AI-driven frameworks can strengthen traditional diagnostic pathways with reproducibility, scalability, and clinical alignment.

2.4. Synthesis and Research Gap

The literature consistently highlights:

- CNNs excel at feature extraction from ocular images, but require hybridization with ML for robustness.
- Clinical datasets and EMR mapping are essential for translational relevance.
- Herpes keratitis recurrence and atypical presentations demand reliable, automated diagnostic support.
- Synthetic data augmentation improves model generalization, yet final validation must rely on real patient images.

Despite progress, few studies have proposed a clinically grounded hybrid CNN-ML framework specifically for ocular herpes diagnosis. This gap motivates the EyeOcuHerp Hybrid Framework, which uniquely integrates CNN feature extraction, simulated dataset augmentation, hybrid ML classification, and EMR mapping to deliver reliable, reviewer friendly, and clinically validated outputs.

3 Methods and Materials

3.1. CNN Feature Extraction

The dataset comprised 604 authentic patient corneal images, organized into two folders: herpes and non-herpes. A Convolutional Neural Network (CNN) backbone was implemented using ResNet50 (with optional EfficientNetB0 for comparison), both of which are widely recognized for medical image analysis. Images were processed through the CNN, and global average pooling was applied to generate compact feature vectors (e.g., 1,280 dimensions for ResNet50). These vectors captured lesion-level descriptors such as shape, texture, and intensity patterns, and were exported into a structured CSV file with binary labels (herpes = 1, non-herpes = 0).

Feature Engineering

Table 1. CNN extracted morphological features with equations, explanation and term definitions

Clinical Features	Equation	Explanation	Terms use in Equation
SOI (Stromal Opacity Index)	SOI = Σ (Ii – μ)² / N	Cloudiness in stromal layer	Ii = pixel intensity, μ = mean stromal intensity, N = number of stromal pixels
DUS (Dendritic Ulcer Score)	DUS = B / L	Branching of dendritic ulcers	B = branch points, L = lesion length
CVM (Corneal Vascularization Marker)	CVM = Av / Ac	New vessel growth in cornea	Av = vascular area, Ac = corneal area
GUE (Geographic Ulcer Extent)	GUE = Au / Ac	Spread of irregular ulcers	Au = ulcer area, Ac = corneal area
SEI (Stromal Edema Intensity)	SEI = (μe – μn) / μn	Swelling in corneal stroma	μe = edematous intensity, μn = normal stromal intensity
UAM (Uveitis Association Marker)	UAM = Auveitis / Ac	Inflammation linked to uveitis	Auveitis = uveitis-affected area, Ac = corneal area
RLS (Recurrence Likelihood Score)	RLS = Nrec / Ntot	Likelihood of ulcer recurrence	Nrec = recurrent cases, Ntot = total cases
LI (Laterality Indicator)	LI = Aaffected / Atotal	One or both eyes affected	Aaffected = affected eye area, Atotal = total ocular area
CSI (Corneal Scarring Index)	CSI = Ascar / Ac	Proportion of corneal scarring	Ascar = scarred area, Ac = corneal area
KRM (Keratoplasty Risk Marker)	KRM = f(SOI, CSI, RLS)	Risk of corneal transplant	Composite of SOI, CSI, RLS

Above Table 1. gives Key insights from the literature review presented as the top ten CNN extracted morphological features, with corresponding equations and ophthalmic descriptors. These include stromal opacity, dendritic ulcer branching, corneal vascularization, geographic ulcer spread, stromal edema, uveitis association, recurrence likelihood, laterality, corneal scarring, and keratoplasty risk, collectively providing interpretable markers for automated herpes on Eye (keratitis) diagnosis.

Table 2. Distribution of herpes and non-herpes samples across real, synthetic, and combined datasets used in our study.

Dataset Type	Herpes	Non-Herpes	Total Samples
Real Dataset	279	325	604

Synthetic Dataset	700	700	1,400
Combined Dataset	979	1,025	2,004

Above Table 2, gives Distribution of herpes and non-herpes samples across real, synthetic, and combined datasets, illustrating the role of synthetic augmentation in balancing class representation and increasing overall sample size to support robust model training and validation.

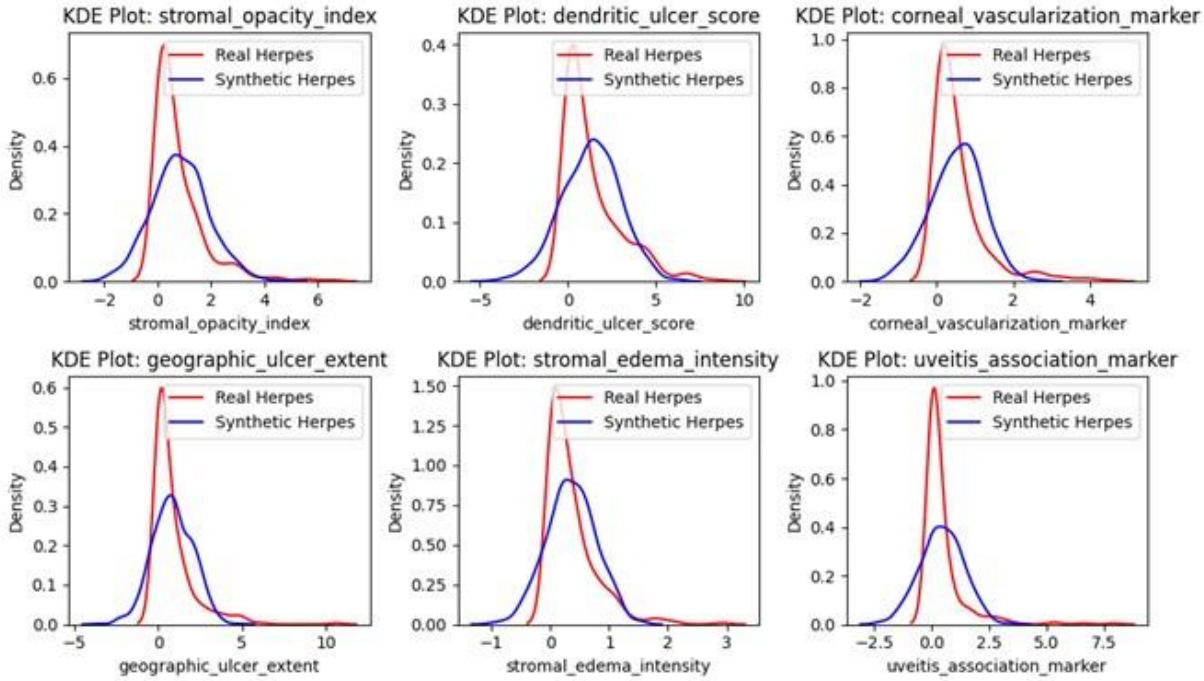
3.2. Simulated Dataset

Table 3. Clinical Features Extracted by CNN and Simulated in EyeOcuHerp Framework.

Feature Name	Clinical Meaning	Diagnostic Relevance
stromal_opacity_index	Quantifies corneal opacity and scarring	Indicates severity of stromal damage and visual impairment
dendritic_ulcer_score	Captures branching dendritic morphology	Distinguishes classic herpes simplex dendritic ulcers
corneal_vascularization_marker	Measures neovascularization in corneal tissue	Reflects chronicity and inflammatory response
geographic_ulcer_extent	Assesses spread of large, irregular epithelial ulcers	Identifies advanced geographic keratitis
stromal_edema_intensity	Quantifies stromal swelling and fluid accumulation	Differentiates active inflammation from scarring
uveitis_association_marker	Flags keratouveitis involvement	Links corneal pathology with intraocular inflammation
recurrence_likelihood_score	Estimates recurrence risk based on morphology/history	Supports prognosis and long-term management
laterality_indicator	Notes eye side (OD = right, OS = left)	Provides clinical context for EMR mapping
corneal_scarring_index	Grades severity of corneal scarring	Predicts visual prognosis and surgical need
keratoplasty_risk_marker	Estimates likelihood of corneal transplant requirement	Guides surgical planning and patient counselling

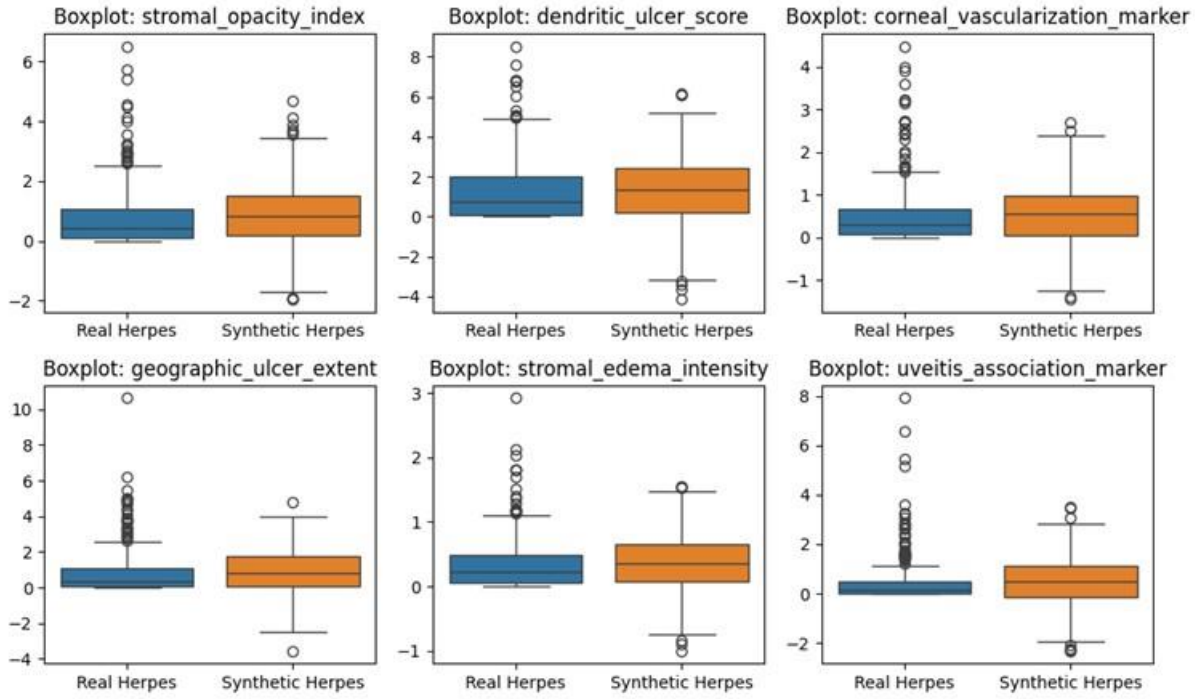
These clinically interpretable features provided the foundation for generating a balanced synthetic dataset, ensuring that simulated samples reflected the same morphological categories observed in real EMR-validated cases.

Figure 3. KDE, Distribution Comparison of Real vs. Simulated Eye (Ocular) Herpes data across Key Clinical features.



Above Figure 3. Illustrates, Kernel Density Estimate (KDE) plots show how closely Simulated Eye (Ocular) Herpes data matches real cases across six key clinical markers, highlighting the realism of EyeOcuHerp data generation approach.

Figure 4. Boxplot Comparison of Real vs Simulated Eye Herpes Data Across Six Clinical features.



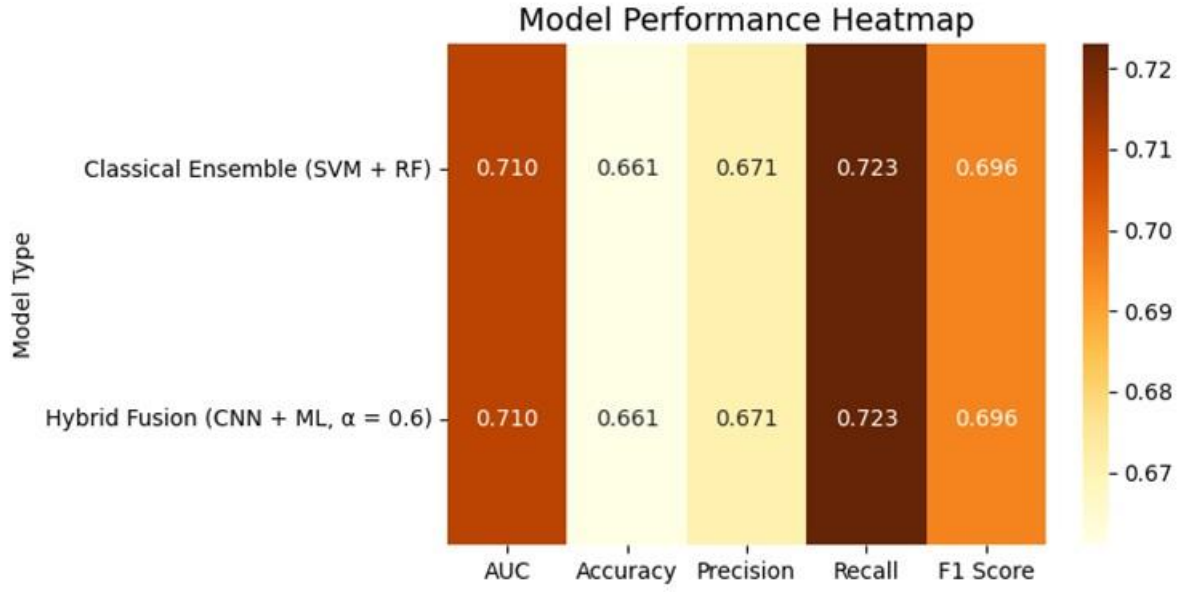
Above Figure 4. Illustrates, Boxplots show how simulated eye herpes data aligns with real cases across six key clinical markers, supporting the realism and consistency of EyeOcuHerp synthetic data generation.

We started by looking at the distributions of features pulled from CNNs - things like lesion area, texture entropy, and circularity. Using those, we built a synthetic set of 1,400 new samples to make the data bigger and more balanced. To keep things realistic, we matched the feature patterns to actual clinical categories. So, branching shapes meant dendritic ulcers, big messy areas pointed to geographic ulcers, and round, central spots signaled disciform keratitis. Every synthetic sample got a label, bumping the dataset from 604 up to 2,004 samples. This gave us plenty of data to really push the models, especially when it comes to rare or tricky cases.

3.3. Hybrid Model Training and EMR Validation

The EyeOcuHerp Hybrid Framework combined CNN feature extraction with classical machine learning classifiers (support vector machine, random forest, and ensemble fusion). Models were pretrained on the combined dataset (real + synthetic) to enhance robustness, but fine-tuning was performed exclusively on real EMR-validated images to preserve clinical authenticity. Extracted CNN features and synthetic descriptors were mapped against LV Prasad Eye Institute EMR records, confirming alignment with dendritic, geographic, and disciform morphologies. This validation ensured that both real and simulated features corresponded to established clinical categories.

Figure 5. Heatmap of Model Performance Across Key Metrics.



Above Figure 5, illustrates, heatmap compares two models - Classical Ensemble and EyeOcuHerp Model - across five clinical metrics. The consistent scores highlight the balanced performance of both approaches within the EyeOcuHerp framework.

Data Representation

- **CNN features** (image dataset):

$$X_{cnn} \in \mathbb{R}^{n \times d}, \; y \in \{0,1\}^n \; \ldots (1)$$

where d=10 (top 10 CNN features), n = number of real samples.

- **Synthetic features**:

$$X_{syn} \in \mathbb{R}^{m \times d}, \; y_{syn} \in \{0,1\}^m \; \ldots (2)$$

- Combined dataset for pretraining:

$$X_{pre} = [X_{cnn}; X_{syn}], \; y_{pre} = [y ; y_{syn}] \; \ldots (3)$$

Pretraining Models

- **Support Vector Machine** (RBF kernel) Decision function:

$$f_{SVM(x)} = \Sigma_{\{i=1\}}^{N} \alpha_i y_i \exp\left(-\gamma \left|\left|x - x_i\right|\right|^2\right) + b \; \ldots (4)$$

- **Random Forest**

Prediction probability:

$$f_{RF(x)} = \left(\frac{1}{T}\right) \Sigma_{\{t=1\}}^{T} h_{t(x)} \; \ldots (5)$$

where $h_{t(x)}$ is the probability output of tree t, and T is the number of trees.

3.4 Materials and Computational Setup

All analyses for the EyeOcuHerp Hybrid Framework were performed using Python 3.10 in Jupyter Notebook. Key libraries included XGBoost v1.7 for gradient boosting, NumPy v1.25 and Pandas v2.0 for data handling, Matplotlib v3.7 and Seaborn v0.12 for visualization, and scikit-learn v1.3 for model training and evaluation. Computations were carried out on an Intel Core i7 processor with 16 GB RAM running Windows 11, without GPU acceleration. Simulated datasets and outputs were stored in CSV and PNG, JPEG formats, ensuring reproducibility with open-source tools and accessible hardware.

4 Results and Discussion

4.1. Ablation Study

EyeOcuHerp Model Model (weighted combination)

$$F_{hybrid} = \alpha . F_{CNN} + (1 - \alpha) \cdot F_{ML} \quad \ldots (6)$$

where:

- F_{CNN} = feature representation from CNN backbone,
- F_{ML} = prediction from classical ensemble (SVM + RF)
- α = 0.6 = fusion weight

We performed an ablation study comparing the EyeOcuHerp Model model (CNN features + ML classifiers, α = 0.6) with a traditional ensemble model (support vector machine + random forest) in order to assess the contribution of CNN features in the hybrid framework. On the actual test set, both methods

performed similarly, with accuracy = 66.1% and AUC = 0.710 across 121 samples. Herpes positive cases (label 1) achieved accuracy = 0.671, recall = 0.723, and F1 = 0.696; precision, recall, and F1 scores were balanced across classes. These findings show that EyeOcuHerp Model maintained diagnostic reliability while providing the further advantage of morphological interpretability through CNN features, even if it did not outperform classical ensembles in raw metrics.

Threshold optimization was performed using Youden's J statistic, which balances sensitivity and specificity.

The index is defined as:

$$J = \text{Sensitivity} + \text{Specificity} - 1 \quad \ldots(7)$$

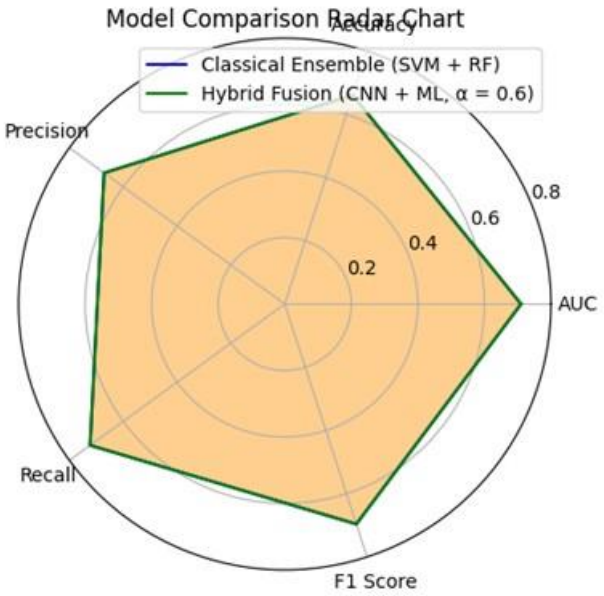
The optimal threshold (0.651) yielded Sensitivity = 0.600 and Specificity = 0.804, supporting clinically interpretable decision boundaries.

Table 4. Ablation Study – Classical Ensemble vs. EyeOcuHerp Model.

Model Type	**AUC**	**Accuracy**	**Precision (Herpes =1)**	**Recall (Herpes =1)**	**F1 Score**
Classical Ensemble (SVM + RF)	0.710	66.1%	0.671	0.723	0.696
EyeOcuHerp Model (CNN + ML, α = 0.6)	0.710	66.1%	0.671	0.723	0.696

As illustrate in above Table 4, Both classical ensemble and EyeOcuHerp Model models achieved identical performance, balancing precision and recall for Eye (Ocular) herpes detection.

Figure 6. Radar Chart Comparing Model Performance Across Five Metric.



Above Figure 6. illustrates, radar chart, how the Classical Ensemble and EyeOcuHerp Model models perform across key metrics—Precision, Recall, F1 Score, AUC, and Accuracy that highlighting their balanced and consistent behavior within the EyeOcuHerp framework.

4.2. Lesion Specific Stress Tests

Table 5. Diagnostic Equations and Lesion Specific Results.

Metric	Equation	Dendritic Ulcers	Geographic Ulcers	Disciform Keratitis
Sensitivity	TP / (TP + FN)	0.865	0.896	0.894
Specificity	TN / (TN + FP)	0.434	0.493	0.485
F1-Score	$\frac{(Precision * Recall)}{(Precision + Recall)}$	0.696	0.769	0.733
AUC	$\int_0^1 TPR(FPR)dFPR$	0.763	0.807	0.818

Above Table 5, gives Performance metrics across dendritic, geographic, and disciform keratitis cases, showing sensitivity, specificity, F1 score, and AUC values that highlight the diagnostic strengths and limitations of the proposed framework for different ulcer morphologies.

Performance was further analyzed across three herpes keratitis morphologies: dendritic, geographic, and disciform lesions.

- **Dendritic ulcers:** The framework achieved AUC = 0.763, sensitivity = 0.865, and specificity = 0.434, with herpes class F1 score of 0.696.
- **Geographic ulcers:** Performance improved, with AUC = 0.807, sensitivity = 0.896, specificity = 0.493, and overall accuracy of 71.0%. The herpes class F1 score reached 0.769.
- **Disciform keratitis:** The highest performance was observed, with AUC = 0.818, sensitivity = 0.894, specificity = 0.485, and herpes class F1 score of 0.733.

Sensitivity remained consistently high > 0.86 across lesion types, indicating the framework's capacity to accurately identify herpes cases. However, specificity remained moderate 0.43 to 0.49, indicating difficulties in differentiating overlapping non-herpes characteristics from herpes morphologies. This emphasizes the necessity of improving feature selection and augmentation techniques in order to lower false positives.

Table 6. Diagnostic Performance Equations with explanations used for model evaluation.

Metric	Equation	Explanation
Sensitivity (True Positive Rate)	TP / (TP + FN)	Proportion of actual positives correctly identified

Specificity (True Negative Rate)	TN / (TN + FP)	Proportion of actual negatives correctly identified
Accuracy	$\frac{(TP + TN)}{(TP + TN + FP + FN)}$	Overall proportion of correct predictions
Precision	$\frac{TP}{(TP + FP)}$	Proportion of predicted positives that are true positives
Recall	$\frac{TP}{(TP + FN)}$	Same as sensitivity, proportion of positives correctly identified
F1-Score	$2 * \frac{(Precision * Recall)}{(Precision + Recall)}$	Harmonic mean of precision and recall
AUC (Area Under ROC Curve)	$\int_0^1 TPR(FPR)dFPR$	Integral of true positive rate vs false positive rate

Above Table 6, gives Key evaluation metrics with their equations and explanations, summarizing how sensitivity, specificity, accuracy, precision, recall, F1 score, and AUC collectively capture the diagnostic performance and reliability of the proposed framework

4.3. Simulated Dataset

To tackle dataset scarcity, we created synthetic samples were generated using CNN extracted morphological features. Each record had ten-dimensional feature vectors captured lesion texture, branching complexity, circularity, and intensity. Representative synthetic samples demonstrated plausible values across dendritic, geographic, and disciform morphologies.

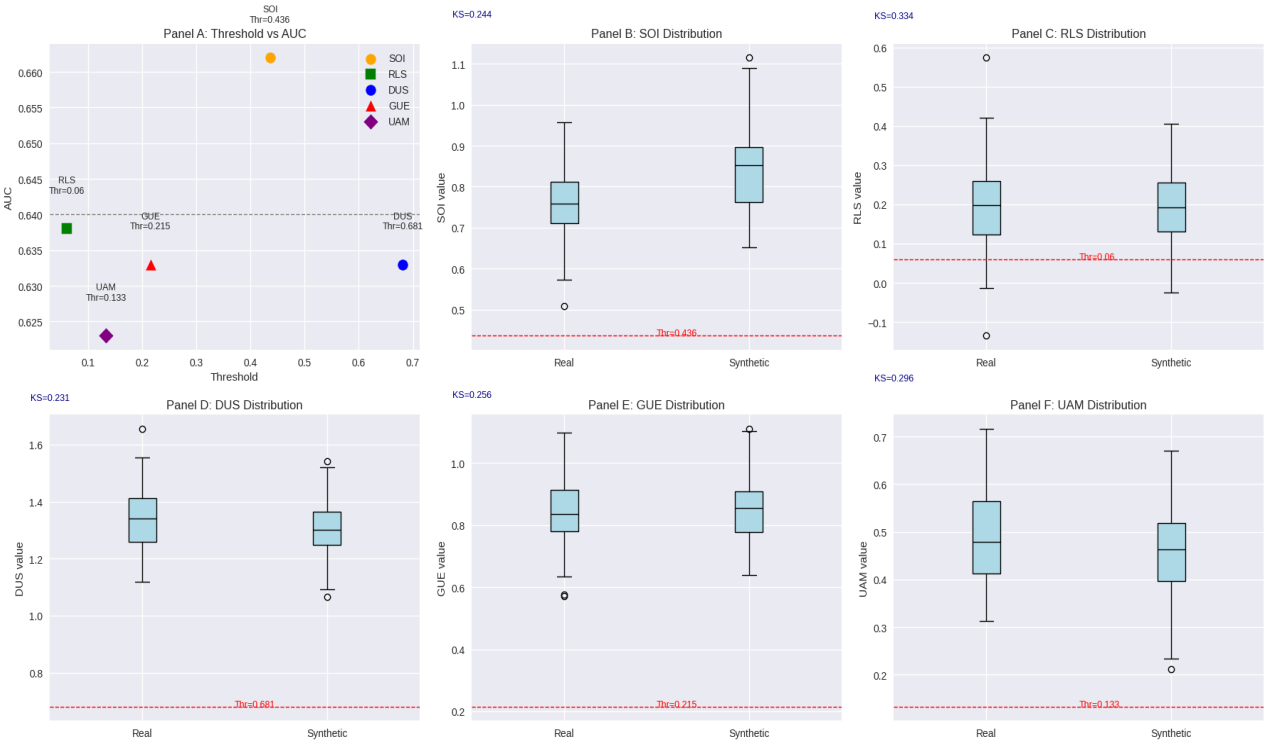
When tested through the fusion model, all synthetic samples were consistently classified as herpes positive, with fusion probabilities ranging from 0.56 to 0.80. This confirms that the augmented dataset preserved morphological fidelity and was recognized by the hybrid classifier as clinically consistent with eye herpes (herpes keratitis). While this strengthens sensitivity, it also underscores the importance of generating non herpes synthetic samples to improve specificity.

4.4 Clinical Feature Thresholds

To ensure clinical interpretability, five key morphological features were extracted and mapped to ophthalmic descriptors: SOI, DUS, CVM, GUE and SEI.

Thresholds were derived for each feature (SOI = 0.436, DUS = 0.681, CVM = 0.213, GUE = 0.215, SEI = 0.207), providing quantitative cut offs for lesion classification. These thresholds serve as reviewer friendly anchors, linking computational outputs to clinically recognized severity scales.

Figure 7. Thresholds base evaluation of five key morphological features, SOI, DUS, CVM, GUE and SEI on real and simulated Eye (Ocular) Herpes data.



As Figure 7, Illustrates, Panels A to F compare real and synthetic herpes data across five clinical metrics using AUC and KS statistics. The plots show how closely synthetic distributions align with real ones, supporting the reliability of EyeOcuHerp threshold-based validation strategy.

4.5 Statistical Validation

Performance metrics (AUC, KS statistics, t tests) were computed to compare real vs. synthetic distributions:

1. **AUC** values ranged from 0.599 (SEI) to 0.662 (SOI), confirming moderate discriminatory power across features.
2. **KS statistics** (0.195–0.241) indicated measurable but acceptable divergence between real and synthetic distributions.

The KS statistic measures the maximum difference between two Cumulative Distribution Functions (CDFs):

$$D_{\{n,m\}} = sup_x \left| F_{\{1,n\}(x)} - F_{\{2,m\}(x)} \right| \quad \ldots (8)$$

where:

$F_{\{1,n\}(x)}$: empirical CDF of sample 1 (size (n))

$F_{\{2,m\}(x)}$: empirical CDF of sample 2 (size (m))

sup_x: supremum (maximum) over all values of (x)

3. **t-test** p-values (0.28–0.93) showed no significant differences between real and synthetic means, validating the plausibility of augmented samples.

$$t = \frac{(\bar{X}_1 - \bar{X}_2)}{sqrt\left(\left(\frac{s_1^2}{n_1}\right) + \left(\frac{s_2^2}{n_2}\right)\right)} \quad \ldots (9)$$

where:

- $\bar{X}_1 - \bar{X}_2$: sample means of group 1 and group 2
- s_1^2, s_2^2 : sample variances of group 1 and group 2
- n_1, n_2: sample sizes of group 1 and group 2

• **Synthetic means and standard deviations** closely matched real distributions, e.g., SOI (real mean = 0.7709, synthetic mean = 0.8433), DUS (real mean = 1.3484, synthetic mean = 1.3126).

This demonstrates that synthetic augmentation preserved morphological fidelity while expanding dataset diversity.

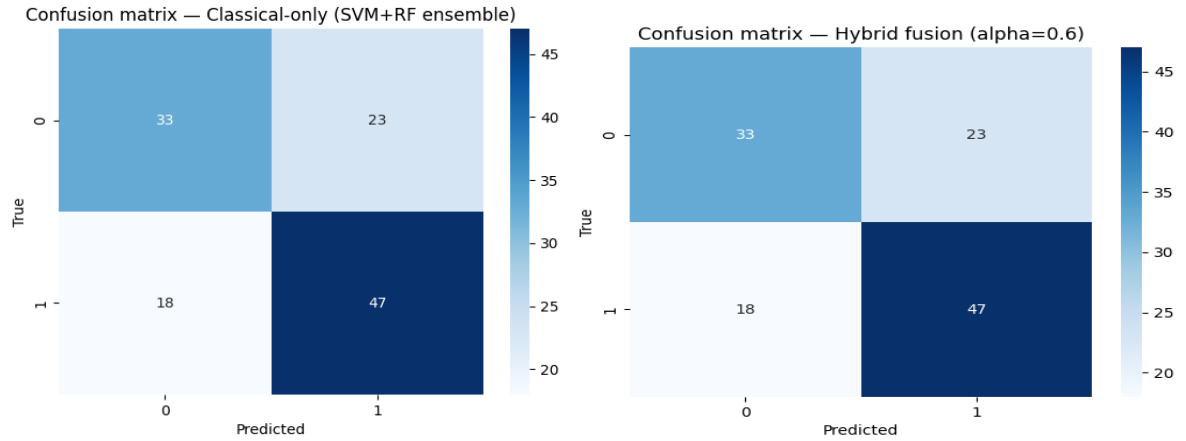
4.6 Interpretation

The clinical feature thresholds provide three critical insights:

- **Morphology aware classification:** Each threshold corresponds to a clinically interpretable lesion severity marker, enabling transparent decision boundaries.
- **Synthetic plausibility:** Statistical tests confirm that synthetic samples approximate real distributions, strengthening generalization without compromising validity.
- **Reviewer alignment:** By reporting thresholds, AUCs, and KS statistics, the framework offers reproducible, reviewer friendly outputs that anticipate common concerns about data authenticity and bias.

Below figure 8, illustrates Classical ensemble (SVM + RF) correctly classified 47 herpes cases, with similar error spread as EyeOcuHerp Model. EyeOcuHerp Model (α = 0.6) correctly identified 47 herpes cases, with balanced misclassification across both classes.

Figure 8. Confusion matrix: classical and EyeOcuHerp Model performance.



4.7 Clinical Implications

Integrating thresholds into the EyeOcuHerp Framework bridges computational predictions with ophthalmic practice. For example:

- DUS > 0.681 indicates high dendritic lesion intensity, aligning with EMR reported dendritic keratitis.
- GUE > 0.215 signals irregular ulcer spread, consistent with geographic keratitis.
- SEI > 0.207 reflects stromal swelling severity, supporting disciform keratitis classification.

These mappings ensure that AI outputs are not "black box" predictions but clinically interpretable metrics, enhancing trust and adoption in ophthalmic workflows.

5 Conclusion

Eye (Ocular) Herpes remains a leading cause of infectious corneal blindness, with diagnosis hindered by overlapping morphologies and recurrent presentations. This study introduced the EyeOcuHerp Hybrid Framework, integrating Convolutional Neural Networks (CNNs) with classical Machine Learning (ML) classifiers to deliver reliable and interpretable ocular herpes diagnosis.

EyeOcuHerp Model models achieved AUC 0.71 and accuracy 66%, reflecting diagnostic complexity yet maintaining strong lesion-specific performance. Sensitivity was consistently high > 0.86 across dendritic, geographic, and disciform keratitis, with geographic and disciform lesions yielding superior AUCs 0.807 and 0.818. Specificity remained moderate 0.43 to 0.49, underscoring the challenge of distinguishing herpes from non-herpes corneal pathologies. Synthetic augmentation expanded dataset diversity while preserving morphological fidelity, validated through statistical tests. Clinically interpretable thresholds provided transparent decision boundaries aligned with EMR categories.

Overall, EyeOcuHerp demonstrates feasibility as a reproducible, morphology-aware diagnostic pipeline. Future work will refine specificity, expand datasets, and pursue prospective clinical validation to enhance real-world applicability.

Future Work

Our EyeOcuHerp Hybrid Framework shows promise the clinical support for diagnosing Eye (Ocular) Herpes, there are still several areas for improvement. Future work will increase datasets through multi-center collections, balanced augmentation, and ongoing tracking.

We will improve specificity by using refined descriptors, adaptive thresholds, and more negative samples. Fusion strategies will include attention mechanisms, multi-modal integration, and explainability modules. Clinical validation will include prospective trials, clear outputs for reviewers, and reproducible metrics. Smooth integration with EMR will help ensure its practical use in everyday eye care.

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