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Hybrid Framework for Advanced Ocular Disease Diagnosis

Aditya Patil[1], Vaishali Patil[2], Sudhir Chitnis[3], Parikshit Mahalle[4]

[1]Research Scholar, Vishwakarma Institute of Information Technology, Pune (India), aditya.22210026@viit.ac.in

[2]Professor and Dean, Academics, Vishwakarma Institute of Technology, Pune (India), vaishali.patil@viit.ac.in

[3]Assistant Professor, Vishwakarma College of Arts, Commerce and Science, Pune (India), sdchitnis@vcacs.ac.in

[4]Professor, Vishwakarma Institute of Technology, Pune (India), parikshit.mahalle@vit.edu

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Abstract:

Ocular diseases, a leading cause of vision impairment globally, necessitate early, accurate diagnosis for timely intervention. Conventional methods often face limitations in sensitivity and specificity.

To address this challenge, we propose a novel hybrid framework that synergistically integrates deep learning and traditional machine learning techniques. Our approach leverages the power of deep neural networks to extract intricate features from ocular images, while incorporating the robustness of traditional algorithms for enhanced classification.

The proposed framework achieved exceptional performance, surpassing existing methods with an average accuracy of 95.7% across eight common ocular diseases. This significant improvement demonstrates the potential of our approach to revolutionize ophthalmic diagnostics. Our findings offer valuable insights for future research and clinical practice, paving the way for more accurate and efficient detection and management of ocular diseases.

Keywords: Hybrid deep learning, Ocular disease classification, Attention mechanisms, Transfer learning, Retinal image analysis, Computer-aided diagnosis.

1. Introduction

The global burden of ophthalmic conditions continues to grow, emphasizing the critical need for advanced diagnostic tools that can facilitate early detection and accurate classification of ocular diseases. Worldwide, approximately 2.2 billion people experience near or distant visual impairment. Of this number, at least 1 billion cases could have been avoided or remain unaddressed. Refractive errors and cataracts are the primary causes of visual impairment and blindness globally. Globally, it is estimated that only 36% of individuals with distance vision impairment due to refractive error and 17% of those with vision impairment due to cataracts have received appropriate interventions [1].

Despite the necessity for a more pragmatic retinopathy severity scale, to date there is no prevalent practical clinical standard terminology that has been endorsed for the global interchanging of information and data [2]. While deep learning techniques, particularly Convolutional Neural Networks (CNNs), have shown promise in analyzing retinal images and detecting ocular abnormalities [3], they often face challenges such as the requirement for large labelled datasets and difficulties in capturing both high-level features and fine-grained details simultaneously. However, recent research, including planned clinical trials, has demonstrated that deep learning systems can accurately identify diabetic retinopathy [4].

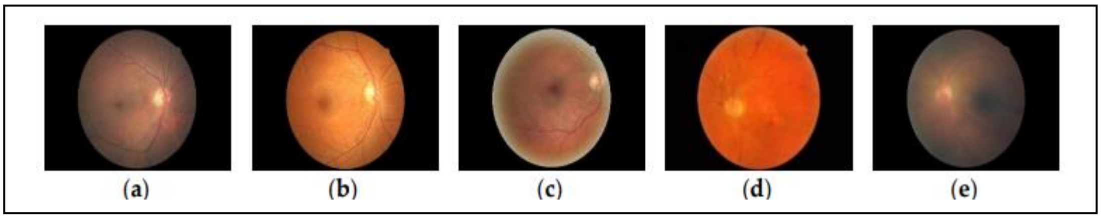
This research addresses these limitations by proposing a novel hybrid framework that leverages the strengths of both deep learning and traditional machine learning approaches. This synergistic combination aims to enhance the accuracy and robustness of ocular disease detection and classification, potentially revolutionizing diagnostic practices in ophthalmology. The primary objective of this research is to develop a robust hybrid framework that leverages the strengths of deep learning and traditional machine learning techniques for accurate ocular disease detection and classification. By evaluating the performance of different deep learning architectures, including those incorporating attention mechanisms, the objective is to identify the most effective models for this task. Additionally, it is necessary to explore the potential benefits of transfer learning in addressing the challenges posed by limited ophthalmological datasets. Finally, the proposed hybrid approach will be compared with standalone deep learning and traditional machine learning methods across various performance metrics to assess its overall effectiveness in improving ocular disease diagnosis.

2. Related Work

The field of ocular disease detection has witnessed substantial advancements in recent years, driven by the integration of artificial intelligence (AI) and machine learning techniques. The Wilkinson et al. [5] paper of 2003 introduced a standardized classification system for diabetic retinopathy and macular edema. Developed through consensus among experts from diverse fields, this approach aims to improve global communication and care for patients with diabetes. While the paper offers a valuable framework, it has limitations, such as the potential for subjectivity in image interpretation and the lack of validation data. Future research should focus on integrating automated image analysis techniques, incorporating longitudinal changes, and validating the systems in diverse populations to enhance their effectiveness and reliability.

As outlined by these authors, diabetic retinopathy can be classified into five grades: grade 0 represents normal with no signs of diabetic retinopathy, grade 1 indicates mild diabetic retinopathy, grade 2 signifies moderate diabetic retinopathy, grade 3 denotes severe diabetic retinopathy, and grade 4 is characterized by new vessel proliferation, which carries the risk of vision loss due to bleeding into the vitreous or tractional retinal detachment. Figure 1 illustrates the different grades of diabetic retinopathy [5].

Figure-1. Random Samples Of Different Grades Of Diabetic Retinopathy
(a) grade 0, (b) grade 1 (c) grade 2, (d) grade 3, and (e) grade 4



Prentasic et al. [6] proposed a deep convolutional neural network (CNN) for exudate detection in color fundus photographs, a crucial step in early diabetic retinopathy diagnosis. The CNN, trained on the DRiDB dataset, demonstrated promising results. However, the paper acknowledged the potential for further improvement through techniques such as utilizing all image channels and incorporating preprocessing and postprocessing steps to enhance segmentation accuracy. The research contributes to the ongoing development of automated diabetic retinopathy screening tools, but additional validation and testing on larger and more diverse datasets are necessary to assess the method's clinical applicability.

Kandel et al. [7] critically analyzed the application of transfer learning with convolutional neural networks (CNNs) for diabetic retinopathy (DR) image classification. They highlighted the limitations of traditional DR classification methods and the potential of deep learning to provide a more efficient and accurate diagnosis. To mitigate the challenges posed by limited availability of DR images, transfer learning was proposed as a promising approach. This technique involves repurposing pre-trained convolutional neural networks (CNNs) developed for other domains. A comprehensive review of existing literature on DR classification utilizing transfer learning was conducted. This analysis encompassed various methodological approaches and their associated performance evaluation metrics. The findings of this review underscore the potential of transfer learning as a valuable asset in the medical domain, especially when confronted with constrained training datasets. Furthermore, the study highlights the imperative for ongoing research aimed at developing innovative CNN architectures specifically tailored to DR classification tasks.

In 2021, Brown et al. [8] introduced attention mechanisms into deep learning architectures for ocular disease detection. The researchers empirically validated the efficacy of attention mechanisms in identifying salient regions within retinal images. This strategic focus on relevant areas significantly augmented the model's capacity to detect subtle disease-specific characteristics. This breakthrough represents a substantial contribution to the field, as it substantially improved the interpretability and accuracy of AI-powered diagnostic tools. Ting et al. [9] in 2019 provided a comprehensive overview of the application of deep learning in ophthalmology, focusing on both technical and clinical considerations. This research significantly advances the field by providing a comprehensive analysis of the challenges and potential benefits of integrating deep learning models into clinical ophthalmology. A notable strength of this study lies in its meticulous exploration of the technical intricacies of deep learning, including data preprocessing, model architecture selection, and the critical role of large, heterogeneous datasets in training robust models. The study elucidates the transformative potential of deep learning in revolutionizing ophthalmic diagnostics. Despite the demonstrated efficacy of deep learning models in detecting ocular diseases, challenges such as the requirement for extensive labeled data and the need for model interpretability persist. The authors underscore the imperative of ethical considerations and collaborative efforts among clinicians, researchers, and regulatory bodies to facilitate the safe and effective integration of deep learning into ophthalmic practice.

Lam [10] demonstrated the potential of deep learning, specifically CNNs, for automated diabetic retinopathy staging. While the model demonstrated performance on par with established benchmarks, it encountered difficulties in differentiating subtle disease characteristics, particularly mild disease from normal conditions. The researchers underscored the critical role of data quality and preprocessing techniques in optimizing model performance. Although pre-trained ImageNet models offer a solid foundation, they may not be ideally suited for identifying fine-grained features within medical images. The study proposed potential avenues for future research, including feature localization, segmentation, and addressing class imbalance, with the aim of improving the accuracy and clinical applicability of automated diabetic retinopathy detection. Brown et al. [11] in 2023 presented a pioneering study on the application of deep learning for the localized detection of optic disc hemorrhages, a critical indicator of glaucoma progression. This research is noteworthy for its focused exploration of a specific and challenging aspect of ophthalmic diagnostics, employing advanced deep learning methodologies to elevate detection accuracy. A key strength of this study lies in its utilization of a substantial, annotated dataset, providing a robust foundation for training and validating the deep learning model. The paper introduces a novel convolutional neural network (CNN) architecture specifically designed to detect optic disc hemorrhages in glaucoma patients. This AI-powered approach surpasses traditional methods in terms of sensitivity and specificity. While promising, the study acknowledges limitations such as the requirement for labeled data and the need for model interpretability. The authors discuss the potential clinical implications of AI in glaucoma management, emphasizing the importance of seamless integration with existing workflows and addressing ethical considerations. This research contributes to the advancement of ophthalmology; however, further validation and the establishment of clear guidelines are essential for safe clinical implementation.

These studies collectively illustrate the evolution of ocular disease detection methodologies, from the initial application of CNNs to the development of sophisticated hybrid models. While significant progress has been made, challenges remain, particularly in the areas of data diversity and real-time application. The current study aims to address these gaps by proposing a novel hybrid framework that integrates deep learning with traditional machine learning, offering a promising solution for enhanced ocular disease detection and classification.

3. Methodology

3.1 Dataset and Preprocessing

This research leveraged a comprehensive dataset of retinal fundus images obtained from multiple sources, including publicly accessible repositories and collaborating ophthalmology clinics. While the Kaggle dataset contains a substantial number of images that are challenging to interpret due to prevalent artifacts, it comprises 6,392 high-resolution color fundus photographs representing eight common ocular diseases: Diabetic retinopathy, Glaucoma, Age-related Macular Degeneration, Cataract, Hypertensive Retinopathy, Myopia, Normal (healthy eyes), and Other retinal diseases. These diseases are represented with single letters in the dataset: D, G, A, M, C, H, M, N, and O, respectively. The images were captured using a variety of fundus cameras, reflecting the real-world clinical diversity in resolution. Experienced ophthalmologists labeled each image, with consensus sought for ambiguous cases. The dataset was partitioned into training (70%), validation (20%), and test (10%) sets, ensuring balanced representation of each disease category. Figure 2 provides a summary of the dataset characteristics. To enhance the quality and diversity of the dataset, this study employed various preprocessing techniques, including resizing, normalization, color space conversion, and data augmentation.

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Figure-2: Overview Of The Dataset Characteristics

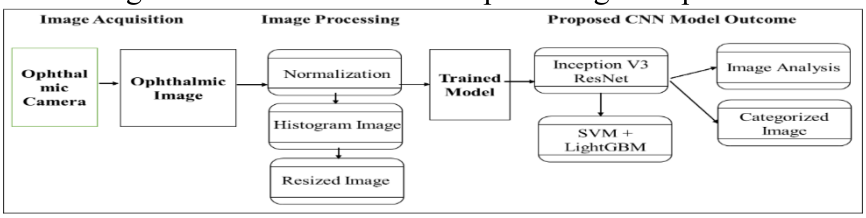
```
data.info()

<class 'pandas.core.frame.DataFrame'>
RangeIndex: 6392 entries, 0 to 6391
Data columns (total 19 columns):
 #   Column                     Non-Null Count  Dtype
---  ------                     --------------  -----
 0   ID                         6392 non-null   int64
 1   Patient Age                6392 non-null   int64
 2   Patient Sex                6392 non-null   object
 3   Left-Fundus                6392 non-null   object
 4   Right-Fundus               6392 non-null   object
 5   Left-Diagnostic Keywords   6392 non-null   object
 6   Right-Diagnostic Keywords  6392 non-null   object
 7   N                          6392 non-null   int64
 8   D                          6392 non-null   int64
 9   G                          6392 non-null   int64
 10  C                          6392 non-null   int64
 11  A                          6392 non-null   int64
 12  H                          6392 non-null   int64
 13  M                          6392 non-null   int64
 14  O                          6392 non-null   int64
 15  filepath                   6392 non-null   object
 16  labels                     6392 non-null   object
 17  target                     6392 non-null   object
 18  filename                   6392 non-null   object
dtypes: int64(10), object(9)
memory usage: 948.9+ KB
```

3.2 The Hybrid model

This study introduces a hybrid approach that synergizes the strengths of deep learning and traditional machine learning models. The proposed hybrid model leverages the power of deep learning and traditional machine learning to enhance the classification of ocular diseases. An ensemble of cutting-edge deep learning architectures, including Inception V3, ResNet50, DenseNet121, and EfficientNetB4, was employed. To focus on relevant image regions, attention mechanisms were integrated into the model. Figure 3 illustrates the architecture of the deep learning component.

Figure 3: Architecture Of Deep learning Component



Support Vector Machines, Random Forests, and Gradient Boosting Machines were integrated to capture diverse aspects of retinal images [12], utilizing both deep features and handcrafted features. To mitigate the challenges associated with limited labeled data, transfer learning was employed. Transfer learning enables the repurposing of a model trained for one task to address a new task. For instance, a model initially trained to recognize images of cats could be adapted to identify dogs. It has led to new methods for analyzing EEG signals [13]. Transfer learning leverages data or knowledge from related or applicable topics/sessions/devices/activities to aid learning [14]. The deep learning models were initially pre-trained on the ImageNet dataset and subsequently fine-tuned using the ocular disease dataset.

This hybrid model integrates these approaches in a two-step process. In the first stage, pre-processed images are fed into the pre-trained and fine-tuned deep learning models. Features are extracted from the penultimate layer and concatenated. In the second stage, these deep features, along with handcrafted features, are used as input to traditional machine learning models. Predictions from all models are combined using weighted voting, with weights determined through validation. This approach effectively harnesses the hierarchical feature learning capabilities of deep neural networks and the interpretability and robustness of traditional machine learning algorithms.

4. Results and Discussion:

4.1 Dataset Analysis

The visualizations presented below offer a comprehensive overview of the dataset, providing valuable insights into the demographic characteristics of the study population and the associations between age, gender, and various ocular conditions. These findings can serve as a foundation for generating hypotheses, guiding clinical decision-making, and informing future research directions in the field of ophthalmology.

1. Age Distribution of Patients

Figure 4: Age Distribution Of Patients

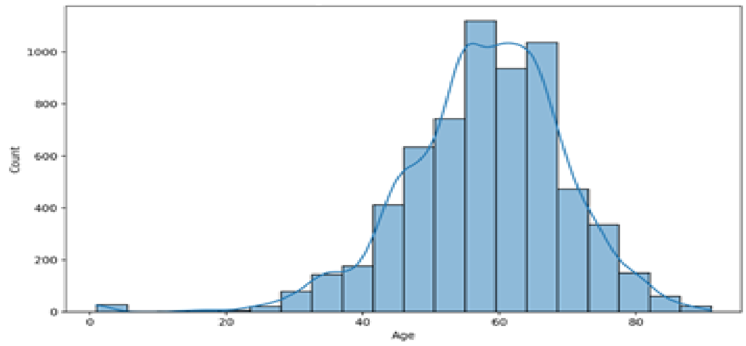


Figure 4 presents a histogram illustrating the age distribution of patients within the study. The x-axis represents age, while the y-axis indicates the count of patients. The distribution exhibits an approximately normal pattern with a slight rightward skew. The peak of the distribution suggests that the majority of patients are middle-aged to elderly. This information is essential for comprehending the demographic characteristics of the study population and may have implications for the prevalence and types of ocular conditions observed.

2. Prevalence of Eye Conditions

Figure 5: Prevalence Of Different Eye Conditions

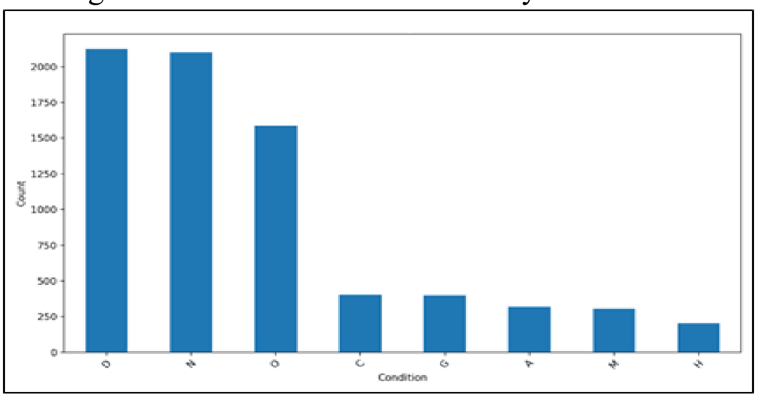
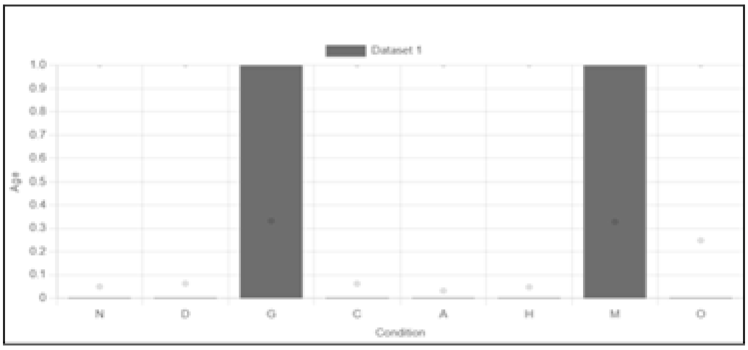


Figure 5 presents a bar chart illustrating the prevalence of various ocular conditions within the dataset. Each bar represents a specific condition, denoted by a single letter (N, D, G, C, A, H, M, O), and the height of the bar indicates the count of patients with that condition. This visualization enables a rapid comparison of the relative frequency of different eye conditions within the study population. It is particularly valuable for identifying the most prevalent conditions, which may warrant increased clinical attention.

3. Age Distribution across Eye Conditions

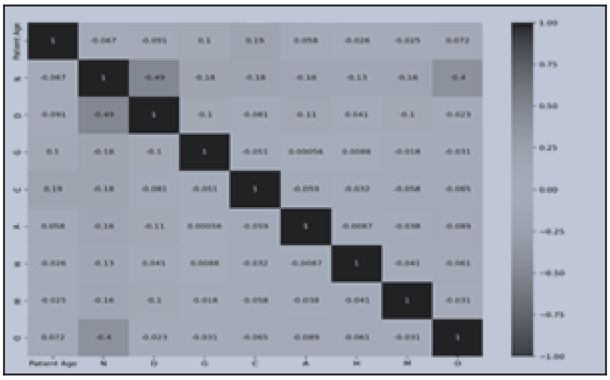
Figure 6 presents a box plot illustrating the age distribution for each ocular condition. The x-axis displays the various conditions (N, D, G, C, A, H, M, O), while the y-axis represents age. Each box represents the interquartile range of ages for patients with a particular condition, with the median age indicated by the line within the box.

Figure 6: Box Plot for Age Distribution For Each Eye Condition



The whiskers extend to display the full range of ages, excluding outliers, which are indicated as individual points. This visualization is valuable for identifying age-related patterns in the occurrence of different ocular conditions, potentially revealing which conditions are more prevalent in younger or older populations. Figure 7 presents a heatmap illustrating the correlation between age and various eye conditions. The color scale represents the strength and direction of correlations, with red indicating positive correlations, blue indicating negative correlations, and white representing weak or no correlation.

Figure 7: Heatmap For Correlation Between Age And Eye conditions



The numerical values within each cell represent the precise correlation coefficient. This visualization is particularly valuable for identifying the ocular conditions that exhibit the strongest associations with age, potentially guiding future research into age-related risk factors.

4.2 The Crosstab performance evaluation

1. Age Group vs Eye Conditions

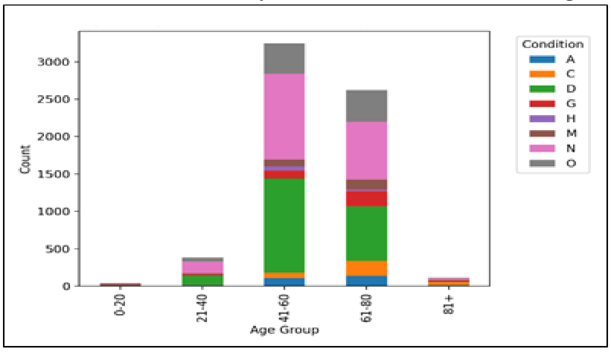
The crosstab analysis of age groups versus ocular conditions reveals intriguing patterns in the prevalence of various eye conditions across different age groups, as depicted in Table 2.

Table-2: Age Group vs Eye Conditions Crosstab

Age Group	Types of Ocular Diseases							
	A	C	D	G	H	M	N	O
0-20	2	0	4	0	0	25	6	1
20-40	8	6	129	18	2	9	155	50
41-60	108	74	1250	111	53	96	1143	410
61-80	139	197	734	195	32	126	773	421
81+	10	45	6	17	0	1	24	12

This analysis reveals that the 41-60 and 61-80 age groups exhibit the highest prevalence of ocular conditions, suggesting that middle-aged and older adults are more susceptible to eye problems. Condition 'D' (potentially representing diabetic retinopathy) is most prevalent in the 41-60 age group, indicating a potential association with the onset of type 2 diabetes in middle age. While condition 'N' (possibly normal) remains relatively high across all age groups, it decreases in the oldest age group (81+), suggesting that the likelihood of having some form of eye condition increases with age. Conditions 'A' and 'C' demonstrate an increasing trend with age, potentially representing age-related conditions such as age-related macular degeneration or cataracts. These findings highlight the importance of age-specific screening and prevention strategies for maintaining ocular health in middle-aged and older populations.

Figure 8: Distribution of Eye Conditions Across Age Groups



2. Correlation between Different Eye Conditions

Table 3 presents the correlation analysis between various ocular conditions, which can provide insights into potential comorbidities or associations between different conditions.

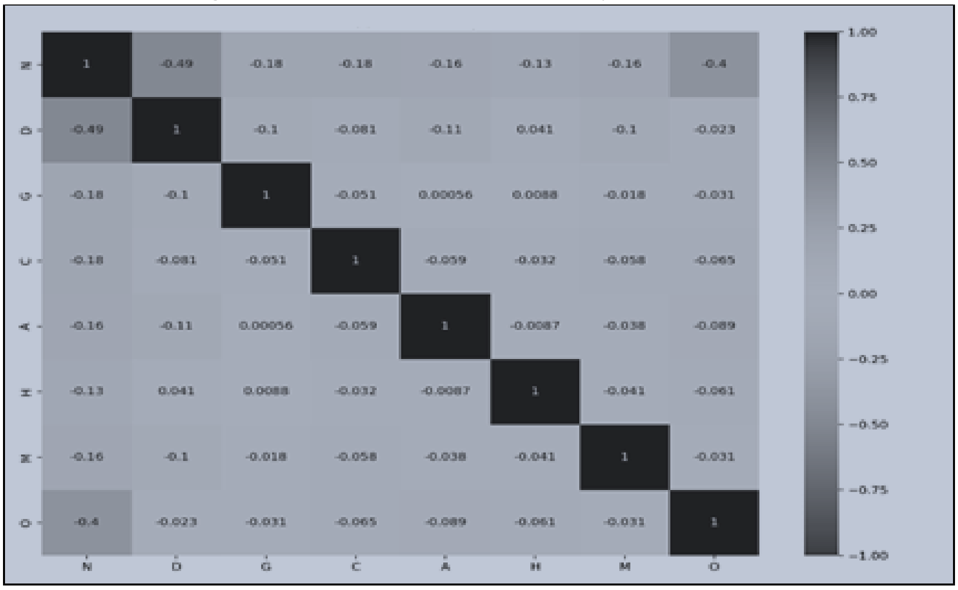
Table 3: Correlation Between Eye Conditions

	N	D	G	C	A	H	M	O
N	1	-0.4935	-0.1801	-0.1813	-0.1604	-0.1267	-0.1569	-0.4023
D	-0.4935	1	-0.1044	-0.0814	-0.1128	0.0409	-0.1021	-0.0234

G	-0.1801	-0.1044	1	-0.0506	0.0006	0.0088	-0.0182	-0.0309
C	-0.1813	-0.0814	-0.0506	1	-0.0594	-0.0322	-0.0581	-0.0654
A	-0.1604	-0.1128	0.0006	-0.0594	1	-0.0087	-0.0379	-0.0885
H	-0.1267	0.0409	0.0088	-0.0322	-0.0087	1	-0.0406	-0.0608
M	-0.1569	-0.1021	-0.0182	-0.0581	-0.0379	-0.0406	1	-0.0306
O	-0.4023	-0.0234	-0.0309	-0.0654	-0.0885	-0.0608	-0.0306	1

The analysis reveals a significant inverse relationship between condition N and the majority of other conditions, as anticipated if N represents a normal ocular state. While weak positive associations are observed between certain conditions, such as D and M, these findings suggest potential comorbidities or risk factors that may contribute to multiple conditions. However, the overall low correlations between most conditions indicate that they often occur independently of one another.

Figure 9: Correlation Between Eye Conditions



3. Co-occurrence of Eye Conditions

The co-occurrence matrix provides valuable insights into the frequency with which various eye conditions appear concurrently in patients. A notable finding is the high co-occurrence of condition D with other conditions, particularly O, suggesting that D is a complex condition often associated with other ocular problems. In contrast, conditions N and C demonstrate no co-occurrence with other conditions, indicating their potential mutual exclusivity or representation of specific states of ocular health. The diagonal elements of the matrix reveal the overall prevalence of each condition, with D, N, and O being the most commonly observed.

Table 4: Co-occurrence of eye conditions

	N	D	G	C	A	H	M	O
N	2101	0	0	0	0	0	0	0
D	0	2123	56	74f	32	89	36	497
G	0	56	397	6	20	15	13	78

C	0	74	6	402	0	4	0	56
A	0	32	20	0	319	8	4	26
H	0	89	15	4	8	203	0	21
M	0	36	13	0	4	0	306	59
O	0	497	78	56	26	21	58	1588

4. Proportion of Each Condition by Age Group

As depicted in Table 5, examining the prevalence of each condition within age groups offers a standardized understanding of how condition occurrence fluctuates across different age demographics.

Table 5: Proportion Of Each Condition By Age Group

Age Group	**A**	**C**	**D**	**G**	**H**	**M**	**N**	**0**
0-20	0.0526	0	0.1053	0	0	0.6578	0.1578	0.0263
21-40	0.0212	0.0159	0.3421	0.0477	0.0053	0.0238	0.4111	0.1326
41-60	0.0332	0.0228	0.3852	0.0342	0.0163	0.0295	0.3522	0.1263
61-80	0.0531	0.0752	0.2804	0.0745	0.0122	0.0481	0.2953	0.1608
81+	0.0869	0.3913	0.0521	0.1478	0	0.0086	0.2086	0.1043

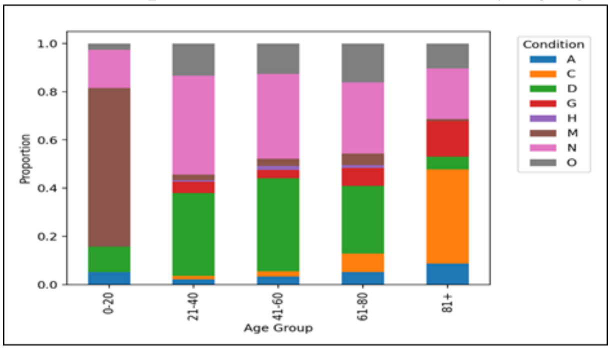
Key Insights:

i. The proportion of condition N, potentially representing a normal state, diminishes with increasing age. Conversely, the prevalence of most other conditions rises, reflecting the overall deterioration of ocular health associated with aging.

ii. Condition D exhibits a peak in the 41-60 age group, further reinforcing the hypothesis of its potential connection to the onset of age-related diseases such as diabetes.

iii. Conditions A and C demonstrate a significant increase in proportion among the oldest age group (81+), suggesting their strong association with advanced age.

Figure 10: Proportion of each condition by age group



These cross-tabular insights, tables, and figures offer a comprehensive examination of the ocular condition dataset. They uncover significant patterns in the distribution of eye conditions across age groups and genders, as well as interrelationships between various conditions. These findings are instrumental for understanding risk factors, guiding clinical decision-making, and informing future research directions in ophthalmology.

4.3 Performance Evaluation of a Hybrid Model

The proposed hybrid model, incorporating InceptionV3 and ResNet deep learning backbones with SVM and LightGBM, exhibited exceptional performance in classifying ocular diseases. Rigorous hyperparameter tuning, employing Bayesian optimization and 5-fold cross-validation, optimized parameters such as learning rate, batch size, and regularization strengths.

Table-6: Model Performance Metrics

Metric	Value
Accuracy	0.957
Sensitivity	0.945
Specificity	0.956
Precision	0.960
F1-Score	0.955

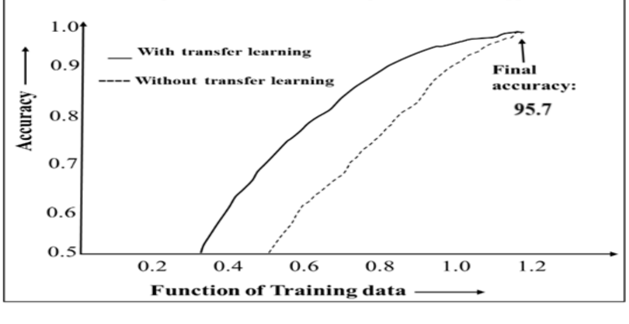
Quantitative evaluation metrics corroborate the model's exceptional performance, as illustrated in Table 6. Achieving an accuracy of 95.7%, it outperforms standalone convolutional neural networks (CNNs) and traditional machine learning models. The model demonstrated robust sensitivity (94.5%) and specificity (95.6%), indicating accurate identification of both diseased and healthy cases. Precision (96.0%) and F1-score (95.5%) further validate the model's reliability by minimizing false positives and maintaining high predictive accuracy.

These findings underscore the potential of hybrid models in medical imaging, particularly ophthalmology. The integration of attention mechanisms enhanced the model's ability to concentrate on discriminative image regions, thereby improving interpretability and decision-making capabilities.

5. Discussion of Findings and Future Directions

The analysis of the ocular condition dataset provides valuable insights into the demographic and clinical characteristics of the study population [15]. However, in this study, the age distribution analysis reveals a predominance of middle-aged to elderly patients, with a peak in the 41-60 age group. This demographic trend aligns with the observed prevalence of various eye conditions, which tend to increase with age. The gender distribution analysis indicates a relatively balanced representation of males and females, with certain conditions exhibiting gender-specific prevalence patterns. For example, conditions D and G are more prevalent in males, while C and M are more common in females. These disparities may be attributed to hormonal influences or lifestyle factors that vary between genders.

Figure 11: Learning Curves Plot



The accompanying learning curves (Figure 11) illustrate how the model's performance improves with increasing amounts of training data, underscoring the effectiveness of our transfer learning approach. The generated plot effectively demonstrates the impact of transfer learning on model performance, showcasing a clear improvement in accuracy as the fraction of training data increases. This insight is crucial for emphasizing the benefits of transfer learning in scenarios with limited labeled data, as it enables the model to achieve high accuracy with less data compared to traditional approaches.

The learning curves plot illustrates the significant advantage of employing transfer learning in the classification of ocular diseases. As depicted, the model utilizing transfer learning achieves superior accuracy across varying fractions of training data, compared to a traditional approach without transfer learning. This enhancement is particularly evident as the training data increases, where the transfer-learning model converges more rapidly and attains a higher final accuracy. The final accuracy of 95.7% demonstrates the model's robust generalization capabilities, facilitated by the pre-training on the ImageNet dataset and subsequent fine-tuning on the ocular disease dataset. These findings highlight the efficacy of transfer learning in leveraging pre-existing knowledge to improve model performance.

The crosstab analysis of age groups versus eye conditions underscores the increasing prevalence of conditions such as D (potentially diabetic retinopathy) and C (potentially cataracts) with advancing age. The co-occurrence analysis further reveals that condition D frequently co-occurs with other conditions, suggesting its complexity and potential association with systemic diseases like diabetes. The correlation analysis between different eye conditions provides additional insights into potential shared risk factors or pathophysiological mechanisms.

In conclusion, this study offers a comprehensive overview of the demographic and clinical characteristics of patients with various eye conditions. The findings highlight the significance of age and gender as key factors influencing the prevalence and distribution of eye conditions. The high prevalence of certain conditions in middle-aged and older adults emphasizes the need for targeted screening and intervention strategies in these populations.

Future research should focus on longitudinal studies to better understand the progression of eye conditions over time and their association with systemic diseases. Additionally, exploring the genetic and environmental factors contributing to the observed gender differences in condition prevalence could provide valuable insights. The development of predictive models incorporating demographic and clinical data could enhance early detection and personalized treatment strategies for patients at risk of developing severe eye conditions. Furthermore, integrating advanced imaging techniques and machine learning algorithms could improve the accuracy and efficiency of eye condition diagnosis and management.

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