Segmentation of Hard exudates & Disease Staging of Diabetic Retinopathy Using UNET architecture

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Abstract- **Diabetic retinopathy (DR) remains a significant cause of vision loss globally, necessitating accurate diagnosis and timely intervention. This research presents a comprehensive methodology leveraging the U-Net architecture for retinal lesion segmentation, disease staging, and treatment recommendation in diabetic retinopathy. The U- Net model is trained on annotated fundus images from the IDRID dataset, enabling precise segmentation of retinal lesions, particularly hard exudates. Disease staging is performed based on the quantified area of retinal lesions, classified into three stages: Non-proliferative DR, diabetic macular edema, and proliferative DR. Treatment recommendations, including medications, surgeries, and laser treatments, are tailored to each disease stage. Evaluation of the methodology encompasses segmentation accuracy, disease staging performance, and treatment recommendation validity. Key metrics such as Intersection over Union, Dice coefficient, and classification metrics are employed to assess model performance**

Keywords: **Diabetic Retinopathy, UNet Architecture, Disease Staging, Deep Learning, Medical Imaging, Hard Exudates.**

I. INTRODUCTION

Diabetic retinopathy (DR) is a prevalent complication of diabetes mellitus and a leading cause of vision impairment worldwide. Early detection and accurate management of DR are crucial to prevent irreversible vision loss and mitigate the burden of this debilitating condition. However, the complex nature of DR lesions and the variability in disease progression pose significant challenges to effective diagnosis and treatment. Traditional methods of DR assessment often rely on manual examination of fundus images by ophthalmologists, which can be time-consuming and prone to Subjectivity. In recent years, advancements in artificial intelligence (AI) and deep learning techniques have shown promise in revolutionizing DR diagnosis and management. Among these techniques, convolutional neural networks (CNNs) have emerged as powerful tools for automated image analysis, particularly in segmenting retinal lesions and assisting in disease staging. One of the CNN architecture widely used in medical image analysis is the U-Net architecture, known for its effectiveness in semantic segmentation tasks.This research aims to harness the potential of the U-Net architecture for the segmentation of retinal lesions in fundus images and subsequent disease staging in diabetic retinopathy. By leveraging annotated datasets such as the Image Database for Retinal Lesion Segmentation (IDRID), the U-Net model can be trained to accurately delineate retinal lesions, including hard exudates, which are indicative of DR severity. The segmentation results can then be utilized to classify the disease into distinct stages, Non-proliferative Diabetic Retinopathy (stage-1), Diabetic Macular Edema (Stage-2), Proliferative Diabetic Retinopathy (Stage-3) based on the extent of retinal lesions. In addition to segmentation and disease staging, this research also incorporates a treatment recommendation system tailored to each disease stage. The system provides recommendations for medications, surgical interventions, laser treatments, and other therapeutic modalities, thereby assisting healthcare providers in making informed decisions regarding patient management. Overall, this study addresses the pressing need for accurate and efficient methods for DR diagnosis and management by leveraging one of the state-of-the art architecture, UNET architecture. Through the development and evaluation of a comprehensive methodology encompassing lesion segmentation, disease staging, and treatment recommendation, this research aims to contribute to improved clinical outcomes and vision preservation for individuals with diabetic retinopathy.

1.1 Background:

Diabetic retinopathy is a diabetes complication that affects the eyes. It's caused by damage to the blood vessels of the light- sensitive tissue at the back of the eye (retina). In people with diabetes, consistently high blood sugar levels can cause damage to blood vessels throughout the body, including the tiny blood vessels in the retina. Over time, these blood vessels may swell, leak, or close off completely, leading to changes in vision or even blindness if left untreated. One of the hallmark signs of diabetic retinopathy is the presence of hard exudates in the retina. Hard exudates are yellowish-white deposits that form in the retina as a result of leakage from damaged blood vessels. They consist of

lipids (fats) and proteins that accumulate in the retinal tissue. The presence of hard exudates in the retina is a significant clinical finding as it indicates the severity of diabetic retinopathy and the risk of vision loss. Treatment options for diabetic retinopathy, including interventions to manage macular edema and prevent further progression of the disease, may be recommended based on the presence and severity of hard exudates. Traditionally, the assessment of DR has relied on manual examination of fundus images by experienced ophthalmologists,   a process that is not only labor-intensive and time- consuming but also subject to inter-observer variability. Moreover, the global shortage of eye care specialists, particularly in resource-limited settings, exacerbates the challenges associated with timely DR screening and management. With the advancements in computer vision and machine learning techniques, automated image analysis systems have emerged as promising tools for assisting clinicians in DR screening and diagnosis. It In recent years, the emergence of artificial intelligence (AI) and deep learning techniques has offered a promising solution to overcome these obstacles. Among various automated approaches, deep learning-based methods, particularly convolutional neural networks (CNNs), have shown remarkable success in DR lesion segmentation. Among the various CNN architectures, the U-Net model has garnered significant attention for its effectiveness in semantic segmentation tasks, making it well-suited for delineating retinal lesions and assisting in disease staging. The unique architecture of U-Net, characterized by a contracting path for capturing context and an expansive path for precise localization, enables robust and accurate segmentation of complex structures within medical images.The contraction path, also known as the encoder, involves successive convolutional and pooling layers to extract hierarchical features and reduce spatial dimensions. Conversely, the expansion path, or decoder, employs upsampling and concatenation operations to gradually recover spatial information and generate segmentation masks with precise boundaries. This symmetrical architecture allows U- Net to effectively capture contextual information while preserving fine details, making it a popular choice for medical image segmentation tasks like diabetic retinopathy detection.In addition to lesion segmentation, precise disease staging is crucial for effective DR management. The main stages include non-proliferative diabetic retinopathy (NPDR), Diabetic Macular Edema(DME) and proliferative diabetic retinopathy (PDR) based on the extent and characteristics of retinal lesions. In this context, our research endeavors to develop a comprehensive deep learning-based system for automated DR diagnosis and management. While various models excel in lesion segmentation, our work uniquely focuses on integrating staging to categorize DR severity and provide personalized treatment recommendations based on clinical guidelines. Leveraging established metrics, such as lesion area coverage thresholds (e.g., below 10% for NPDR, 10-20% for DME, and beyond 20% for PDR), our system aims to streamline the diagnosis and management of DR, enhancing both efficiency and accuracy in clinical decision-making processes. Furthermore, personalized treatment recommendations are essential for optimal DR management. Treatment modalities for DR span from pharmacotherapy to laser interventions, with therapeutic decisions guided by disease severity, lesion attributes. Automated recommendation systems leverage clinical guidelines and expert knowledge to devise treatment plans tailored to the diagnosed disease stage and lesion distribution. Through rigorous evaluation and validation, this study seeks to demonstrate the efficacy and clinical utility of the proposed system in enhancing the efficiency and accuracy of DR diagnosis and treatment decision- making.
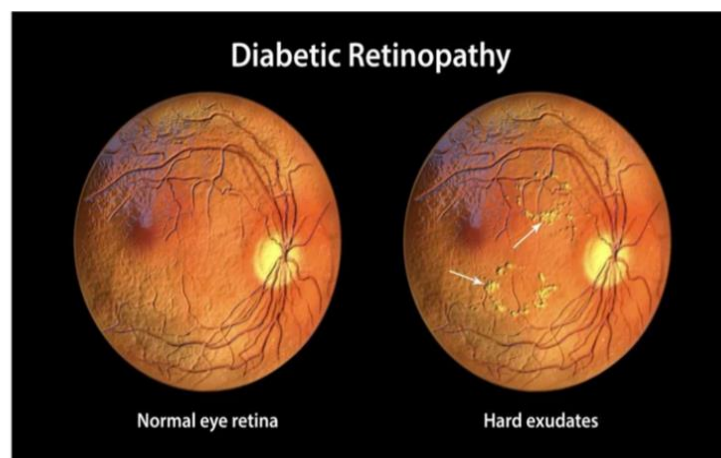

Fig-1 : Hard Exudates in Diabetic Retinopathy

II. IMPLEMENTATION:

The Entire System has been implemented in multiple Phases.Each phase corresponds to a set of Workflow Activities to build the Parts of the entire Solution.The implementation phase involoves following three phases:

1.Training phase
2.Inference phase
3.Application Development

1.   **Training Phase**

Training Phase deals with the Workflow activities that are related to the Training of the UNET Model to perform Semantic Segmentation on Fundus Images.

i.**Data Collection:** The Data Collection phase involves gathering annotated segment images of diabetic retinopathy from the IDRID dataset, which includes both hard exudate images and corresponding ground truth annotations of the lesions. During this phase, particular attention is given to collecting a diverse range of lesion images, encompassing both positive and negative instances, with varying sizes to ensure a representative distribution in the dataset.During the Data Preprocessing stage, the collected data is divided into training and testing sets using an 80-20 split ratio. Furthermore, both the images and their corresponding ground truth masks are resized to a resolution of 256x256 pixels to align with the input requirements of our customized UNet architecture. This step ensures consistency and compatibility between the data and the segmentation model.
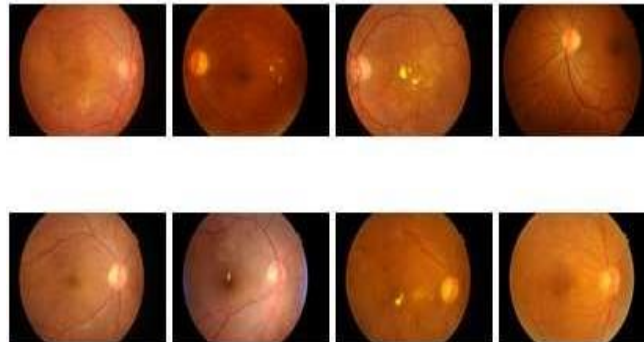
Fig-1: Sample images of Dataset

ii.**Data Preprocessing:** During the Data Preprocessing stage, the collected data is divided into training and testing sets using an 80-20 split ratio. Furthermore, both the images and their corresponding ground truth masks are resized to a resolution of 256x256 pixels to align with the input requirements of our customized UNet architecture. This step ensures consistency and compatibility between the data and the segmentation model.

iii.**Defining UNET Architecture:** During the phase of defining the UNet model architecture, we engage in experimentation and implement the architecture using the TensorFlow (Keras) framework. The UNet model constructed consists of a 12 convolutional blocks, organized into specific segments: 5 blocks for the encoder, 2 for the bridge, 4 for the decoder, and 1 for the output. This design aims to strike a balance between capturing detailed features through the encoder, facilitating information flow through the bridge, and reconstructing the segmented output through the decoder.
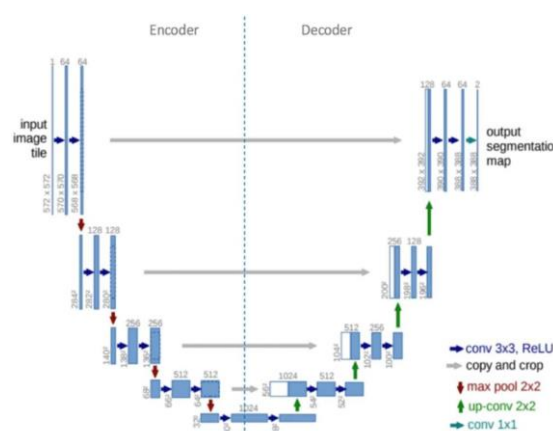

Fig-2:UNET Architecture

iv.**Training UNET Model:** During the Training Phase, the UNet model undergoes training using training images. This process involves optimizing the model parameters using the ADAM optimizer over a span of 10 epochs, continuing until the validation loss converges to its minimum value. Through this iterative process, the model learns to accurately segment retinal lesions in DR images.

v.Evaluating Model Performance: In the Evaluation Phase, the performance of the model is assessed using various metrics including the Dice Coefficient, Intersection over Union (IOU) Loss, Precision, and Recall. These metrics provide insights into the model's ability to accurately segment retinal lesions in diabetic retinopathy images. By analyzing these performance indicators, we can gauge the effectiveness of the model in capturing lesion boundaries, minimizing false positives, and maximizing true positives.

2. Inference Phase

The Inference Phase encompasses the workflow activities associated with using the trained UNet model to perform semantic segmentation on unseen fundus images. This phase involves applying the model to new data to generate segmentation prediction.

i.**Evaluating Model Performance:** During the Data Preprocessing phase, the images undergo resizing to achieve a resolution of 256x256 pixels, ensuring compatibility with the input specifications of our customized UNet model. Additionally, normalization is applied to standardize the pixel intensity values across the images.

ii.**Inference:** During the Inference stage, the pretrained UNet model is loaded into memory. Subsequently, inference is performed on unseen preprocessed images. This process involves utilizing the UNet model's learned features to predict the regions of lesions within the unseen images

iii.**Result Interpretation:** In the Result Interpretation phase, the predicted lesion region area serves as the basis for staging the lesion disease. Specifically, if the lesion area covers less than 10% of the total retinal area, it indicates non-proliferative diabetic retinopathy (NPDR). Lesion areas ranging between 10% and 20% indicate diabetic macular edema (DME), while those beyond 20% suggest proliferative diabetic retinopathy (PDR).

3. Application Development

The Application Development Phase encompasses the workflow activities dedicated to encapsulating the solution as a web application for end users. This phase involves the development and deployment of a user-friendly web interface that enables users to interact with the solution seamlessly.

i.**Streamlit Application Development:** During the Streamlit Application Development Phase, a user- friendly web interface is crafted to showcase the solution. This involves integrating backend functionalities seamlessly and implementing solution features such as interactive visualizations and result displays.
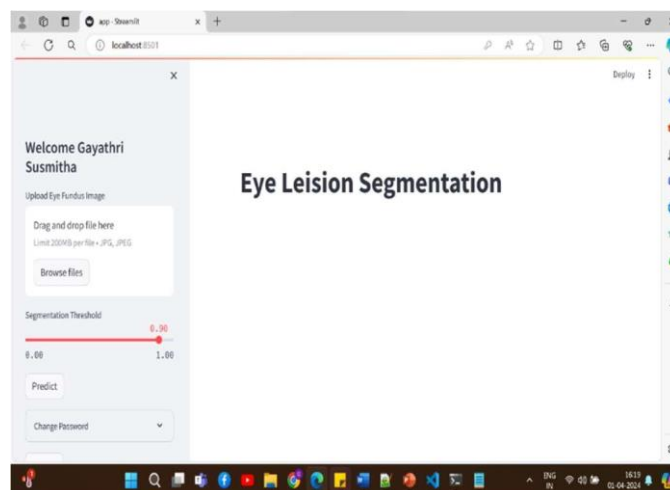

Fig-3: Streamlit Application

III. RESULTS AND DISCUSSION

The system provides a comprehensive analysis for each stage of diabetic retinopathy, offering five key components:

1. **Original Retinal Image**: The system presents the original retinal image captured during the examination process, providing clinicians with a baseline for visual assessment.
2. **Predicted Lesion Region**: Using the UNET architecture,the system identifies and highlights the areas of retinal lesions within the image, aiding in the precise localization of pathological features.

3. **Retinal Lesion Overlay on Original Image**: By overlaying the segmented lesion regions onto the original retinal image, the system visually enhances the identification and visualization of retinal abnormalities for clinicians.
4. **Stage of DR Disease**: The system categorizes the severity of diabetic retinopathy into Non-Proliferative Diabetic Retinopathy, Diabetic Macular Edema and Prolifertaive dIabetic Retinopathy based on the identified lesion area.
5. **Diagnosis and Medication Recommendation**: Based on the identified stage of diabetic retinopathy, the system offers tailored recommendations for further clinical management, including treatment options such as medicines, surguries, laser treatment, injections. These recommendations are aligned with established guidelines and clinical best practices, guiding clinicians in making informed decisions regarding patient care.

Stage-1(Non-Proliferative Diabetic Retinopathy)

Fig-1 displays the original fundus image of the retina obtained from the IDRID Dataset. This image corresponds to the stage-1 of Diabetic Retinopathy (Non-proliferative Diabetic Retinopathy). This image serves as the foundational reference for all subsequent analyses and diagnostic assessments corresponding to stage-1. This the user uploaded retinal image while using the application.
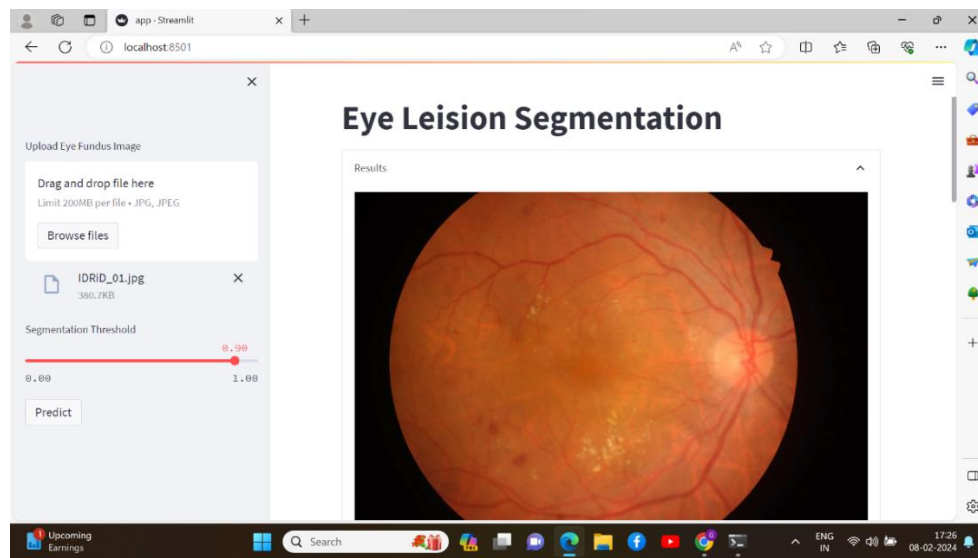
Fig-1: Original Stage-1 Retinal Image

Fig-2 shows the retinal lesions, specifically hard exudates, are delineated and accentuated. The delineation process employs an autoencoder-decoder architecture, specifically the UNet Architecture, which analyzes the original retinal image (Fig- 1) to identify and highlight these lesions.
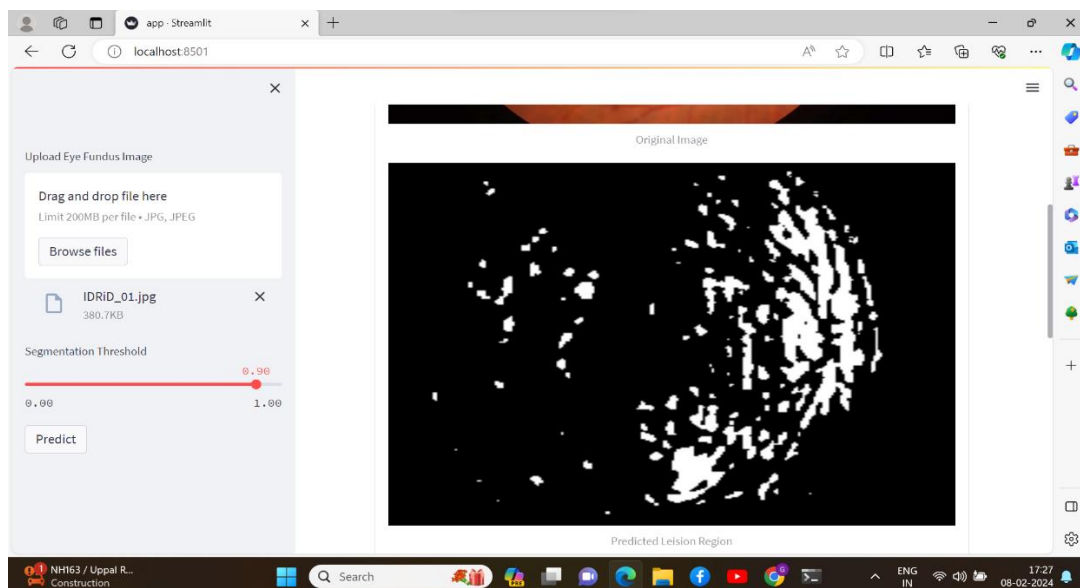

Fig-2: Predicted Lesion Region

Fig-3,this composite image merges the original retinal image (Fig-1) with the delineated lesions (Fig-2) superimposed on it. By overlaying the segmented lesions onto the original retinal image, it offers a comprehensive visual depiction of how the identified lesions correspond to the anatomical features of the retina.
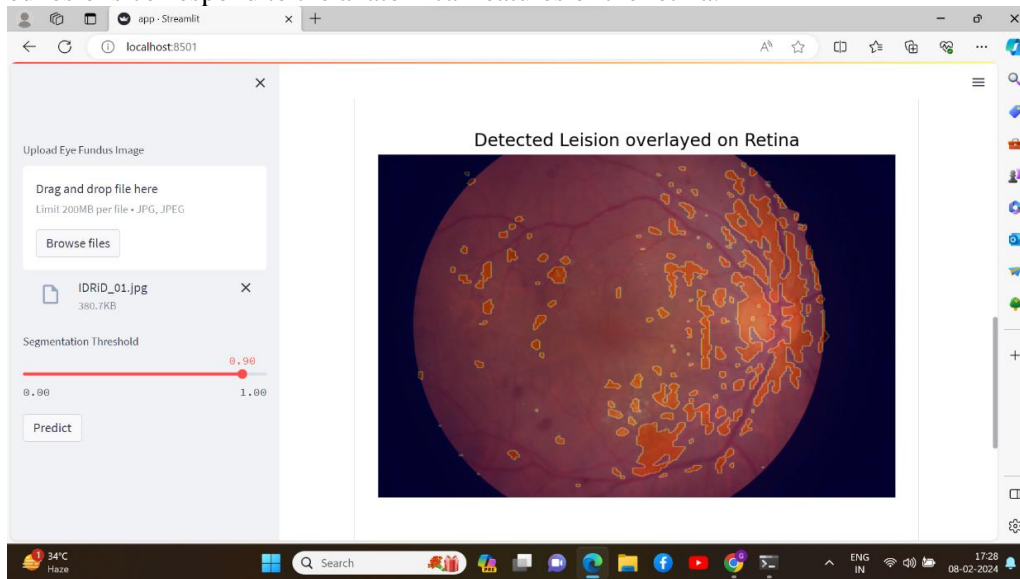

Fig-3: Detected Lesion overlayed on Retina

Fig-4 depicts the stage diagnosis of the disease based on the segmented lesions. It categorizes the severity of diabetic retinopathy into stages such as non-proliferative diabetic retinopathy (NPDR), diabetic macular edema (DME), or proliferative diabetic retinopathy (PDR). The current image shows the diagnosis for stage-1 Diabetic Retinopathy. The image displays the treatment recommendations and medication prescribed based on the stage diagnosis of diabetic retinopathy. It outlines the therapeutic interventions, such as medication, surgery, laser treatments, or injections, tailored to the specific disease stage .
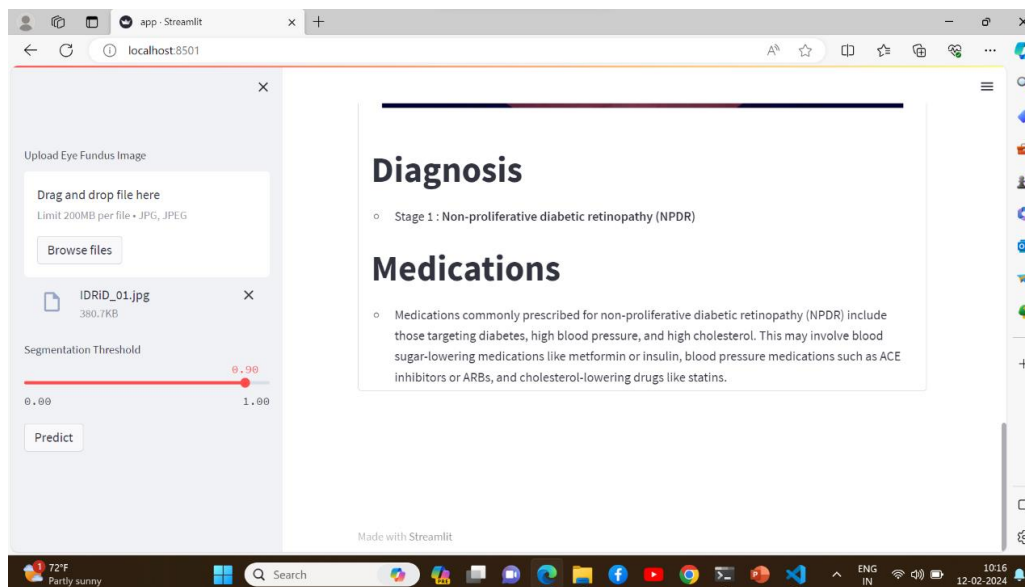
Fig-4:Stage-1 Diagnosis and medication recommendation

Lesion identification and staging occur by assessing the area of the lesion within the retinal image. Lesions covering less than 10% of the retinal area correspond to stage-1 diagnosis. This staging criterion forms the basis for categorizing the severity of the retinal disease and determining appropriate treatment interventions.
From Fig-2, the identified lesions occupy less than or about 10% of the retinal area. So, the identified stage of the Diabetic Retinopathy is Stage-1 (Non-proliferative Diabetic Retinopathy).

Stage-2 (Diabetic Macular Edema)

Fig-5 displays the original fundus image of the retina obtained from the IDRID Dataset. This image corresponds to the stage- 2 of Diabetic Retinopathy (Diabetic Macular Edema). This image serves as the foundational reference for all subsequent analyses and diagnostic assessments corresponding to stage2. User uploads this image while using the application.
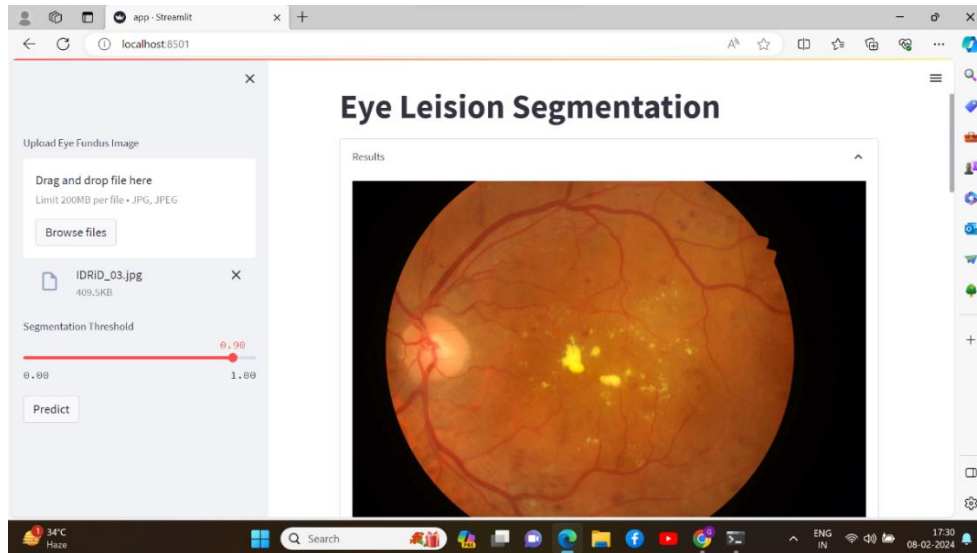

Fig-5: Original Stage-2 Retinal Image

Fig-6 illustrates the segmented lesions, specifically hard exudates, extracted from the original retinal image using the U-Net architecture. The area occupied by these lesions falls within the range of 10-20%, indicating a moderate degree of diabetic retinopathy severity which corresponds to the stage- 2 of Diabetic Retinoapthy.
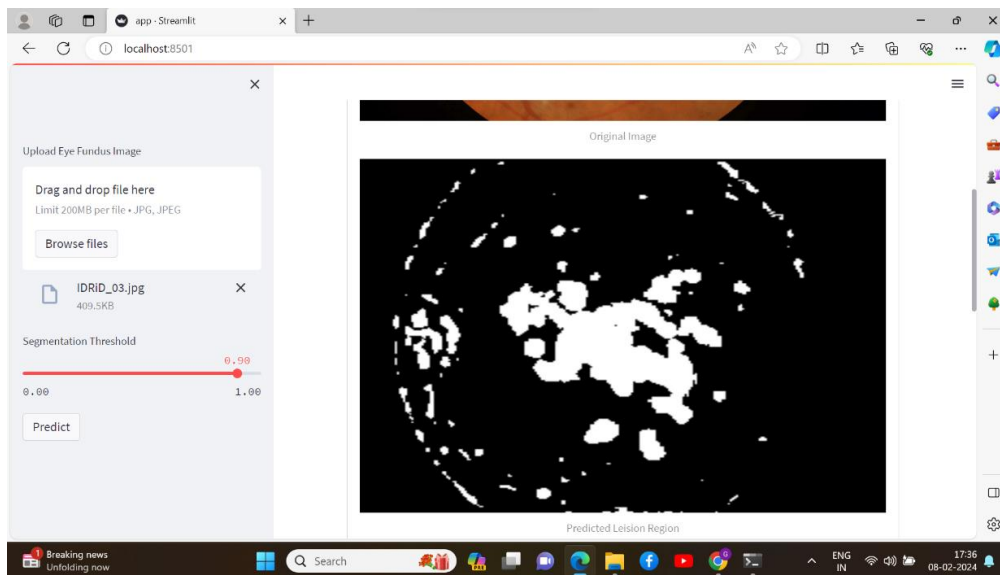
Fig-6: Detected lesion (white pixels)

In Fig-7, the original retinal image (Fig-5) is combined with the delineated lesions (Fig-6) overlaid on top. This composite image provides a detailed visual representation of how the segmented lesions align with the anatomical structures of the retina. By superimposing the segmented lesions onto the original retinal image, it enhances the interpretation of the segmentation outcomes, offering valuable insights into the spatial distribution and localization of the identified lesions within the retinal structure.
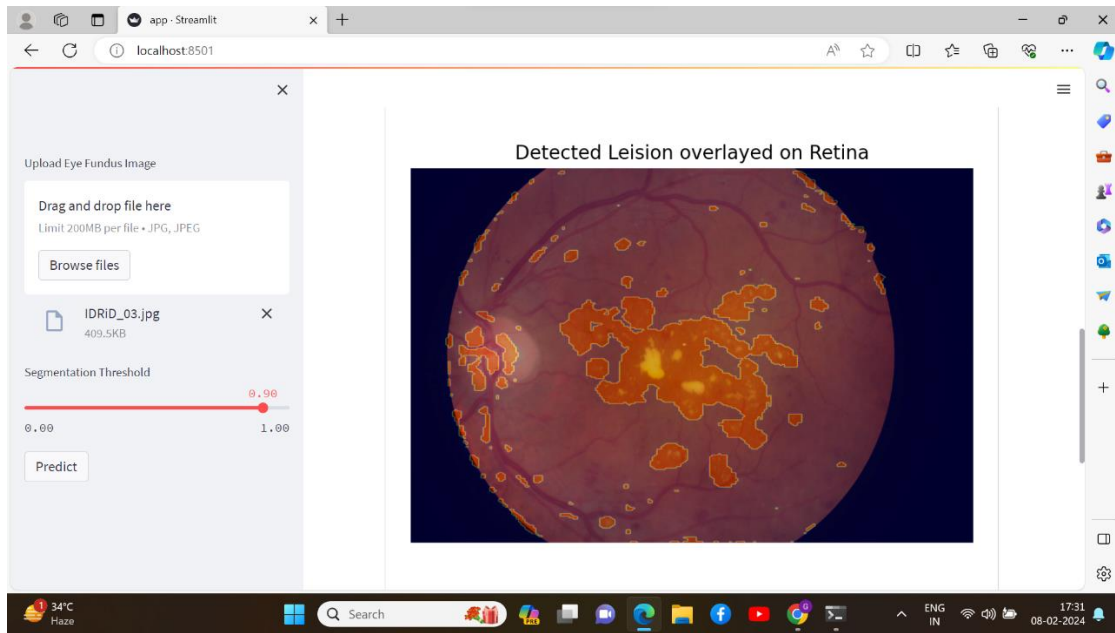
Fig-7: Detected Lesion overlayed on Retina

Figure 8 provides an overview of the disease staging process for diabetic retinopathy, which is based on the analysis of segmented lesions. In this instance, the diagnosis indicates stage-2 Diabetic Retinopathy. Moreover, the image presents tailored treatment recommendations and medication prescribed in accordance with the diagnosed disease stage. These recommendations encompass various therapeutic interventions, including medication, surgery, laser treatments, or injections, customized to address the specific stage of diabetic retinopathy.
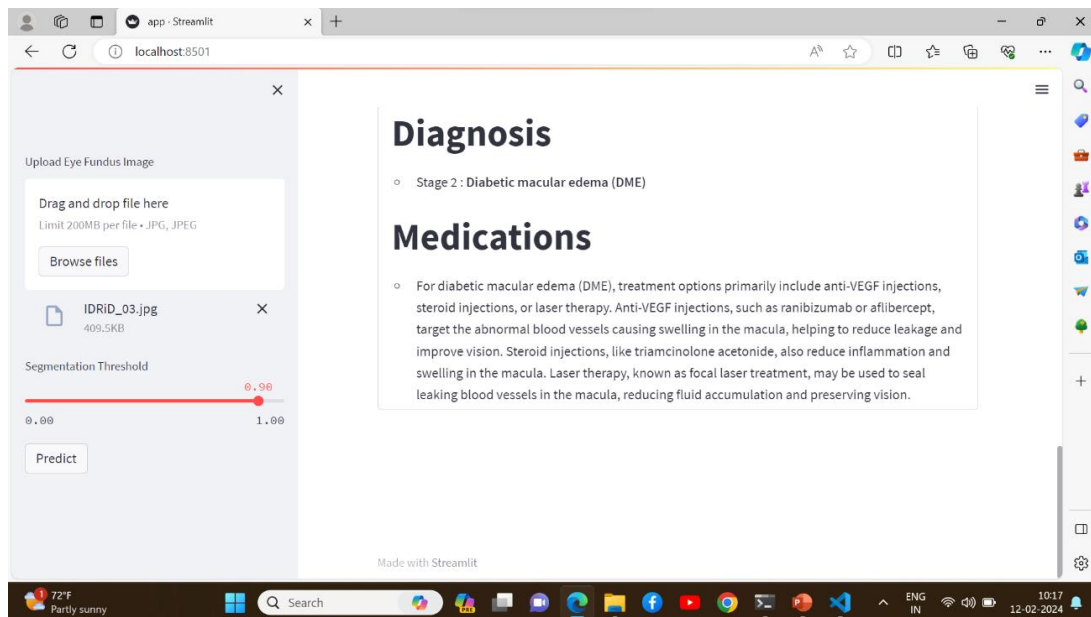
Fig-8: Stage-2 Diagnosis and medication Recommendation

The disease is staged based on the extent of lesion coverage, with stage 2 indicating a moderate severity level. At this stage, corresponding to Diabetic Macular Edema (DME), lesions occupy between 10% to 20% of the retinal area, necessitating targeted interventions to mitigate vision-threatening complications. The final recommendation encompasses a tailored treatment plan associated with DME.

Stage-3 (Proliferative Diabetic Retinopathy)

Fig-9 displays the original fundus image image corresponding to the stage-3 of Diabetic Retinopathy (Proliferative Diabetic Retinopathy). This image serves as the foundational reference for all subsequent analyses and diagnostic assessments corresponding to stage-3. This image is uploaded by the user while using the application.
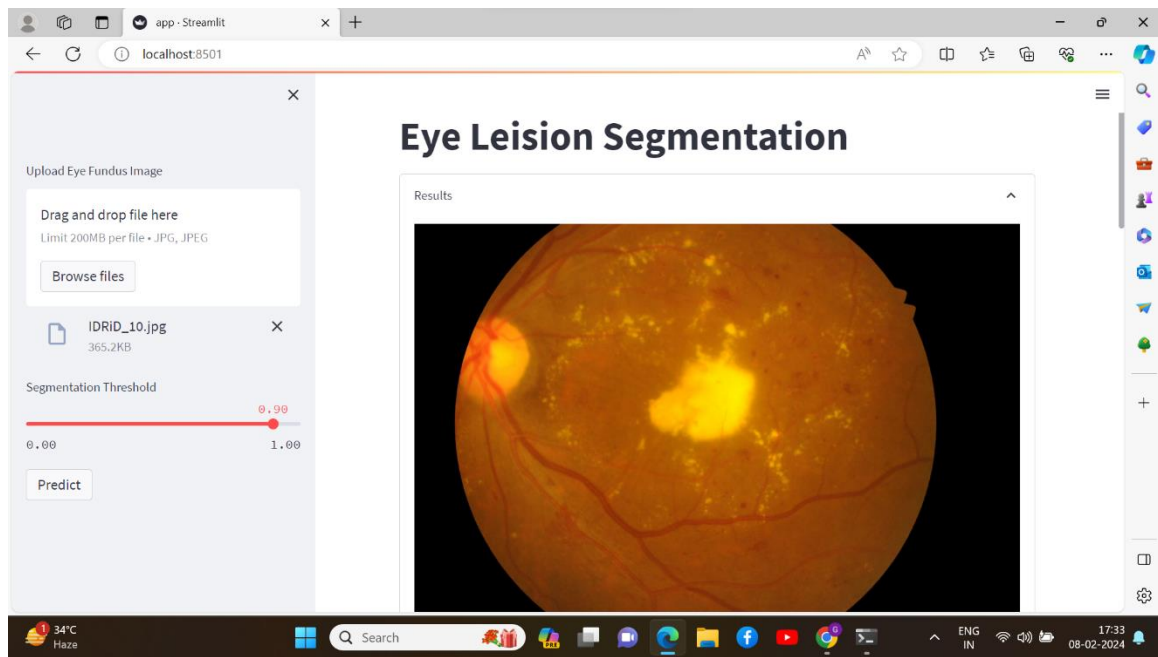
Fig-9: Original Stage-3 Retinal image

Fig-10 showcases the delineated hard exudates, extracted from the original retinal image through the implementation of the U-Net architecture. The extent of lesion coverage surpasses 20%, indicative of a severe manifestation of diabetic retinopathy, aligning with stage-3 diagnosis.
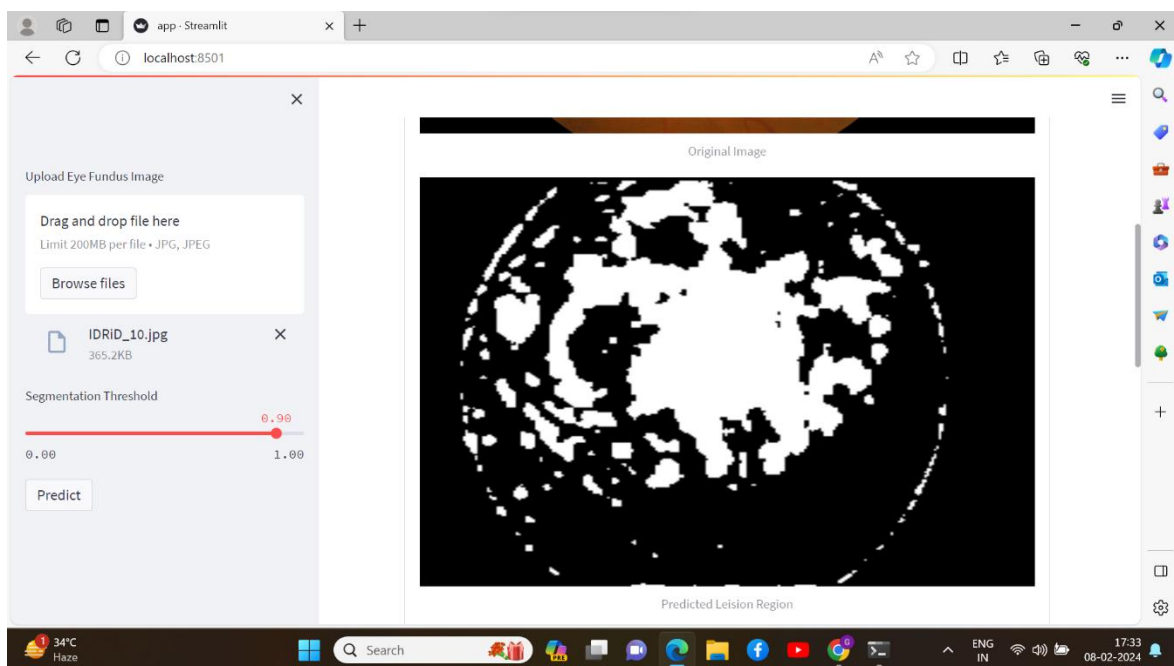

Fig-10: Predicted Lesion Region

Figure 11 presents a composite image merging the original retinal image (Figure 9) with the delineated lesions (Figure 10) overlaid on top. This visualization offers a comprehensive view of how the segmented lesions correspond to the retinal anatomy. By superimposing the lesions onto the original image, it facilitates a deeper understanding of their spatial distribution and localization within the retina, aiding in the interpretation of the segmentation results.
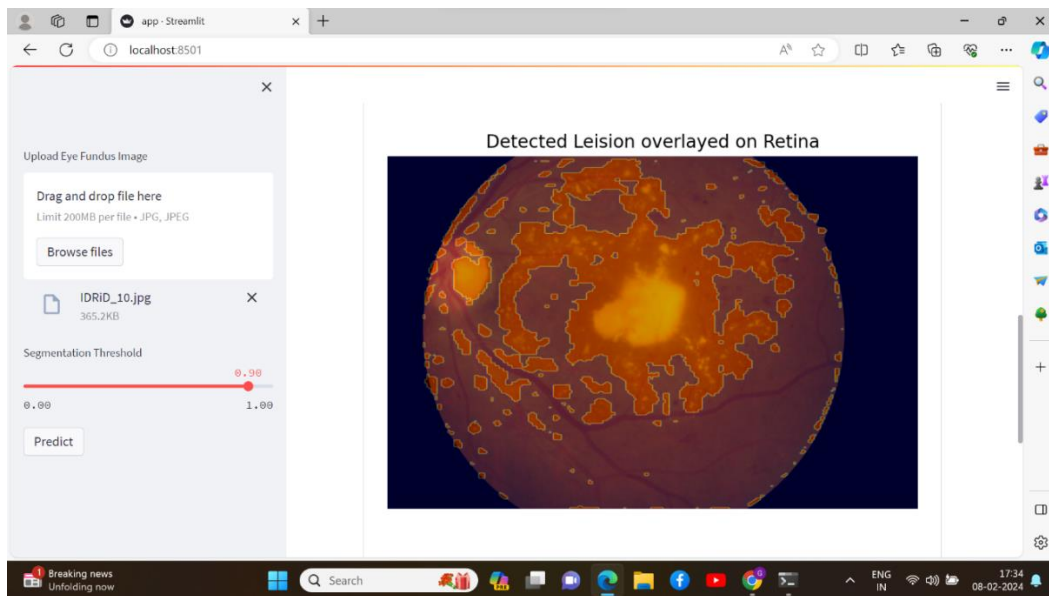
Fig-11: Detected Lesion overlayed on Retina

Figure 12 illustrates the disease staging process for diabetic retinopathy, which relies on the analysis of segmented lesions. The severity of the condition is classified into one of the three stages of Diabetic Retinopathy based on the extent of lesion coverage. In this particular case, the diagnosis indicates stage-3 Diabetic Retinopathy. Additionally, the image presents personalized treatment recommendations and medication prescribed according to the diagnosed disease stage. These recommendations encompass a range of therapeutic interventions, including medication, surgery, laser treatments, or injections, tailored to address the specific stage of diabetic retinopathy and fulfill the individual patient's requirements, thereby facilitating effective management of the condition.
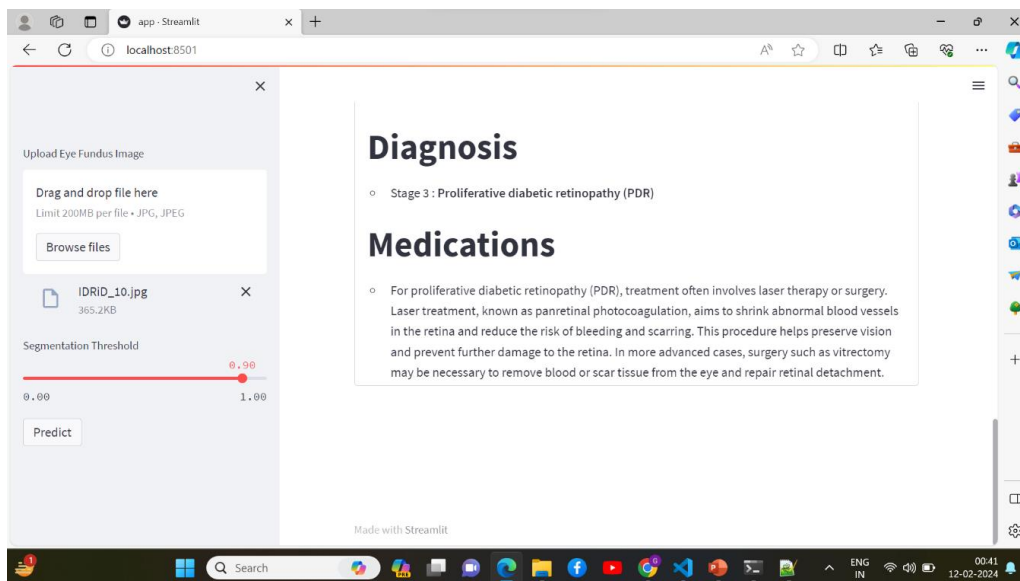

Fig-12: Stage-3 Diagnosis and Recommendation

Staging of the disease is determined by the extent of lesion coverage, with stage 3 denoting a moderate level of severity. In this stage, corresponding to PDR, lesions occupy more than 20% of the retinal area, necessitating specific interventions to address potential vision-threatening complications. The ultimate recommendation entails a customized treatment plan tailored to address the challenges associated with PDR.

IV. MODEL EVALUATION METRICS

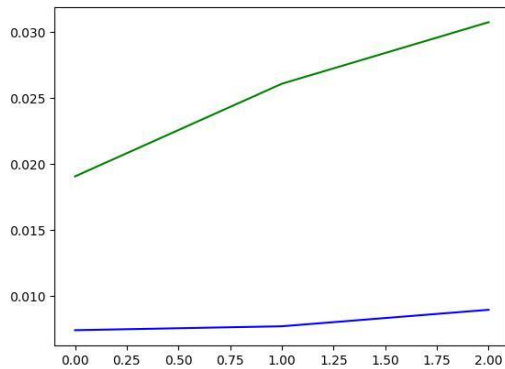| Metric	Value
Precision	0.15
Recall	0.95

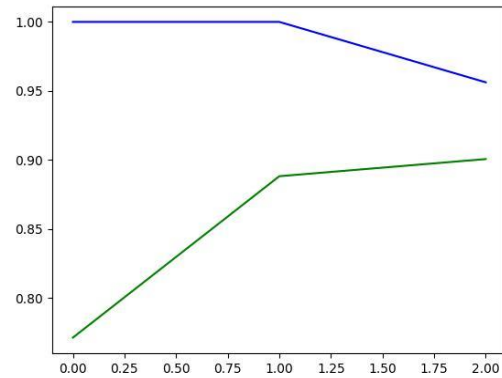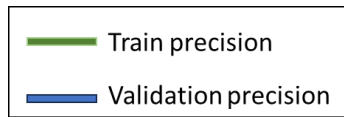| Dice coefficient | 0.7 |
| IOU loss | 0.4 |

Table-1: performance metrics
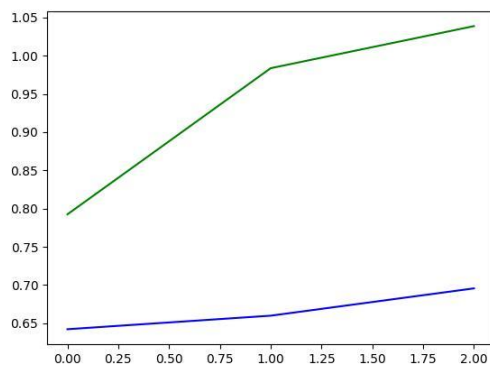

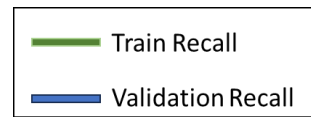Fig-1 Precision graph

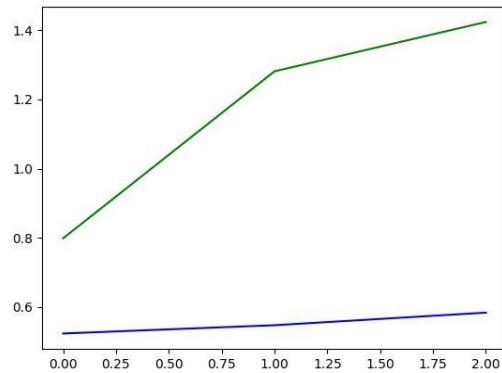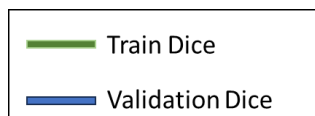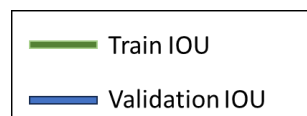Fig-2: Recall graph

Fig-3: Dice graph

Fig-4: IOU graph

As depicted in the table above, the evaluation metrics for the UNet model reveal a notable trend: while the model exhibits relatively lower precision compared to recall, indicating a higher rate of false positives, it demonstrates a robust capability in detecting the actual lesion regions. This discrepancy suggests that the model tends to encompass a larger area surrounding the true lesion as part of the segmented region. While this slight overestimation may lead to false positives, it ensures comprehensive coverage of the actual lesion regions, minimizing the risk of missing critical abnormalities. The observed trade-off between precision and recall underscores the model's inclination towards prioritizing sensitivity over specificity, thereby favoring inclusivity in lesion detection. While higher precision is desirable for minimizing false positives and enhancing specificity, the emphasis on recall ensures that the model captures a greater proportion of true positive instances, thereby reducing false negatives and enhancing sensitivity. This characteristic aligns with the objective of automated lesion segmentation, where the priority lies in detecting all potential abnormalities to facilitate thorough screening and diagnosis. To address the observed performance characteristics and further enhance the model's efficacy, several avenues for future improvement can be explored. One approach involves refining the architecture of the UNet model by introducing more complex configurations with an increased number of filters. By augmenting the model's capacity to extract and represent intricate features from the input images, such enhancements may lead to more precise lesion segmentation while maintaining high recall rates.

Additionally, the incorporation of spatial attention mechanisms within the convolutional stages of the UNet architecture presents another promising avenue for improvement. Spatial attention modules enable the model to dynamically adjust its focus during feature extraction, directing attention towards regions of interest while suppressing irrelevant or redundant information. By integrating such attention mechanisms, the model can enhance its discriminative ability and optimize lesion localization, thereby potentially improving both precision and recall metrics. Furthermore, expanding the training dataset by collecting additional annotated images can significantly contribute to model refinement. A more diverse and comprehensive dataset allows the model to learn from a broader range of lesion characteristics, including variations in size, shape, and texture. Through exposure to a more extensive and representative dataset, the model can generalize better to unseen data and exhibit improved performance in real-world scenarios.

V. CONCLUSION

In this study, we have developed a comprehensive system for the automated diagnosis and management of diabetic retinopathy (DR) leveraging advanced deep learning techniques, specifically the U-Net architecture. The system encompasses robust lesion segmentation, accurate disease staging, and personalized treatment recommendations tailored to individual patient needs.The UNet architecture employeed demonstrated high precision and recall rates, effectively delineating retinal lesions from fundus images. By incorporating expert recommendations and clinical guidelines, the system provided accurate di sease staging, enabling precise categorization of DR severity into non-proliferative diabetic retinopathy (NPDR), diabetic macular edema (DME), and proliferative diabetic retinopathy (PDR) stages. The results of our study highlight the potential of artificial intelligence-driven solutions in transforming DR diagnosis and management, offering improved clinical outcomes and vision preservation for patients. Moving forward, further refinement such as integration of multimodal imaging data will enhance the system's performance and applicability in diverse clinical settings. Integrating multimodal imaging data, such as optical coherence tomography (OCT) and fluorescein angiography, could enhance the system's diagnostic capabilities and provide a more comprehensive assessment of DR progression.

REFERENCES:

1. Soomro, Toufique & Afifi, Ahmed J. & Zheng, Lihong & Soomro, Shafiullah & Gao, Junbin & Hellwich, Olaf & Paul, Manoranjan. (2019). Deep Learning Models for Retinal Blood Vessels Segmentation: A Review. IEEE Access. 7.71696-71717.10.1109/ACCESS.2019.2920616.
2. Mary Dayana A., Sam Emmanuel W.R. (2020) A Patch - Based Analysis for Retinal Lesion Segmentation with Deep Neural Networks. In: Pandian A., Palanisamy R., Ntalianis K. (eds) Proceeding of the International Conference on Computer Networks, Big Data and IoT (ICCBI - 2019). ICCBI 2019. Lecture Notes on Data Engineering and Communications Technologies, vol 49. Springer, Cham. https://doi.org/10.1007/978-3-030-43192-1_75
3. Wisaeng, Kittipol & Sa-Ngiamvibool, Worawat. (2018). Automatic Detection of Exudates in Retinal Images using Region-Based, Neighborhood and Block Operation. Journal of Computer Science. 14. 438-452. 10.3844/jcssp.2018.438.452.4
4. Y. Zong et al., (2020) "U-net Based Method for Automatic Hard Exudates Segmentation in Fundus Images Using Inception Module and Residual
5. Sambyal, Nitigya & Saini, Poonam & Syal, Rupali & Gupta, Varun. (2020). Modified U-Net architecture for semantic segmentation of diabetic retinopathy images. Biocybernetics and Biomedical Engineering. 40. 10.1016/j.bbe.2020.05.006
6. Caixia Kou, Wei Li, Wei Liang, Zekuan Yu, Jianchen Hao, (2019) "Microaneurysms segmentation with a U- Net based on recurrent residual convolutional neural network," J. Med. Imag. 6(2), 025008, doi: 10.1117/1.JMI.6.2.025008.
7. Khojasteh, P., Aliahmad, B. & Kumar, (2018) D.K. Fundus images analysis using deep features for detection of exudates, hemorrhages and microaneurysms. BMC Ophthalmol 18, 288. https://doi.org/10.1186/s12886- 018-0954-4.
8. Ronneberger, O., Fischer, P., Brox, T. (2015): U-Net: Convolutional Networks for Biomedical Image Segmentation. In: International Conference on Medical Image Computing and Computer-Assisted Intervention, pp. 234{241, Springer.
9. Prasanna Porwal, Samiksha Pachade, Ravi Kamble, Manesh Kokare, Girish Deshmukh, Vivek Sahasrabuddhe, Fabrice Meriaudeau, April 24, 2018, "Indian Diabetic Retinopathy Image Dataset (IDRiD)", IEEE Dataport, doi: https://dx.doi.org/10.21227/H25W98.
10. Silva, C.; Colomer, A.; Naranjo Ornedo, V. (2018). Deep Learningbased Approach for the Semantic Segmentation of Bright Retinal Damage. En Intelligent Data Engineering and Automated Learning - IDEAL 2018. Springer. 164-173. https://doi.org/10.1007/978-3-030- 03493-1 18