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NON-INVASIVE VS. INVASIVE: ASSESSING THE POWER OF SLIT LAMP BIOMICROSCOPY IN DETECTING DIABETIC RETINOPATHY COMPARED TO FUNDUS FLUORESCEIN ANGIOGRAPHY

Ophthalomology

Dr. Arushi Prakash* Consultant Ophthalmologist Shantived Institute of Medical Sciences, Agra. *Corresponding Author

Dr. Sanya Garg Consultant Ophthalmologist Darshan Superspeciality Hospital Bhatinda.

Dr. Nisha Dulani Head of the Department, Ophthalmology RUHS-CMS, Jaipur.

Dr. Kishor Kumar Senior Professor RUHS-CMS, Jaipur.

ABSTRACT

Background: Diabetic retinopathy (DR) is a leading cause of blindness among working-age adults. Early detection is crucial for effective management and prevention of vision loss. This study compares the efficacy of slit lamp biomicroscopy (SLB) and fundus fluorescein angiography (FFA) in detecting and grading DR. **Methods:** This observational cross-sectional study involved 102 eyes from 52 diabetic patients at KLES Prabhakar Kore Hospital, Belagavi, from January 1, 2014, to December 31, 2014. Patients underwent comprehensive ophthalmic examinations, including SLB and FFA. DR severity was graded using the International Clinical Diabetic Retinopathy (ICDR) scale. Sensitivity, specificity, and agreement between SLB and FFA were assessed using kappa statistics. **Results:** The study found a high agreement between SLB and FFA in grading DR, with a kappa statistic of 0.836. SLB identified DR severity in 86.2% of cases, with a sensitivity of 89.7% and a positive predictive value of 95.6%. SLB also demonstrated 100% sensitivity and specificity in detecting clinically significant macular edema (CSME), aligning perfectly with FFA findings. **Conclusions:** SLB is a reliable, non-invasive, and cost-effective alternative to FFA for detecting and grading DR, especially in resource-limited settings. Future research should explore integrating SLB with advanced imaging techniques like OCTA to enhance early detection and management of DR.

KEYWORDS

INTRODUCTION

Diabetes mellitus is a major global health issue and the primary cause of blindness among adults in the working age.[1] It is projected that by 2045, India alone could have up to 124.9 million people living with diabetes.[2] A national survey has revealed that the prevalence of diabetic retinopathy (DR) among persons with diabetes in India is 15.5%, the prevalence of sight threatening DR is 5.3%.[3] Despite the high prevalence, existing screening programs for DR are insufficient, often failing to diagnose and treat patients before they experience significant vision loss. Consequently, DR remains the leading cause of blindness that can be registered in this demographic.

The lag between the onset of diabetes and the emergence of symptoms in DR underscores the importance of early detection. Research indicates significantly better outcomes when the disease is identified during this asymptomatic phase.[4] Efficient early detection of DR not only helps in managing the disease more effectively but is also cost-effective, particularly in preventing blindness among the working-age population.

The methods used to diagnose DR are varied and subject to ongoing debate. The primary diagnostic tools include direct ophthalmoscopy, retinal photography, slit lamp biomicroscopy (SLB) and fundus fluorescein angiography (FFA).[4-6] Microaneurysms are often the first sign of DR, detectable through ophthalmoscopy.[7] Early vascular alterations are further detailed through fluorescein angiography, which highlights issues like dye leakage, capillary dilation, and filling defects.[8]. However, FFA has its drawbacks: it is invasive, expensive, time-intensive, and not universally accessible. There's also a risk of hypersensitivity reactions, although these are rare.[9]

Optical Coherence Tomography Angiography (OCTA) in the recent years has emerged as a non-invasive imaging technique that provides detailed images of retinal and choroidal vasculature without the need for dye injection. Further, OCTA provides high-resolution images and has proven effective in early DR detection.

This study aims to compare the clinical and angiographic findings of FFA with those of SLB to evaluate the latter's sensitivity in the accurate detection and grading of DR. By doing so, we intend to assess whether SLB could serve as a viable alternative to FFA in settings where the latter is impractical due to equipment limitations, cost issues, or potential health risks to patients.

METHODOLOGY

This observational cross-sectional study was conducted at KLES Prabhakar Kore Hospital in Belagavi from January 1, 2014, to December 31, 2014, and involved 102 eyes of 52 patients."02 eyes of 52 patients. Institutional review board committee approval was taken and participation was voluntary, with the option to withdraw at any time. Patients included had a known diabetic history and signs of DR identified through Indirect Ophthalmoscopy. Exclusions included those with significant ocular media opacity, other fundus degenerative conditions, previous treatments for DR (intravitreal anti-vascular endothelial growth factor injections/ laser treatment), contraindications for fluorescein dye (renal insufficiency or history of allergic reactions), and unwillingness to consent.

Upon obtaining informed consent, comprehensive medical and ocular histories were collected, including details on diabetes duration, HbA1c levels, current medications, and other relevant conditions. A general physical examination and thorough ophthalmic assessment followed, including visual acuity assessments (uncorrected, best corrected, and near vision), torchlight and slit lamp examinations of the anterior segment, and intraocular pressure measurements were performed.

After mydriasis with Tropicamide 0.8% and Phenylephrine 5%, participants underwent SLB using a Zeiss slit lamp and Volk Superfield NC lens to evaluate the posterior pole for microaneurysms, retinal hemorrhages, venous beading, IRMA, neovascularization, hemorrhages, and macular edema. Findings were documented and graded using the International Clinical DR (ICDR) scale.[10] Also, late phase images were taken at 7 and 10 minutes to evaluate the macula which were similarly graded.

The consistency and diagnostic value of SLB and FFA were compared. The sensitivity of SLB in grading DR was calculated, and kappa statistics measured the agreement between SLB and FFA grading. Associations of diabetic age, hypertension, and HbA1c with the severity of DR were also determined.

RESULTS

This observational study was conducted on 52 patients with DR who met the inclusion criteria and presented to the ophthalmology department of KLES Dr. Prabhakar Kore Hospital and Medical Research Centre between January 1, 2014, and December 31, 2014. Among these patients, 5 had Type 1 Diabetes Mellitus (T1DM), and 47 had Type 2 Diabetes Mellitus (T2DM), involving a total of 102 eyes.

The age distribution of the patients ranged from 21 to 77 years, with a

mean age of 55.88 years (standard deviation 12.21). The largest age group was 61-70 years, comprising 34.6% of the participants. There was a male predominance in the study group, with 29 males (55.7%) and 23 females (44.3%), resulting in a male-to-female ratio of 1.26:1.

The severity of DR was assessed using FFA. Mild Non-Proliferative Diabetic Retinopathy (NPDR) was observed in 9.8% of eyes, moderate NPDR in 35.3%, severe NPDR in 17.6%, very severe NPDR in 9.8%, early Proliferative Diabetic Retinopathy (PDR) in 16.7%, and high-risk PDR in 10.8%. [Graph 1]. Moderate NPDR was the most common form, affecting more than one-third of the patients.

Clinically Significant Macular Edema (CSME) was present in 28.43% of the eyes, all of which had T2DM. None of the T1DM patients had CSME.

The mean age at diagnosis of diabetes for T1DM patients was 16.8 years (standard deviation 6.8), and for T2DM patients, it was 58.5 years (standard deviation 5.0). The age of onset of diabetes ranged from 6 to 72 years.

The duration of diabetes among the patients varied from 0 to 22 years, with a mean duration of 10.37 years (standard deviation 5.94 years).

The severity of retinopathy correlated with the duration of diabetes. Mild NPDR was more common in patients with a diabetic age of less than 10 years, while severe NPDR and PDR were more prevalent in patients with a diabetic age of more than 10 years.

Regarding treatment, 65.8% of participants were on oral hypoglycemic agents (OHAs) alone, 18% were on insulin alone, and 13% were on both OHA and insulin. Two patients (3.8%) were not on any treatment.

Hypertension was present in 58 out of 52 patients, and its correlation with retinopathy severity was not statistically significant ($p = 0.161$). The mean HbA1c level was 8.73% (standard deviation 1.50), with higher levels associated with increased severity of retinopathy.

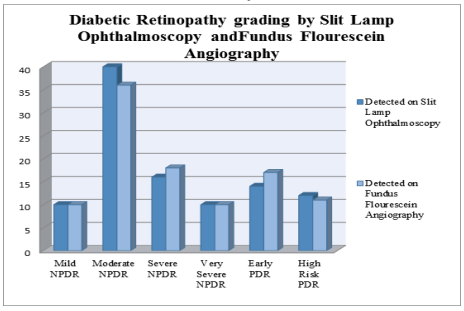
The mean fasting blood sugar levels also increased with the severity of retinopathy. For mild NPDR, the mean fasting blood sugar was 156.00 mg/dL (standard deviation 55.70), while for high-risk PDR, it was 170.00 mg/dL (standard deviation 18.83).

Table 1: Correlation Between Slit Lamp Ophthalmoscopy And Fundus Flourescein Angiography for Grading of Diabetic Retinopathy Slit Lamp Ophthalmoscopy * Fundus Flourescein Angiography Crosstabulation

		Fundus Flourescein Angiography						Total Total
		Mild NPDR	Mod NPDR	Severe NPDR	Very Severe NPDR	Early PDR	High Risk PDR	
Slit Lamp Ophathmoscopy	Mild NPDR	10	0	0	0	0	0	10
	% co-relation	100%						
	Moderate NPDR	0	35	5	0	0	0	40
	% co-relation		97.2%	27.8%				
	Severe NPDR	0	0	13	0	3	0	16
	% co-relation			72.2%		17.6 %		
	V.Severe NPDR	0	0	0	8	2	0	10
	% co-relation				80%	11.7 %		
	Early PDR	0	0	0	2	12	0	14
	% co-relation					70.6 %		
	High Risk PDR	0	1	0	0	0	11	12
	% co-relation		2.8%				100%	
Total		10	36	18	10	17	11	102

SLB graded 102 eyes with DR as follows: 9.8% were classified as mild NPDR, 39.2% as moderate NPDR, 15.7% as severe NPDR, 9.8% as very severe NPDR, 13.7% as early PDR, and 11.8% as high-risk PDR [Graph 1]. These findings indicate a strong correlation between SLB and FFA, as evidenced by a chi-square value of 383.731 ($p < 0.001$) and a Kappa statistic of 0.836, demonstrating excellent agreement between the two methods.

Overall, SLB agreed with FFA grading in 88 cases (86.2%) [Table 1]. There were 10 cases underdiagnosed and 4 cases overdiagnosed by SLB. Sensitivity was calculated at 89.7%, with a positive predictive value of 95.6%. Specificity and negative predictive value could not be calculated due to the absence of true negatives (patients without DR) in this study. FFA, being an invasive procedure, was not performed on patients without DR as detected by ophthalmoscopy; thus, such patients were excluded from the study.



Graph 1: Comparison of Diabetic Retinopathy grading by Slit Lamp Biomicroscopy and FFA

Furthermore, SLB detected clinically significant macular edema (CSME) in 29 eyes, which corresponded 100% with the FFA detection of CSME. The remaining 73 eyes did not show signs of CSME on either test, resulting in a sensitivity and specificity of 100% for SLB in detecting CSME.

DISCUSSION

The findings of this study highlight the significant correlation between slit lamp biomicroscopy (SLB) and fundus fluorescein angiography (FFA) in grading diabetic retinopathy (DR). The high agreement, with a kappa statistic of 0.836, underscores SLB's potential as a non-invasive, cost-effective alternative to FFA, particularly in resource-limited settings where FFA may not be readily available.

COMPARISON OF SLB AND FFA

Our results demonstrate that SLB accurately identified DR severity in 86.2% of cases, with a sensitivity of 89.7% and a positive predictive value of 95.6%. These findings align with previous studies (Khalaf et al., 2007; Nanda et al., 2017)[7,9] indicating the reliability of SLB for DR screening.

CSME is a major cause of vision loss in patients with diabetes, and early detection is crucial for preventing progression (Hannouche et al., 2008).[11] The high concordance between SLB and FFA in detecting clinically significant macular edema (CSME) further supports the use of SLB as a dependable diagnostic tool.

CLINICAL IMPLICATIONS

Given the prevalence of DR and its potential to cause blindness among working-age adults, efficient and accessible screening methods are crucial. The study underscores SLB's utility in clinical practice, offering a practical solution for early DR detection and management. This is particularly important in settings where FFA's invasiveness, cost, and accessibility pose significant barriers.

FACTORS INFLUENCING DR SEVERITY

The study also explored the correlation between DR severity and patient characteristics, such as diabetes duration, HbA1c levels, and hypertension. Consistent with previous research (Rema et al., 2005; Wong et al., 2008)[12,13], a longer duration of diabetes and higher HbA1c levels were associated with more severe DR. However, the correlation between hypertension and DR severity was not statistically significant, suggesting the need for further investigation into these relationships (UKPDS Group, 1998).[14]

Interestingly, the study found a male predominance among the

participants, with a male-to-female ratio of 1.26:1. This finding is consistent with other studies (Qian et al., 2022; Cherchi et al., 2020)[15,16] that suggest males may have a higher risk of developing DR, though the exact reasons for this gender difference remain unclear .

LIMITATIONS AND FUTURE DIRECTIONS

Despite its strengths, the study has limitations, including its observational nature, small sample size, single-center design, and the absence of a control group (diabetic patients without DR). Larger, multi-center studies are necessary to validate these findings across diverse populations and settings. Additionally, future research should explore integrating SLB with advanced imaging techniques like Optical Coherence Tomography Angiography (OCTA). OCTA offers high-resolution imaging and can detect early microvascular changes, potentially enhancing DR management. The integration of OCTA with artificial intelligence[17] holds promise for detecting subclinical cases and improving patient outcomes.

CONCLUSIONS

SLB proves to be a reliable and effective method for DR detection and grading, presenting a viable alternative to FFA in resource-constrained environments. Emphasizing the importance of regular screening and optimal management of diabetes, this study advocates for the broader adoption of SLB in clinical practice. Future research should focus on enhancing SLB's diagnostic capabilities by incorporating advanced imaging technologies to further improve early DR detection and patient care.

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