Journal of Cardiovascular Disease Research

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

Original Research Article

Evaluation of Peripheral Fundus Auto Fluorescence Changes Using Ultra-Wide field Retinal Imaging in Patients with Age Related Macular Degeneration

Dr. Felix Lal R.V.[1], Dr. Rohan Rajan[2]

[1]Assistant Professor, Department of Ophthalmology, Dr. Moopen's Medical College, Wayanad, Kerala, India.
[2]Consultant, Department of Ophthalmology, Aravind eye hospital, Coimbatore, Tamil Nadu, India.

Corresponding Author
Dr. Felix Lal R.V., Assistant Professor, Department of Ophthalmology, Dr. Moopen's Medical College, Wayanad, Kerala, India.

Received: 20-08-2024 / Revised: 31-08-2024 / Accepted: 01-10-2024

ABSTRACT

Background
Age-related macular degeneration (AMD) is a leading cause of vision loss worldwide. Traditional imaging focuses on central retinal changes, but ultra-wide field imaging has revealed peripheral retinal involvement. This study aimed to identify the prevalence and characteristics of peripheral fundus autofluorescence (FAF) changes in AMD patients using ultra-wide field imaging in Kerala, India.

Methods
This cross-sectional study included 126 eyes of 65 AMD patients aged 50–90 years attending a tertiary eye care hospital in Thiruvananthapuram from December 2018 to December 2019. Patients with no fundus view were excluded. Ultra-wide field imaging using the Optos 200Tx system captured peripheral FAF patterns. Lesions were classified as hyper, hypo, or mixed auto fluorescence, and quadrant involvement was recorded. Data were analyzed using SPSS.

Results
Peripheral retinal lesions were present in 53.17% of eyes. Non-neovascular AMD accounted for 76.11% of these cases, while 23.88% were seen in neovascular AMD. Hyper FAF was the most common pattern (50.74%), followed by mixed FAF (28.35%) and hypo FAF (20.89%). One quadrant was involved in 47.76% of eyes, and involvement of two or more quadrants occurred in the remaining cases.

Conclusion
Ultra-widefield imaging revealed significant peripheral retinal changes in AMD, highlighting the necessity of examining the peripheral retina in addition to the macula. These findings may contribute to better AMD management strategies, though further longitudinal studies are required.

Keywords: Age-Related Macular Degeneration (Amd), Peripheral Fundus Autofluorescence, Ultra-Wide Field Imaging, Retinal Lesions, Kerala.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

INTRODUCTION

Age-related macular degeneration (AMD) emerged as the primary cause of blindness in industrialized countries[1–6] and the third most common cause of blindness globally.[7] With projected population growth and increasing life expectancy, the number of patients experiencing significant visual loss due to AMD was expected to escalate over time. Initial research in AMD predominantly focused on retinal pigment epithelial changes in the central retinal region (macula), but advancements in Wide Field Retinal Imaging and Fundus Auto Fluorescence (FAF) enabled identification of diverse AMD disease phenotypes by imaging the retinal periphery.[8–11]

AIM AND OBJECTIVES

The study aimed to determine the prevalence of peripheral fundus auto fluorescence changes in patients with age-related macular degeneration using Ultra-Wide field Retinal Imaging. The objectives were to investigate peripheral retinal lesions and explore potential modifications in AMD phenotyping and management strategies.

MATERIALS AND METHODS

A hospital-based cross-sectional study was conducted at the Regional Institute of Ophthalmology, Thiruvananthapuram, Kerala, from December 2018 to December 2019. The study population comprised AMD patients attending the outpatient department. The study was initiated after obtaining clearance from the Human Ethics Committee of RIO, Thiruvananthapuram. Informed consent was obtained from patients in their local languages, and patient confidentiality was maintained throughout the study.

Inclusion and Exclusion Criteria

Patients with AMD attending the RIO OPD for management were included in the study. Patients with no fundus view on examination and those with a history of other retinal diseases were excluded.

Sample Size Calculation

The sample size was calculated using the formula $n = 4pq/d^2$, where n is the sample size, p is the prevalence of AMD, q is 100-p, and d is 20% of p. Based on the study by Colin S Tan et al 12 which reported the prevalence of 68.9%, the calculated sample size was 45 patients.

Data Collection Technique

The data collection process was comprehensive and systematically designed to capture detailed patient information. Socio-demographic details were obtained through a structured interview schedule, providing essential background context for each participant. A thorough comprehensive ophthalmological examination was conducted to assess overall eye health and specific AMD-related characteristics. Best Corrected Visual Acuity was meticulously measured using the standard Snellen's Chart, enabling precise documentation of each patient's visual capabilities. Fundus examination was performed using Indirect Ophthalmoscopy, which allowed for a detailed assessment of the retinal structures. Subsequently, high-resolution Peripheral Retinal Images were captured using the advanced Optos 200Tx Ultra-Wide field Retinal Imaging Device, ensuring a comprehensive and detailed documentation of retinal changes associated with Age-related Macular Degeneration.

Statistical Analysis

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

The collected data were entered into an Excel sheet and analysed using SPSS software.

RESULTS

Peripheral Retinal Lesions	Number of eyes	PERCENTAGE
Absent	59	46.82
Present	67	53.17
Total	126	100
Table 1: Peripheral Retinal Lesions Distribution		

In our study, 53.17% of examined eyes demonstrated peripheral retinal lesions, indicating a significant proportion of patients with extramacular involvement in Age-related Macular Degeneration (AMD).

Type of ARMD	Number of eyes	Percentage
Non neovascular	51	76.11
Neovascular	16	23.88
Total	67	100
Table 2: Type of AMD and Peripheral Retinal Lesions		

Peripheral retinal lesions were predominantly observed in non-neovascular AMD patients, accounting for 76.11% of cases compared to 23.88% in neovascular AMD.

Type of FAF	Number of eyes	Percentage
Hypo Autofluorescence	14	20.89%
Hyper Autofluorescence	34	50.74%
Mixed Autofluorescence	19	28.35%
Total	67	100
Table 3: Fundus Auto Fluorescence (FAF) Characteristics		

Hyper autofluorescence was the most prevalent finding, observed in 50.74% of peripheral retinal lesions. Hypo autofluorescence was evident in 20.89% of eyes, while mixed autofluorescence was observed in 28.35% of cases.

Quadrant	Number of eyes	Percentage
One	32	47.76%
Two	26	38.80%
Three	6	8.95%
Four	3	4.47%
Total	67	100
Table 4: Quadrant Involvement in Peripheral Retinal Lesions		

The distribution of peripheral retinal lesions revealed a gradual decrease in frequency as the number of involved quadrants increased.47.76% of eyes had lesions in one quadrant, 38.80% of eyes showed involvement of two quadrants, 8.95% of eyes exhibited lesions in three quadrants, 4.47% of eyes demonstrated comprehensive four-quadrant involvement.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

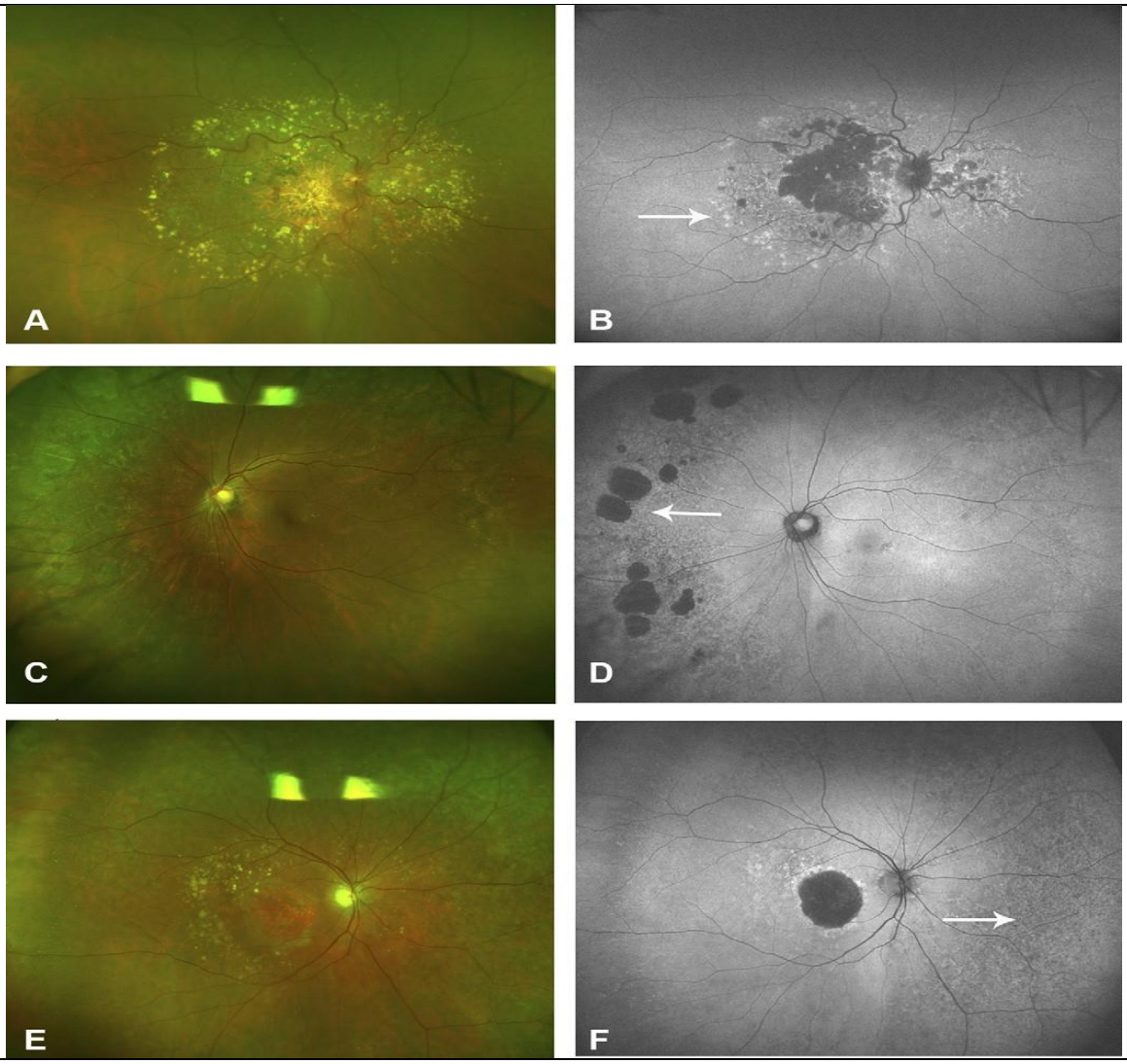

Figure 1. Color and autofluorescence photographs illustrating fundus autofluorescence (FAF) abnormalities and the associated clinical features.
Figure A: Color fundus photography illustrating peripheral drusen.
Figure B: FAF image showing granular increased autofluorescence corresponding to the drusen (white arrow).
Figure C: Areas of retinal pigment epithelium (RPE) atrophy in the nasal periphery.
Figure D: FAF image showing areas of nummular decreased autofluorescence (white arrow) corresponding to the RPE atrophy.
Figure E: Areas of RPE depigmentation in the periphery of the fundus. Small peripheral drusen are seen temporally.
Figure F: FAF image demonstrating large areas of mottled decreased autofluorescence (white arrow) corresponding to the area of RPE depigmentation. Fine granular FAF is also seen temporally corresponding to peripheral drusen.

DISCUSSION

Tan et al.[13] significant findings were observed regarding peripheral FAF abnormalities. They documented that 68.9% of individuals exhibited distinct peripheral FAF abnormality patterns. Notably, these abnormalities were more prevalent in neovascular AMD, with 86% of eyes showing abnormal FAF patterns, compared to 72.8% in non-neovascular AMD and only

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

18.4% in normal eyes. This aligns closely with the current study's findings, which revealed peripheral retinal lesions in 53.17% of eyes.

The current study provides a more detailed breakdown of FAF patterns. While Tan et al. focused on the presence of abnormalities, this research delved deeper into the characteristics of these abnormalities. Specifically, 50.74% of peripheral retinal lesions displayed hyper-fundus autofluorescence, 20.89% showed hypo-FAF, and 28.35% exhibited a mixed FAF pattern. Interestingly, the distribution of lesions was also examined, with 47.76% of eyes involving only one quadrant, 38.80% spanning two quadrants, and a small percentage affecting three or four quadrants.

Holz et al. (2007) [14] and Bindewald et al. (2005) [15] established early groundwork in classifying abnormal fundus autofluorescence patterns, particularly in the junctional zones of geographic atrophy.

Delori et al.'s pioneering research (1995, 2001)[16,17] demonstrated the critical role of lipofuscin accumulation in retinal aging. Their studies revealed the in vivo fluorescence characteristics of the ocular fundus and age-related spatial distribution of lipofuscin in RPE. Our current research corroborates these findings, showing how lipofuscin variations manifest in different FAF patterns – with 50.74% displaying hyper-fundus autofluorescence, 20.89% hypo-FAF, and 28.35% mixed FAF patterns.

The epidemiological perspectives provided by Klein et al. (2007) [18]and van Leeuwen et al. (2003) [19]offer crucial context to our findings. While these studies focused on the cumulative incidence and epidemiology of age-related maculopathy, our research provides a more nuanced view of peripheral retinal changes. Notably, we observed peripheral retinal lesions in 53.17% of eyes, with a higher prevalence in non-neovascular AMD (76.11%) compared to neovascular AMD (23.88%).

Ambati et al. (2003)[20] extensively discussed AMD's etiology and pathogenesis. Our study complements their work by demonstrating the variable involvement of retinal quadrants – 47.76% of eyes had lesions in one quadrant, 38.80% in two quadrants, and smaller percentages in three or four quadrants.

Stangos et al. (1995)[21], Holz et al. (1995)[22], and Midena et al. (1994)[23] explored contrast sensitivity and visual field deficits in AMD patients. Our ultra-widefield imaging approach offers a novel perspective on peripheral retinal changes, suggesting that peripheral lesions might be more extensive and complex.

Drawing from Bird's (1996)[24] and Knudtson et al.'s (2004)[25] work on macular disease progression, our research emphasizes the need for longitudinal studies. The observed peripheral retinal changes warrant further investigation to understand their relationship with macular progression and overall disease trajectory.

The global perspective provided by Resnikoff et al. (2004)[7] on visual impairment underscores the significance of our research. We also acknowledge the study's limitations, including the potential distortion from the Optos system's ellipsoid mirror and the need for more comprehensive imaging techniques.

LIMITATIONS

The study encountered several methodological constraints. The Optos system's ellipsoid mirror distorts peripheral retinal imaging, creating topographic mismatches with limited superior and inferior views. We exclusively evaluated green-light fundus autofluorescence (FAF), which restricts comprehensive abnormality detection.

Significant imaging artifacts from eyelids, eyelashes, floaters, intraocular lens optics, and lens opacities can potentially compromise peripheral lesion identification. No standardized reference exists for comparing imaging patterns.

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

FAF imaging presents inherent limitations, including low signal strength and autofluorescence artifacts from anterior segment structures. While blue-light excitation may raise concerns about patient discomfort and potential retinal toxicity, no formal studies have confirmed adverse effects.

CONCLUSION

Age-related macular degeneration (AMD) is a degenerative disease that significantly impacts the quality of life for older patients and appears to be increasing in prevalence within our society.

Despite being a potentially vision-threatening condition, AMD is frequently overlooked until severe vision loss occurs. This underscores the critical importance of early diagnosis and consistent follow-up.

Ultra-widefield imaging demonstrated a non-contact method of detecting peripheral retinal lesions in 52.31% of AMD patients. This finding emphasizes the necessity of comprehensive retinal examination, extending beyond the traditional central 30-degree focus.

The research highlights the value of peripheral retinal assessment in understanding and managing AMD, potentially revolutionizing our approach to diagnosing and monitoring this sight-threatening condition.

REFERENCES

1. Prokofyeva E, Zrenner E. Epidemiology of major eye diseases leading to blindness in Europe: a literature review. Ophthalmic Res 2012;47:171– 88.
2. Wong TY, Loon SC, Saw SM. The epidemiology of age related eye diseases in Asia. Br JOphthalmol 2006;90:506–11.
3. Rothe Nissen K, Sjolie AK, Jensen H, et al. The prevalence and incidence of visual impairment in people of age 20-59years in industrialized countries: a review. Ophthalmic Epidemiol 2003;10:279 –91.
4. Xu L, Wang Y, Li Y, et al. Causes of blindness and visual impairment in urban and rural areas in Beijing: the Beijing Eye Study. Ophthalmology 2006;113:1134–41.
5. Eye Diseases Prevalence Research Group. Causes and prevalence of visual impairment among adults in the United States. Arch Ophthalmol 2004;122:477– 85.
6. Maberley DA, Hollands H, Chuo J, et al. The prevalence of low vision and blindness in Canada. Eye (Lond) 2006;20:341–6.
7. Resnikoff S, Pascolini D, Etya'ale D, et al. Global data on visual impairment in the year 2002. Bull World Health Organ 2004;82:844 –51.
8. von Ruckmann A, Fitzke FW, Bird AC. Fundus autofluorescence in age-related macular disease imaged with a laser scanning ophthalmoscope. Invest Ophthalmol Vis Sci 1997; 38:478–86.
9. Holz FG, Bellmann C, Margaritidis M, et al. Patterns of increased in vivo fundus autofluorescence in the junctional zone of geographic atrophy of the retinal pigment epithelium associated with age-related macular degeneration. Graefes Arch Clin Exp Ophthalmol 1999;237:145–52.
10. Bindewald A, Jorzik JJ, Loesch A, et al. Visualization of retinal pigment epithelial cells in vivo using digital highresolution confocal scanning laser ophthalmoscopy. Am J Ophthalmol 2004;137:556–8.
11. Jorzik JJ, Bindewald A, Dithmar S, Holz FG. Digital simultaneous fluorescein and indocyanine green angiography, autofluorescence, and red-free imaging with a solid-state laserbased confocal scanning laser ophthalmoscope. Retina 2005

ISSN: 0975-3583,0976-2833 VOL15, ISSUE 12, 2024

12. Tan CS, Ngo WK, Chay IW, Ting DS, Sadda SR. Neovascular Age-Related Macular Degeneration (nAMD): A Review of Emerging Treatment Options. Clin Ophthalmol. 2022 Mar 25;16:917-933. doi: 10.2147/OPTH.S231913. PMID: 35368240; PMCID: PMC8965014.
13. Coupat C, Allard E. Beyond stages: Comment on Tan et al. (2024) 'Stages of readiness for advance care planning: Systematic review and meta-analysis of prevalence rates and associated factors'. Int J Nurs Stud. 2024 Aug;156:104782. doi: 10.1016/j.ijnurstu.2024.104782. Epub 2024 May 3. PMID: 38744149.
14. Holz FG, Bindewald-Wittich A, Fleckenstein M, et al, FAMStudy Group. Progression of geographic atrophy and impact of fundus autofluorescence patterns in age-related macular degeneration. Am J Ophthalmol 2007;143:463–72.
15. Bindewald A, Schmitz-Valckenberg S, Jorzik JJ, et al. Classification of abnormal fundus autofluorescence patterns in the junctional zone of geographic atrophy in patients with age related macular degeneration. Br J Ophthalmol 2005;89:874–8.
16. Delori FC, Dorey CK, Staurenghi G, et al. In vivo fluorescence of the ocular fundus exhibits retinal pigment epithelium lipofuscin characteristics. Invest Ophthalmol Vis Sci 1995;36:718–29.
17. Delori FC, Goger DG, Dorey CK. Age-related accumulation and spatial distribution of lipofuscin in RPE of normal subjects.Invest Ophthalmol Vis Sci 2001;42:1855– 66.
18. Klein R, Klein BE, Knudtson MD, Meuer SM, Swift M, Gangnon RE. Fifteen-year cumulative incidence of age-related macular degeneration: the Beaver Dam Eye Study. Ophthalmology. 2007;114:253–262
19. Van Leeuwen R, Klaver CC, Vingerling JR, Hofman A, de Jong PT. Epidemiology of age-related maculopathy: a review. Eur J Epidemiol. 2003;18:845–854.
20. Ambati J, Ambati BK, Yoo SH, Ianchulev S, Adamis AP. Age-related macular degeneration: etiology, pathogenesis, and therapeutic strategies. Surv Ophthalmol. 2003;48:257–293.
21. Stangos N, Voutas S, Topouzis F, Karampatakis V. Contrast sensitivity evaluation in eyes predisposed to age-related macular degeneration and presenting normal visual acuity. Ophthalmologica. 1995;209:194–198.
22. Holz FG, Gross-Jendroska M, Eckstein A, Hogg CR, Arden GB, Bird AC. Colour contrast sensitivity in patients with age-related Bruch’s membrane changes. Ger J Ophthalmol. 1995;4:336– 341.
23. Midena E, Segato T, Blarzino MC, Degli Angeli C. Macular drusen and the sensitivity of the central visual field. Doc Ophthalmol. 1994;88:179–185.
24. Bird A. Age-related macular disease. Br J Ophthalmol. 1996; 80:2–3.
25. Knudtson MD, Klein R, Klein BE, Lee KE, Meuer SM, Tomany SC. Location of lesions associated with age-related maculop-athy over a 10-year period: the Beaver Dam Eye Study. Invest Ophthalmol Vis Sci. 2004;45:2135–2142.