SHORT COMMUNICATION

Assessment of visual and cognitive function among patients with Stargardt Disease

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Abstract

This study aimed to assess the association between visual and cognitive impairment in patients with Stargardt Disease at the Low Vision Rehabilitation Centre, Al-Shifa Trust Eye Hospital, Rawaalpindi. It was a cross-sectional study conducted from September to December 2023 which included 32 patients (mean age 20.34 ± 7.9 years). Visual function was evaluated using LogMAR (Logarithm of the Minimum Angle of Resolution), Pelli Robson Chart, and Pseudo Isochromatic Plates, while cognitive function was assessed using the Montreal Cognitive Assessment (MoCA) and Ray Auditory Verbal Learning Test (RAVLT). MoCA scores indicated cognitive impairment in 59.38% of patients. Pearson correlation showed no significant association between MoCA scores and visual acuity ($p = 0.768$) and between most RAVLT variables and visual acuity, except for RAVLT forgetting ($p = 0.007$). Although visual acuity was not directly linked to cognitive decline, many patients exhibited impairment, suggesting other contributing factors. Further research with a larger sample size is needed.

MeSH Words: Visual acuity, Low vision, Stargardt Disease, Cognition.

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Introduction

The World Health Organisation's (WHO) 10th revision of the International Statistical Classification of Diseases, Injuries, and Causes of Death (ICD-10) defines "low vision" as visual acuity below 6/18 but at least 3/60 or a visual field loss of less than 20° in the better eye, with functional vision retained.[1] In Pakistan, uncorrected refractive error, cataract, corneal opacity, and retinal abnormalities are the main causes of vision impairment, with a prevalence of (1.7%) and blindness at (0.2%).[2] Loss of vision significantly impacts quality of life by limiting reading, mobility, work, and social interactions.[3] Among individuals with Stargardt Disease (STGD), depressive symptoms are a major factor affecting the quality of life.[4]

STGD, also called juvenile macular degeneration, is a genetic disorder that causes fatty deposits in the macula, impairing central vision. It is the most common inherited macular dystrophy, affecting 1 in 8,000–10,000 individuals. While usually presenting in childhood, milder adult-onset cases also occur.[5] The autosomal-recessive form of STGD often manifests in the first two decades of life.[6] leading to progressive bilateral central vision loss, peaking in infancy and early adulthood.[7] Ophthalmoscopy shows macular atrophy with yellowish-white flecks near the retinal pigment epithelium (RPE).[8] Visual acuity (VA) in STGD correlates with age and disease stage, with stage 1 patients maintaining VA better than 20/200, while those in later stages have VA of 20/200 or worse.[9] High vitamin A intake may worsen retinal degeneration in an STGD1 deletion mouse model.[6] STGD results from over 1,500 distinct ATP-binding cassette subfamily A member 4 (ABCA4) mutations, each affecting ABCA4 protein function to varying degrees. The condition presents with diverse phenotypes, ranging from early blindness to mild macular changes with minimal visual complaints.[10] Macular diseases contribute to both visual impairment and cognitive decline.[11]

Cognitive function includes processes such as perception, memory, and problem-solving, and is a crucial predictor of life outcomes.[12] Alzheimer's disease (AD) is the leading cause of dementia, primarily affecting the brain, but also linked to retinal changes, including macular deposits, thinning of retinal nerve fibres, optic disc cupping, and microvascular abnormalities.[13] Cognitive function is assessed using various tests, including the Rey Auditory Verbal Learning Test (RAVLT) and the Montreal Cognitive Assessment (MoCA). MoCA is a sensitive tool for detecting mild cognitive impairment, including in AD and other cognitive disorders.[14] It effectively identifies cognitive impairment in AD and other conditions.[15] MoCA scores below 26 suggest mild cognitive impairment.

RAVLT assesses verbal learning and memory through three domains: Immediate recall, Learning (difference

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between first and fifth trial recall), and Forgetting (difference between fifth trial recall and delayed recall).[16] Cognitive function declines with increasing macular abnormalities and worsening VA.[17] Advanced age-related macular degeneration (AMD) is associated with cognitive impairment in older adults. AMD, a multifactorial retinal degeneration, shares clinical features with STGD.[18] This study aims to assess visual and cognitive function in STGD patients with low vision.

Patients, Methods and Results

This cross sectional study was conducted in the low vision clinic at the Al Shifa Trust Eye Hospital, Rawalpindi, following the Declaration of Helsinki. Data was collected from September 2023 to December 2023, with a sample size of 32 patients diagnosed with Stargardt Disease. The sample size was calculated using a WHO calculator based on a prevalence of 1 in 8,000, with a (95%) confidence level.[19] Inclusion criteria were patients aged 10 to 40 years, diagnosed with Stargardt disease, and fulfilling the low vision criteria set by the WHO. Exclusion criteria applied to those who, despite meeting all inclusion attributes, had mental impairment, were non-cooperative, or had any syndrome. The study design and statistical analysis accounted for variation by using continuous visual acuity (LogMAR) scores rather than categorical staging, ensuring robust correlation testing. Written consent was obtained from all participants.

Demographic data was collected using a self-designed clinical proforma. Visual acuity (VA) was recorded using the LogMAR chart at distances of 4m, 2m, and 1m, followed by colour vision assessment using Ishihara pseudo-isochromatic plates in a well-lit setting. Contrast sensitivity was assessed with the Pelli-Robson chart.[20] The results for these are mentioned in the table 1. Cognitive function was evaluated using the Montreal Cognitive Assessment (MoCA) and the Rey Auditory Verbal Learning Test (RAVLT). MoCA consists of a 30-point assessment, with sections evaluating memory, drawing, visual association, calculation, word associations, and literacy.[21] A score of 26 or above indicates normal cognitive function. The results of these ae depicted in the form of table 2. RAVLT involves two lists of 15 words each. Patients recall words from List A over five trials, with the sum of scores from the five trials representing RAVLT Immediate. The difference between trial 1 and trial 5 scores gives RAVLT Learning. After List B is presented, a delayed recall test is performed after a 15-minute break to calculate RAVLT Forgetting.

Data were analysed using SPSS version 26, with descriptive statistics for all variables. Pearson's correlation was applied to assess associations between cognitive variables and VA. Results showed that 65.6% of participants were males, with a mean age of 20.34 ± 7.9 years. Most patients were educated and aged 16–20 as described in table 1. Cognitive function was impaired in 19(59.38%) patients, with MoCA scores showing no significant correlation with VA ($p = 0.768$). In the case of RAVLT, no significant association was noted with VA, except for the Forgetting domain which was significant ($p < 0.05$) as described in table 3.

Table-1: Frequency and % of demographics.

		N	%
Gender	Male	21	65.63
	Female	11	34.38
Age (years)	10-15	10	31.3
	16-20	11	34.4
	21-25	4	12.5
	>25	7	21.9
Education	Primary	22	68.8
	Secondary	9	28.1
	Higher	1	3.1

Table-2: Colour vision and contrast sensitivity among Stargardt patients.

		Frequency	%
Colour vision	Defective	30	93.8
	Tri-chromate	2	6.3
Contrast Sensitivity	Defective	30	93.8
	Normal	2	6.3

Table-3: Correlation of MoCA and RAVLT with Visual Acuity

Test	Minimum	Maximum	Mean ± SD	Correlation (R) with Visual Acuity	p-value
MoCA	16	30	23.50 ± 3.34	0.06	0.786
RAVLT Immediate	31	58	43.09 ± 6.87	0.04	0.843
RAVLT Learning	3	10	5.59 ± 1.88	0.08	0.658
RAVLT Forgetting	0	8	3.00 ± 1.92	0.43	0.007

*MoCA: Montreal Cognitive Assessment, RAVLT: Rey Auditory Verbal Learning Test.

Conclusion

This study included 32 patients with Stargardt Disease, aged 10 to 40 years, observed over a four-month period (September to December 2023), irrespective of gender, for an association between cognitive decline and vision loss.

In comparison, another study on age-related macular degeneration (AMD)

reported that of the 38 patients, 66% were at risk of cognitive impairment.[17] In the case of RAVLT, no significant correlation was observed between vision and cognition across most variables ($p > 0.05$), except for RAVLT Forgetting, which demonstrated a significant association ($p = 0.007$).

A study by Aubin and Phillips (2023) suggested that subjects with AMD exhibited poorer cognitive function than expected when compared to sighted counterparts. Findings indicated that elderly individuals with visual impairment demonstrated significantly reduced cognitive abilities, particularly in processing speed, episodic memory, and global cognition.[22] Furthermore, a meta-analysis suggested that diabetic retinopathy (DR) is associated with a higher risk of brain structural abnormalities and cognitive decline, with this correlation remaining significant even after adjusting for blood glucose levels.[23] Existing literature highlights the impact of retinal pathology on cognitive function. While cognitive decline is generally associated with ageing, Stargardt Disease is an inherited retinal dystrophy typically diagnosed within the first two decades of life.[24] It is characterised by progressive bilateral central vision loss, which begins in childhood and progresses into early adulthood.[25] To date, no previous research has explored the link between cognitive function decline and Stargardt Disease, making this the first known study on the subject.

Limitations: This study is limited by its small sample size, which may affect the generalisability of the findings. Additionally, the study design did not allow for longitudinal assessment of cognitive changes over time.

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MM & WS: Concept and design.
MT: Concept, design, final approval and agreement to be accountable for all aspects of the work.
ZB: Data analysis, interpretation and drafting.
FA: Data analysis and interpretation.
SF: Drafting.