

The association between objective vision impairment and mild cognitive impairment among older adults in low- and middle-income countries

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ABSTRACT

Aim: The association between visual impairment and mild cognitive impairment (MCI) has not been investigated to date. Thus, we assessed this association among older adults from six low- and middle-income countries (LMICs) (China, India, Ghana, Mexico, Russia, South Africa) using nationally representative datasets.

Methods: Cross-sectional, community-based data from the WHO Study on global AGEing and adult health (SAGE) were analyzed. Visual acuity was measured using the tumbling ElogMAR chart, and vision impairment (at distance and near) was defined as visual acuity worse than 6/18 (0.48 logMAR) in the better seeing eye. The definition of MCI was based on the National Institute on Ageing-Alzheimer's Association criteria. Multivariable logistic regression was conducted to associations.

Results: Data on 32715 individuals aged ≥ 50 years [mean (SD) age 62.1 (15.6) years; 51.2% females] were analysed. Compared to those without far or near vision impairment, those with near vision impairment but not far vision impairment (OR=1.33; 95%CI=1.16-1.52), and those with both far and near vision impairment (OR=1.70; 95%CI=1.27-2.29) had significantly higher odds for MCI. Only having far vision impairment was not significantly associated with MCI.

Conclusions: Visual impairment is associated with increased odds for MCI among older adults in LMICs with the exception of far vision impairment only. Future longitudinal and intervention studies should examine causality and whether improvements in visual acuity, or early intervention, can reduce risk for MCI and ultimately, dementia.

Key Words: Vision Impairment; Mild Cognitive Impairment; Older Adults; Low- and middle-income countries; Epidemiology

DECLARATIONS

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INTRODUCTION

The World Health Organization (WHO) defines dementia as a syndrome – usually of a chronic or progressive nature – in which there is deterioration in cognitive function (i.e., the ability to process thought) beyond what might be expected from normal ageing [1]. Dementia is one of the major causes of disability and dependency in the older population and also has significant social and economic impacts [2]. However, there are currently no pharmacological interventions to prevent or cure dementia. Therefore, it is essential to understand the correlates of its preclinical stage to plan strategies to prevent or delay the onset of dementia.

An identified precursor to dementia is mild cognitive impairment (MCI). It has been estimated that one or two in every 10 people over 65 years may have MCI [3]. Although not all individuals with MCI will go on and develop dementia, MCI is associated with a high conversion rate to dementia. Specifically, 12%, 20%, and 50% at 1, 3, and 5 years, respectively [3,4].

Previously identified correlates of MCI include factors such as low physical activity, poor diet, alcohol consumption and smoking [5]. However, there are currently no studies on the association between vision impairment and MCI. Vision impairment may increase one's risk of cognitive impairment via barriers in carrying out daily activities, such as reading or driving, and this may consequently negatively impact cognition, owing to decreased brain stimulation [6]. Several previous studies from high-income countries have found that vision impairment is associated with cognitive decline [6-14]. For example, one longitudinal study from Germany measuring vision impairment at baseline found that the onset of severe visual impairment was associated with decline in cognitive function score [9]. However, all these

previous studies only focused on cognitive decline in general and not MCI, which carries a particularly high risk of conversion to dementia.

Therefore, the aim of the present study was to investigate the association between objectively measured visual impairment (far and near) and MCI in adults aged ≥ 50 years from six low- and middle-income countries (LMICs). Examining this association in LMICs is of particular importance as people living with dementia is increasing most rapidly in these settings [15], while the prevalence of visual impairment has been estimated to be higher in LMICs than in high-income countries [16].

METHODS

The survey

Data from the Study on Global Ageing and Adult Health (SAGE) were analyzed. These data are publically available through <http://www.who.int/healthinfo/sage/en/>. This survey was undertaken in China, Ghana, India, Mexico, Russia, and South Africa between 2007 and 2010. Based on the World Bank classification at the time of the survey, all countries were LMICs.

Details of the survey methodology have been published elsewhere [17]. Briefly, in order to obtain nationally representative samples, a multistage clustered sampling design method was used. The sample consisted of adults aged ≥ 18 years with oversampling of those aged ≥ 50 years. Trained interviewers conducted face-to-face interviews using a standard questionnaire. Standard translation procedures were undertaken to ensure comparability between countries. The survey response rates were: China 93%; Ghana 81%; India 68%; Mexico 53%; Russia 83%; and South Africa 75%. Sampling weights were constructed to adjust for the population structure as reported by the United Nations Statistical Division.

Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards. Written informed consent was obtained from all participants.

Visual impairment

Visual acuity was measured using the tumbling ElogMAR chart for distance and near acuity separately for each eye. For distance vision, the participant was asked to be seated in a chair positioned so that the respondent's head is 4 meters from the eye chart. A string was used to measure 40 cm as the test distance for near visual acuity. The interviewer was instructed to check that the vision charts are well lit and to make sure that the surface does not reflect glare. Furthermore, the respondent was instructed to use glasses or contact lenses if they usually wear them. We defined vision impairment (at distance and near) according to the World Health Organization definition for moderate vision impairment, which refers to visual acuity worse than 6/18 (0.48 logMAR) in the better seeing eye [18]. We created different categories of visual impairment based on different combinations of far and near vision impairment. Specifically, the following four categories were created: (a) no far or near vision impairment; (b) only far vision impairment and no near vision impairment; (c) only near vision impairment and no far vision impairment; (d) both far and near vision impairments.

Mild cognitive impairment (MCI) (Outcome)

MCI was ascertained based on the recommendations of the National Institute on Aging-Alzheimer's Association [19]. We applied the identical algorithms used in previous SAGE publications to identify MCI [4,20]. Briefly, individuals fulfilling all of the following conditions were considered to have MCI:

(a) Concern about a change in cognition: Individuals who replied 'bad' or 'very bad' to the question "How would you best describe your memory at present?" and/or those who

answered 'worse' to the question "Compared to 12 months ago, would you say your memory is now better, the same or worse than it was then?" were considered to have this condition.

(b) Objective evidence of impairment in one or more cognitive domains: was based on a <-1 SD cut-off after adjustment for level of education and age. Cognitive function was assessed through the following performance tests: word list immediate and delayed verbal recall from the Consortium to Establish a Registry for Alzheimer's Disease [21], which assessed learning and episodic memory; digit span forward and backwards from the Weschler Adult Intelligence Scale [22], that evaluated attention and working memory; and the animal naming task [21], which assessed verbal fluency.

(c) Preservation of independence in functional abilities: was assessed by questions on self-reported difficulties with basic activities of daily living (ADL) in the past 30 days [23]. Specific questions were: "How much difficulty did you have in getting dressed?" and "How much difficulty did you have with eating (including cutting up your food)?" The answer options were none, mild, moderate, severe, and extreme (cannot do). Those who answered either none, mild, or moderate to both of these questions were considered to have preservation of independence in functional activities. All other individuals were deleted from the analysis (935 individuals aged ≥ 50 years).

(d) No dementia: Individuals with a level of cognitive impairment severe enough to preclude the possibility to undertake the survey were not included in the current study.

Control variables

The control variables used were selected based on past literature and included sex, age, years of education, wealth quintiles based on income, physical activity, smoking (never, current smoking, past smoking), obesity (body mass index $\geq 30\text{kg/m}^2$ based on measured weight and height), diabetes, stroke, hypertension, and depression [24,25]. Levels of physical activity

were assessed with the Global Physical Activity Questionnaire and were classified as low, moderate, and high based on conventional cut-offs [26]. Diabetes and stroke were based solely on lifetime self-reported diagnosis. Hypertension was defined as having at least one of: systolic blood pressure ≥ 140 mmHg; diastolic blood pressure ≥ 90 mmHg; or self-reported diagnosis. Questions based on the World Mental Health Survey version of the Composite International Diagnostic Interview [27] were used for the endorsement of DSM-IV depression [28].

Statistical analysis

The statistical analysis was performed with Stata 14.1 (Stata Corp LP, College station, Texas). The analysis was restricted to those aged ≥ 50 years as MCI is an age-related condition. We included the middle-aged in this analysis as assessment of cognitive function and its risk factors at earlier ages is important for prevention of dementia given that cognitive dysfunction can manifest up to 10 years prior to the actual dementia diagnosis [29], and current evidence shows that intervening in mid-life is important [30-33]. We conducted multivariable logistic regression analysis to assess the association between visual impairment (exposure) and MCI (outcome). The variable on visual impairment was a four-category variable with different combinations of far and near visual impairment. The regression analysis was adjusted for sex, age, education, wealth, physical activity, smoking, obesity, diabetes, stroke, hypertension, depression, and country. Analyses stratified by age groups (50-64 and ≥ 65 years) were also conducted. Adjustment for country was done by including dummy variables for each country in the model as in previous SAGE publications [4,34]. All variables were included in the models as categorical variables with the exception of age and years of education (continuous variables). The sample weighting and the complex study design were taken into account in the analyses. Results from the regression analyses are

presented as odds ratios (ORs) with 95% confidence intervals (CIs). The level of statistical significance was set at $P < 0.05$.

RESULTS

The final analytical sample consisted of 32715 individuals aged ≥ 50 years with preservation in functional abilities. The sample characteristics are provided in **Table 1**. The mean (SD) age of the sample was 62.1 (15.6) years and 51.2% were females. The prevalence of MCI was 15.3%, while the prevalence of the four visual impairment categories were: (a) no far or near vision impairment 55.7%; (b) only far vision impairment and no near vision impairment 5.4%; (c) only near vision impairment and no far vision impairment 29.3%; and (d) both far and near vision impairment 9.7%. The prevalence of MCI was lowest in those without far or near vision impairment (13.4%) and highest among those with both far and near vision impairment (22.3%) (**Figure 1**). The association between different combinations of far and near vision impairment and MCI estimated by multivariable logistic regression is shown in **Table 2**. In the overall sample, compared to those without far or near vision impairment, those with near vision impairment but not far vision impairment (OR=1.33; 95%CI=1.16-1.52), and those with both far and near vision impairment (OR=1.70; 95%CI=1.27-2.29) had significantly higher odds for MCI. Only having far vision impairment was not significantly associated with MCI. Similar results were found for analyses stratified by age groups (i.e., 50-64 and ≥ 65 years).

DISCUSSION

Summary of main findings

In this large sample of older adults from six LMICs, it was found that those with near vision impairment, and those with far and near vision impairment had high odds of MCI whereas those with far vision impairment only did not. Findings from the present study support previous literature that has shown an association between vision impairment and cognitive decline [6-14] and add to the literature by reporting for the first time that an association exists between vision impairment and MCI in older adults residing in LMICs, after controlling for important covariates.

Potential pathways

Two potential pathways likely explain the present findings. First, vision impairment may reduce the number and type of daily activities that one can engage in (e.g. exercise, driving motor vehicles, socializing) [35], consequently resulting in reduced brain stimulation and thus MCI [6]. Indeed, older cognitively impaired adults have improved cognitive function after cataract surgery, probably reflecting better vision and enhanced brain activity as sensory stimulation increased [24]. However, it is important to note that the present study did not find an association between far vision impairment only and MCI. This is in line with a previous longitudinal study conducted among Mexican American older adults [24], and may be reflecting the fact that near vision is more important for intellectually stimulating activities, but more studies are necessary to assess whether this finding can be corroborated. Second, it is also possible that vision impairment and MCI are not causally related but that their association is explained by a shared common pathway, such as inflammation [6].

Despite the fact that far vision alone was not significantly associated with MCI, those with far and near vision impairment simultaneously had the highest odds for MCI. Although the reason for this is unclear, it is possible that those who have far and near vision impairment are more likely to have non-refractory visual impairment (e.g., cataracts, diabetic retinopathy, glaucoma), and thus, more severe visual impairment, which can severely impair their ability to engage in intellectually stimulating activities.

Implications

If visual impairment is confirmed to be a risk factor for MCI/dementia in future longitudinal studies, one measure that may aid in the prevention of MCI is to ensure that there is an adequate provision of correctly prescribed spectacles. Unfortunately, this is a public health challenge in LMICs since there is a paucity of human resources for refraction and optical services, lack of access to refraction services in rural areas, and the cost of spectacles. Low-cost approaches to provide affordable glasses with the correct prescription in developing countries are critical. Possible approaches to overcome this may include increasing the use of focometers and self-adjustable glasses, among other modalities [36].

Strengths, limitations, and directions for future research

Clear strengths of the present study include the objective measure of vision and a large nationally representative sample of older adults from six LMICs. It is important to interpret findings from the present study in light of its limitations. First the study is cross-sectional in design and thus the direction of the association is not known. For example, it is possible that those with MCI are less likely to access health care to correct refractive errors or treat cataracts. Future research of a longitudinal design is required. Second, our study is not able to clinically diagnose dementia. Thus, some people with mild dementia may have been included

in our study. However, the present prevalence of MCI was within previously reported figures [37].

Conclusion

In this large sample of older adults from six LMICs, we showed for the first time that vision impairment increases the odds of having MCI, except for having far vision impairment only. Future longitudinal and intervention studies should examine causality and whether improvements in visual acuity can reduce risk for MCI and ultimately, dementia.

- **Compliance with Ethical Standards:** The study followed the Declaration of Helsinki Ethical Principles for Medical Research Involving Human Subjects.
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- **Conflict of Interest:** None.
- **Ethical approval:** Ethical approval was obtained from the WHO Ethical Review Committee and local ethics research review boards.
- **Informed consent:** Written informed consent was obtained from all participants.

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TABLES AND FIGURES

Table 1 Sample characteristics (overall and by different combinations of far and near vision impairment)

Characteristic		Overall	Vision impairment			
			Far (-) Near (-)	Far (+) Near (-)	Far (-) Near (+)	Far (+) Near (+)
Sex	Female	51.2	47.4	59.1	54.6	58.1
	Male	48.8	52.6	40.9	45.4	41.9
Age (years)	Mean (SD)	62.1 (15.6)	60.4 (14.8)	65.7 (17.4)	62.2 (15.2)	67.3 (16.4)
Education (years)	Mean (SD)	6.1 (8.9)	6.4 (9.2)	4.8 (8.8)	5.1 (8.5)	4.6 (8.1)
Wealth	Poorest	17.1	15.4	25.0	16.5	24.7
	Poorer	19.2	18.3	18.7	19.9	22.9
	Middle	19.6	19.3	21.0	18.9	22.9
	Richer	21.4	22.6	17.7	22.0	15.1
	Richest	22.6	24.5	17.5	22.7	14.4
Physical activity	High	50.0	51.7	43.3	50.6	42.4
	Moderate	23.1	23.7	23.7	21.6	24.2
	Low	26.9	24.6	33.0	27.8	33.4
Smoking	Never	57.9	57.5	56.6	58.2	59.9
	Current smoker	35.8	36.0	38.1	35.3	34.2
	Former smoker	6.4	6.5	5.3	6.5	5.9
Obesity	No	90.1	90.3	89.4	89.6	90.6
	Yes	9.9	9.7	10.6	10.4	9.4
Diabetes	No	93.4	93.8	92.9	92.3	95.1
	Yes	6.6	6.2	7.1	7.7	4.9
Stroke	No	97.4	97.7	97.3	97.5	95.1
	Yes	2.6	2.3	2.7	2.5	4.9
Hypertension	No	45.9	46.8	43.6	45.3	43.6
	Yes	54.1	53.2	56.4	54.7	56.4
Depression	No	94.4	95.3	89.3	94.2	92.0
	Yes	5.6	4.7	10.7	5.8	8.0

Abbreviation: SD Standard deviation

Data are % unless otherwise stated.

Table 2 Association of different combinations of far and near vision impairment and covariates with mild cognitive impairment estimated by multivariable logistic regression (overall and by age group)

Characteristic		Overall (Age ≥50 years)		Age 50-64 years		Age ≥65 years	
		OR	95%CI	OR	95%CI	OR	95%CI
Visual impairment	Far (-) Near (-)	1.00		1.00		1.00	
	Far (+) Near (-)	1.15	[0.87,1.53]	0.99	[0.63,1.56]	1.28	[0.87,1.87]
	Far (-) Near (+)	1.33***	[1.16,1.52]	1.40***	[1.19,1.64]	1.29*	[1.01,1.64]
	Far (+) Near (+)	1.70***	[1.27,2.29]	1.56*	[1.08,2.24]	1.80**	[1.24,2.61]
Sex	Male vs. Female	0.82*	[0.69,0.97]	0.69***	[0.56,0.85]	0.96	[0.73,1.26]
Age (years)		1.02***	[1.01,1.03]	1.03**	[1.01,1.05]	1.05***	[1.03,1.06]
Education (years)		0.98*	[0.96,1.00]	0.97**	[0.95,0.99]	0.99	[0.97,1.02]
Wealth	Poorest	1.00		1.00		1.00	
	Poorer	0.94	[0.78,1.12]	0.92	[0.74,1.14]	0.90	[0.67,1.20]
	Middle	1.00	[0.82,1.22]	0.88	[0.69,1.11]	1.11	[0.81,1.53]
	Richer	0.67***	[0.55,0.81]	0.67**	[0.52,0.85]	0.55***	[0.42,0.72]
	Richest	0.40***	[0.33,0.50]	0.32***	[0.25,0.42]	0.50***	[0.36,0.69]
Physical activity	High	1.00		1.00		1.00	
	Moderate	0.74***	[0.65,0.85]	0.78**	[0.66,0.92]	0.77*	[0.63,0.95]
	Low	1.11	[0.96,1.30]	0.84	[0.68,1.03]	1.52***	[1.22,1.89]
Smoking	Never	1.00		1.00		1.00	
	Current smoker	1.21*	[1.03,1.44]	1.24*	[1.03,1.49]	1.28	[0.94,1.74]
	Former smoker	1.21	[0.97,1.51]	1.15	[0.86,1.55]	1.31	[0.93,1.84]
Obesity	Yes vs. No	1.41**	[1.12,1.78]	1.62***	[1.22,2.15]	1.22	[0.85,1.75]
Diabetes	Yes vs. No	1.04	[0.82,1.31]	1.31	[0.93,1.85]	0.86	[0.65,1.14]
Stroke	Yes vs. No	1.89***	[1.43,2.50]	2.34***	[1.55,3.54]	1.56*	[1.04,2.32]
Hypertension	Yes vs. No	1.07	[0.96,1.19]	1.03	[0.91,1.17]	1.14	[0.95,1.37]
Depression	Yes vs. No	1.01	[0.76,1.34]	0.98	[0.69,1.39]	0.97	[0.63,1.50]

Abbreviation: OR Odds ratio; CI Confidence interval

Models are adjusted for all variables in the Table and country.

* p<0.05, ** p<0.01, *** p<0.001

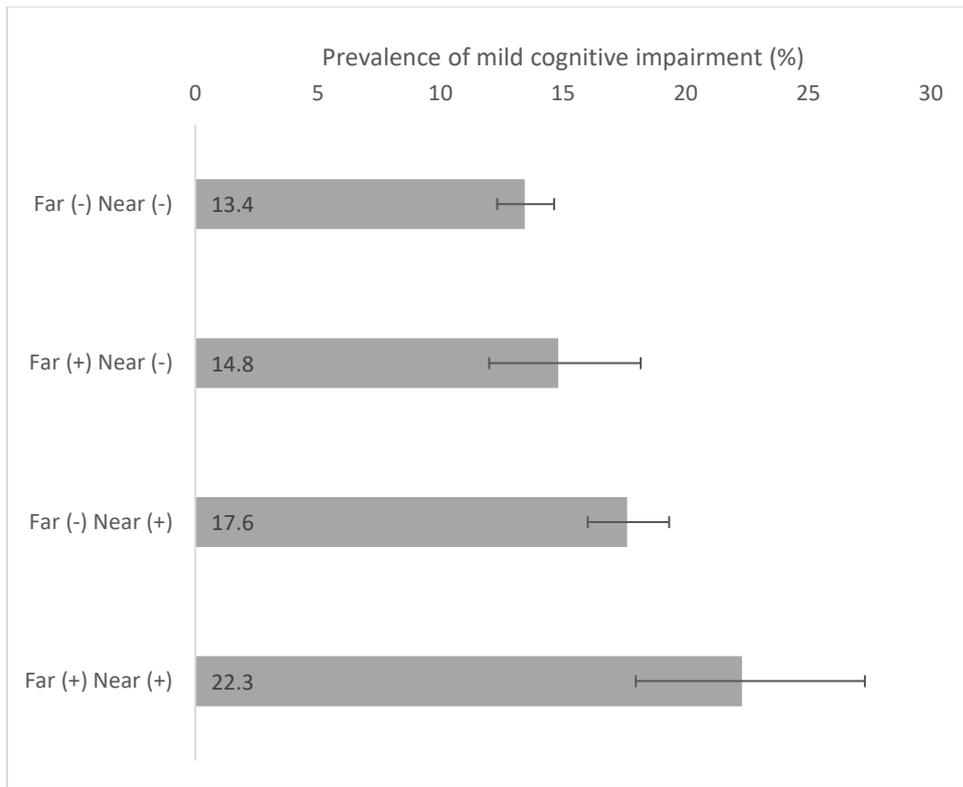


Figure 1 Prevalence of mild cognitive impairment by different combinations of far and near vision impairment. Bars denote 95% confidence interval.