

Epidemiology of Age-Related Macular Degeneration among the Elderly Population in Thailand

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Objective: To estimate the prevalence and associated factors of age-related macular degeneration (AMD) in Thailand.

Material and Method: This cross-sectional survey was undertaken in 2010. Five provinces were selected and people aged 50 years and over were invited for eye examination. Demographic and health behaviors and data from eye examination equipment were registered. Ophthalmologists graded AMD as early or late based on fundus color photograph and image from optical coherence tomography. Logistic regressions were analyzed to establish association factors for AMD.

Results: Of the 7,043 participants, AMD was found in 862 people (12.2%), with more than half (53.1%) found in both eyes. Most cases (94.3%) were early dry, 1.8% early wet, 3.4% late dry, and 0.7% late wet AMD. Factors positively associated with AMD were age (OR 1.03, 95% CI 1.02-1.04), diabetes mellitus (OR 1.20, 95% CI 1.03-1.39), and consumption of yellow vegetable (OR 2.32, 95% CI 1.23-4.39). Factors that conversely associated with AMD were consumption of green vegetable (OR 0.51, 95% CI 0.33-0.79), physical exercise (OR 0.67, 95% CI 0.51-0.87), high blood pressure (OR 0.75, 95% CI 0.63-0.89), and heavy drinking habit (OR 0.45, 95% CI 0.26-0.75).

Conclusion: The prevalence of AMD in Thai population age 50 and over was 12.2%. More than half (53.1%) of the cases were found in both eyes, but few at severe stages. The present study confirmed age and DM as positive associated factors, and green vegetable, exercise as negative associated factors. Further research should investigate the effects of hypertension, yellow vegetable, and alcohol drinking on AMD.

Keywords: Age-related macular degeneration (AMD), Epidemiology, Associated factor, Thailand

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Age-Related Macular Degeneration (AMD) is a leading cause of irreversible blindness in people aged 50 years and older with limited effective cure⁽¹⁾. More than 30 million people worldwide had severe visual loss leading to low quality of life, greater anxiety and depression, and more frequent falls and fractures due to AMD⁽²⁾. The prevalence of AMD rises as age increases; therefore, as our world population is advancing to ageing societies, more people will be diagnosed as AMD.

Epidemiological studies on AMD in the elderly population had been carried out and developed, adopting improved methodologies over years⁽³⁾. Studies

in USA, Europe, and Australia usually focus on larger Caucasian population group⁽⁴⁻⁴⁰⁾, while other existing studies in Asia such as Japan⁽⁴¹⁾, China⁽⁴²⁾, Taiwan⁽⁴³⁾, India⁽⁴⁴⁾, and Singapore⁽⁴⁵⁾ focus on Asian population. The population in these countries is under different circumstances from that in Thailand (e.g., race, climate, food, education, life style, and genetic predisposition). Therefore, previous studies may not be the most accurate reference to be applied for Thailand. At present, literature review reveals that no epidemiological study of AMD in the elderly population has been conducted in Thailand. This paper is to evaluate prevalence of AMD and associated factors for people aged 50 years and older in Thailand.

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Material and Method

The present study was a cross-sectional survey carried out by setting up of a mobile examination

survey unit which registered sample groups' data were taken as follows: (i) visual acuity using logMAR (logarithm of the minimum angle resolution) chart, (ii) refraction using Nidek ARK (Auto Ref/Keratometer) 510A, (iii) ocular tension using Nidek NT (Non-contact Tonometer) 2000, (iv) lens status and cataract grading using digital slit lamp microscope CSO (Costruzione Strumenti Oftalmici S.r.l.)-SL990, (v) 30 degree posterior pole fundus photo using digital color camera Nidek-AFC (Auto Fundus Camera) 230, and (vi) macula using optical coherence tomography (OCT) (Optovue-RTVue 100). The fundus readers were provided with fundus photos and OCT scanned images.

Participants

A random selection of one province in each region was made (Phayao for the north, Phitsanulok for the central, Khon Kaen for the northeastern, Chumphon for the south, and Nonthaburi for the capital suburban areas). Based on calculation of sample size of previous papers, the sample size calculation assumed that 6,000 people are required to detect a prevalence of AMD of $2\% \pm 0.5\%$ at a 95% confidence level. About 2,000 participants in each representative area were invited to participate in ophthalmic examination; the total expected number of participants was (2,000 x 5 regions) 10,000. Field data collection was conducted between December 2009 and October 2010. This research was approved by the Research Ethics Committee of Naresuan University (No. 5202040040, December 2009) in recognition of the Helsinki Declaration on research in human subject.

The criteria for participants were individuals of 50 years and over. Five trained research assistants supervised by a nurse practitioner conducted an interview with closed-ended questions to obtain demographic data (age, sex), health behaviors relevant to AMD (smoking, alcohol intake, consumption of green and yellow vegetables by food frequency questionnaire, physical exercise), and underlying diseases (diabetes and high blood pressure based on medical treatment history). Body measurements were taken before going for eye examinations.

Criteria for AMD diagnosis

Color fundus photographs and 3D (three-dimensional) scanned OCT images, which were recorded on compact disks in a JPG file format, were forwarded to five ophthalmologists for evaluation without giving previous patients' histories or physical

examinations; some normal and abnormal pictures were randomly inserted to check for agreement among ophthalmologists. Evaluation from color fundus photograph and 3D scanned OCT based on lesion size, position, and intra-retinal/sub-retinal depth of each eye was identified as (i) no AMD, or (ii) early AMD, or (iii) late AMD.

Early AMD or dry AMD was diagnosed based on criteria of the International ARM (age-related maculopathy) Epidemiological Study Group⁽⁴⁶⁾. This included soft drusen bigger than 63 micron, area of increased pigment or hyperpigmentation in outer retina or choroid associated with drusen, areas of depigmentation or hypopigmentation of the retinal pigment endothelial (RPE) most often more sharply demarcated than drusen, but without any visibility of choroidal vessels, associated with drusen.

Late AMD or advanced AMD was diagnosed based on the following criteria: non-exudative AMD (soft drusen and geographic atrophy of RPE), exudative or neovascular AMD by RPE detachment or choroidal neovascularization (CNV), with the following clinical CNV characteristics; subretinal fluid, or subretinal pigment epithelial blood, subretinal or intraretinal lipid, subretinal pigment ring, irregular elevation of RPE, subretinal gray-white lesion, cystoid macular edema, sea fan pattern of subretinal small vessels and disciform scar⁽⁴⁷⁾.

Statistical analysis

Descriptive, inferential statistics and logistic regressions were analyzed by R-studio statistical package⁽⁴⁸⁾.

Results

The number of participants in provincial representative areas were, central region (1,679 persons), northern region (2,096 persons), northeastern region (1,842 persons), southern region (2,256 persons), and capital and its suburban areas (958 persons). The AMD diagnosis for the present study was evaluated using 16,131 color fundus photographs and OCT scanned images of 8,831 participants, 1,676 (10.4%) of which were undetermined or did not have picture. The latter could be explained by ocular media opacity, which impeded color fundus photographs or OCT scanning. After validation and verification of input data, 7,043 participants were included in the study, of which 1,998 (28.4%) were male, and 5,045 (71.6%) were female. The average age was 61.9 (SD 8.3, range 50-99) years.

Results were presented into (i) behaviors and other underlying diseases as associated factors for AMD in order to identify, (ii) prevalence and associated factors to AMD.

Health behaviors of participants

Smoking history was very different between male and female participants. However, the current smokers and ex-smokers reported about the same amount of (8 to 14) cigarettes smoked per day for both male and female. Hence, both were classified as the ever-smoke (22% of total were the ever-smoke). More than half (52%) of male were the ever-smoke and 7% of female were the ever-smoke.

The responses on alcohol consumption allowed calculation of gram alcohol consumed. In contrast, gram alcohol consumed was very different between current drinkers and ex-drinkers. Based on World Health Organization's criteria on drinking problem, the cut-off point at 60 grams alcohol per week was adopted to categorize participants into heavy drinkers (4% of total) and non-heavy drinkers (96%). About 10% of male and 2% of female participants were classified as heavy drinkers.

Consumption of green and yellow vegetables was hypothesized to be preventive factor for AMD. Food frequency questionnaire provided data on the number of bowls consumed. The cut-off point of 21 bowls was used to categorize whether the participants consumed antioxidant vegetables adequately. Only 5% of participants consumed green vegetable adequately and only 1% consumed yellow vegetables adequately.

About 80% of male participants and 75% of female participants reported having physical exercise. However, if a cut-off point of exercising 60 minutes or more per week was used for adequate exercise, only 10% of participants had adequate exercise. Body measurements were taken, 7% of participants were obese based on the body mass index higher than 30.

Prevalence of AMD

Based on the number of AMD positive patients and the number of patients with readable fundus and OCT images, the prevalence rate of AMD of Thailand's elderly population from the studied samples was 12.2% (while the figure based on number of images was approximately 9.5% because many patients had only unilateral AMD).

Among 862 people who suffered AMD, 53.1% had bilateral AMD, and 46.9% had unilateral AMD. The findings indicated the proportions of participants at different AMD stages as follows: early dry AMD 94.3%, early wet AMD 1.8%, late dry AMD 3.4%, and late wet AMD 0.7%.

An interesting observation was that the majority of AMD stage in every region was early dry AMD (range 88.3-96.7%). However, a statistically significant difference was found in the central and the northeastern areas, where there were higher proportion of early wet AMD.

Associated factor for AMD

Potential associated factors with AMD were selected for modeling with multivariate logistics analysis as listed in Table 1. Among 7,043 participants

Table 1. Prevalence of associated factors for elderly with and without age-related macular degeneration (AMD)

	AMD	No AMD	<i>p</i> -value
No.	862	6,181	
Age, mean ± SD*	64.06±8.45	61.59±8.24	<0.01
Male (%)	32	28	0.02
Ever smoke (%)	24	21	<0.01
Heavy drink (%)	2	4	<0.01
Eat green vegetable (%)	4	6	0.01
Eat yellow vegetable (%)	2	1	0.17
Adequate physical exercise (%)	7	10	<0.01
Diabetes mellitus (%)	47	42	<0.01
Hypertension (%)	23	29	<0.01
Body mass index (kg/m ²), mean ± SD*	23.43±4.20	23.95±4.00	<0.01

* *p* from independent t-test; others from Chi-square test

Table 2. Odds ratio from logistic regression analysis for age-related macular degeneration (AMD)

	Adjusted odds ratio	95% confidence interval	<i>p</i> -value (LR test)
Age	1.03	1.02, 1.04	<0.01
Male	1.15	0.96, 1.39	0.14
Ever smoke	1.12	0.92, 1.38	0.27
Heavy drink	0.45	0.26, 0.75	<0.01
Green vegetable	0.51	0.33, 0.79	<0.01
Yellow vegetable	2.32	1.23, 4.39	0.01
Physical exercise	0.67	0.51, 0.87	<0.01
Diabetes	1.20	1.03, 1.39	0.02
High blood pressure	0.75	0.63, 0.89	<0.01
Obesity	1.05	0.78, 1.43	0.73

LR = log-likelihood ratio; *p* = probability
Log-likelihood = -2,535.8, number of observations = 6,960

with required variables, the average age for non AMD group was 62 years, 28% were male, 21% were ever-smokers, 4% were heavy drinkers, 4% consumed sufficient amount of necessary daily intake of green vegetable, 1% yellow vegetable, 10% had adequate physical exercise, and 42% were diabetic.

An odds ratio for selected associated factors for AMD (Table 2), showed that among 6,960 participants, the variables that had a statistically significant positive association to AMD were age, diabetes, and eating more yellow vegetable. An increase of age by each year increased the odds of having AMD by 3%. Diabetes increased the odds of having AMD 1.20 times compared to those who were non-diabetic (95% CI 1.03-1.39). Eating yellow vegetable increased the odds of AMD 2.32 times higher (95% CI 1.23-4.39). While protective factors were (i) alcohol consumption (OR 0.45, 95% CI 0.26-0.75), (ii) consumption of green vegetable (OR 0.51, 95% CI 0.33-0.79), (iii) physical exercise (OR 0.67, 95% CI 0.51-0.87), and (iv) high blood pressure (OR 0.75, 95% CI 0.63-0.89).

Discussion

Researchers decided to apply a cross-sectional approach to the study as the entry point for further subsequent clinical research. The cross-sectional nature may limit robust conclusions, but this epidemiological prevalence study was limited to the very gradual and slow development of AMD, which requires 5 to 10 years for prospective incidence studies^(11,14).

Strengths of the present study are (i) the study was the biggest community survey on prevalence of AMD in Asia, and (ii) its results could be used as a reference for national health planning or for further research in Thailand. The sampled populations were mostly rural people as the majority of population in Thailand lived in rural areas. Weaknesses confined to the selection of the participants. Some rural areas attracted more participants than expected because the mobile units were stationed at the community hospitals. The central site hardly recruited participants because of the urban setting and the political instability at the time of community survey. The recruited samples had more female (72%), diabetes (42%), or hypertension (28%). This may be because women are usually more health oriented than men and the clinical guidelines of these two diseases warrant patients to have annual eye examination. Applying stricter criteria of health behaviors, 10% of cases in the present study exercised adequately compared to 20% of total in the national elderly survey⁽⁴⁹⁾, 4% were problem drinker compared to 18%⁽⁴⁹⁾, 5% having adequate green vegetable, and only 1% having adequate yellow vegetable compared to 98% reported having fruits and vegetables⁽⁴⁹⁾. The AMD prevalence of 12.2% in the present study may have been underestimated because the prevalence in male was slightly higher than in female (13.7% vs. 11.7%, *p* = 0.01). On the other hand, it may have been overestimated because of high proportion of sample population were diabetic. The strict measurement of health behaviors, especially smoking and drinking, which are gender-related behaviors, should strengthen the conclusion of odds ratios as risk or protective factors.

The present study employed OCT scanned image to help in AMD diagnosis by allowing clearer visualization of retinal layers. This facilitates the process of AMD diagnosis in an accurate manner without relying on 3D photographing that required multiple different view technique. Five ophthalmologists (retina specialists) independently interpreted the images from each region with acceptable results among tracer pictures randomly inserted to check agreement. Furthermore, 95% of AMD cases were mild stages, the visual acuity (by logMAR) of AMD and non-AMD cases were not significantly different.

Only 10% of the total color fundus photographs and OCT scanned images were reported as “undetermined” by the readers because of no or not clear pictures. This could be due to dense cataract, vitreous hemorrhage, corneal opacity, advanced

pterygium, or eye blinking. Compared to Shihpai study in Taiwan, it was found that 46% of 1,361 participants' image data were ungradable although only 4.3% of them were elderly and suffered dense cataract⁽⁴³⁾.

The multivariate analysis showed that age and diabetes were significant associated factors for AMD. A year older was putting an individual a 3% increase chance of having AMD. Diabetes contributed to a 20% increase chance of having AMD. Male was not a significant associated factor different from Japan study may be because under-representation of male in the present study. As age and sex are non-modifiable factors, it is thus important to look for modifiable independent factors that patients can learn to adopt as new habits in attempts to help them prevent progression of AMD.

Exercise and green vegetable consumption were significant preventive factors for AMD. Preventive measures for diabetes patients such as physical exercise and healthy food consumption should be advocated to help prevent AMD⁽¹⁾. The finding of green vegetable intake adds up to result from the Age-Related Eye Disease Study (AREDS) suggesting that lutein, which is found in green vegetable, can help prevent early stage AMD into wet AMD. Another previous study showed that lutein tends to reduce in macula as age increases. Therefore, it is useful to explore whatever sources of lutein, either from vegetable and animals are more effective in protecting AMD as researchers in Thailand discovered that silkworm cocoon has higher lutein than high-lutein green vegetable (kale, parsley, spinach, and beans)^(50,51). Given the abundance of cocoons in Thailand, there is a potential for Thailand to develop lutein extraction method from cocoons⁽⁵²⁾, which could be used as measures to prevent AMD and development of wet AMD from early AMD. The positive association of yellow vegetable was also skeptical. It raises cautious interpretation as the cross-sectional survey cannot conclude cause and effect.

Alcohol is considered a controversial risk factor for AMD⁽¹⁴⁾. The study tried to find out relevance between pattern of alcohol consumption (according to World Health Organization's criteria, to define heavy drinker, light drinker, and non-drinker using collected data on amount, frequency, and type of alcohol consumed) and prevalence of AMD. While the odds ratio of heavy drinking was a protective factor, nonetheless cautions from cross-sectional study limited confidence conclusion. Hypertension was shown by the study result to be a protective factor. This contradicts with other study and should be repeated or

clinical study in animals to find out mechanism that make hypertension a protective factor may be required.

What is already known on this topic?

Age-related macular degeneration is the condition found in elderly population. There were many cross-sectional studies to estimate the prevalence, and cohort studies to estimate incidence of the problem in developed countries mostly in Caucasian populations. The magnitude of the problem varied from 1 to 12%. The studies in Asia also gave high variation ranging from 3 to 12%. Known risk factors were age, diabetes and known protective factors were physical exercise, eating green vegetable. Factors with controversial effects included gender and drinking alcohol.

What this study adds?

The prevalence of AMD in population aged 50 and above in Thailand was about 12%. About half of cases had AMD in both eyes, and most cases were at early stage.

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Contributions of authors

All authors involved in the planning and designing the research project. Sutheerawatananonda M and Khotcharat R sought funding and managing the expenditure. Khotcharat R, Patikulsilas D, Hanutsaha P, Khiaochoam U, and Ratanapakorn T interpreted the retinal images. Khotcharat R and Pannarunothai S handled data analysis and drafting the manuscript. All authors read, commented, and approved the final manuscript.

Potential conflicts of interest

The present study was funded by the Agricultural Research Development Agency. All authors declared no conflict of interest.

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ระบาดวิทยาของโรคจอประสาทตาเสื่อมในผู้สูงอายุของประเทศไทย

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วัตถุประสงค์: เพื่อประมาณค่าความชุกและปัจจัยที่สัมพันธ์กับโรคจอประสาทตาเสื่อมในผู้สูงอายุของประเทศไทย

วัสดุและวิธีการ: ทำการศึกษาเชิงสำรวจภาคตัดขวางใน พ.ศ. 2553 สุ่มเลือกจังหวัด 5 จังหวัด ใน 5 เขต ของประเทศไทย โดยเชิญประชากรผู้มีอายุตั้งแต่ 50 ปีขึ้นไป เข้ารับการตรวจตา ทำการบันทึกข้อมูลประชากร พฤติกรรมสุขภาพ และข้อมูลจากเครื่องมือตรวจตา จักษุแพทย์อ่านภาพถ่ายสีจากเครื่องมือตรวจจอประสาทตา และภาพสแกนจอประสาทตาจากเครื่อง *optical coherence tomography* เพื่อวินิจฉัยว่าเป็นโรคจอประสาทตาเสื่อมชนิดแรกเริ่มหรือชนิดรุนแรง ใช้สมการลอจิสติกหลายตัวแปรเพื่อวิเคราะห์ปัจจัยเสี่ยงของโรคจอประสาทตาเสื่อม

ผลการศึกษา: จากกลุ่มตัวอย่าง 7,043 คน พบโรคจอประสาทตาเสื่อม 862 คน (12.2%) โดยจำนวนมากกว่าครึ่งหนึ่ง (53.1% ของผู้ที่เป็นโรค) พบโรคทั้งสองตา ผู้ที่เป็นโรคส่วนใหญ่ (94.3%) เป็นชนิดแรกเริ่ม อีกร 1.8% เป็นชนิดแรกเริ่มแบบ *wet* 3.4% เป็นชนิดรุนแรงแบบ *dry* และ 0.7% เป็นชนิดรุนแรงแบบ *late wet* ปัจจัยที่สัมพันธ์กับโรคจอประสาทตาเสื่อมมากขึ้นได้แก่ อายุ (*OR* 1.03, 95% *CI* 1.02-1.04) เบาหวาน (*OR* 1.20, 95% *CI* 1.03-1.39) และการกินผักสีเหลือง (*OR* 2.32, 95% *CI* 1.23-4.39) ปัจจัยที่พบว่าโรคจอประสาทตาเสื่อมลดลง ได้แก่ การกินผักสีเขียว (*OR* 0.51, 95% *CI* 0.33-0.79) การออกกำลังกาย (*OR* 0.67, 95% *CI* 0.51-0.87) ความดันเลือดสูง (*OR* 0.75, 95% *CI* 0.63-0.89) และการดื่มแอลกอฮอล์ (*OR* 0.45, 95% *CI* 0.26-0.75)

สรุป: ความชุกของโรคจอประสาทตาเสื่อมในกลุ่มประชากรอายุ 50 ปีขึ้นไป คือ 12.2% ในจำนวนนี้มากกว่าครึ่งหนึ่ง (53.1%) พบในตาสองข้าง แต่พบระยะรุนแรงไม่มากนัก การศึกษาครั้งนี้ยืนยันว่าปัจจัยที่สัมพันธ์ในทางบวกได้แก่ อายุ และเบาหวาน ปัจจัยที่สัมพันธ์ในทางตรงข้าม ได้แก่ การกินผักสีเขียวและการออกกำลังกาย ควรศึกษาต่อไปถึงผลที่แน่ชัดของความดันเลือดสูง การกินผักสีเหลือง และการดื่มแอลกอฮอล์ ต่อโรคจอประสาทตาเสื่อม
