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**Original Article**

# Vitamin E and Age-related Macular Degeneration in a Randomized Testing of Women in Rewa M.P

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## ABSTRACT

Age related macular degeneration, as the term implies, affects adults and accounts for about half of all vision impairment or blind registrations in the developed world. Its prevalence is increasing with the demographic shift towards an ageing society. Recent evidence from large scale population based epidemiological studies confirms that it is also a major cause of sight loss in the developing world, in countries such as India. This study found that certain nutritional supplements could help some people who have a lot of drusen. These supplements may also help people who have lost a lot of vision from AMD.

**Key words**: Macular Degeneration, Impairment, Epidemiological studies, Drusen

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## INTRODUCTION

Age-related macular degeneration (AMD) is a continual condition of the eye that involves pathological changes in the central region of the retina responsible for high-resolution visual acuity. It is the leading reason of severe irreversible visual injury. Mainly of the vision loss in AMD is because of the advanced form of the disease, either geographic atrophy or neovascular AMD, (1)

Treatment alternatives include laser photocoagulation, photodynamic therapy, and anti-vascular endothelial growth factor therapy, although these options are costly and are limited to a marginal of persons with late-stage, neovascular AMD (2). For these causes, identification of means to prevent AMD start and progression is of particular clinical and public health significance (3).

Though, the new development of anti-vascular endothelial growth factor (VEGF) agents has revolutionized therapy for this situation, and vision loss can now be avoided in more 90% of patients with neovascular AMD, with about one-third of patients experiencing significant improvements in visual acuity (4). Risk factors related with AMD consist of sex, iris colour, heredity, cardiovascular health, nutrient status, body mass index, age and smoking. Foods have a lot of nutrients that could interact on the danger for multi-factorial diseases for example AMD (5).

It has been advised that the condition of AMD may advance in people fed vitamins, antioxidants (carotenoids, vitamins C and E) and minerals (selenium and zinc) affluent diets (6). Age-Related Eye Disease learn (AREDS) suggested that to take an antioxidant supplementation (15 mg β-carotene, 500 mg vitamin C, 400 IU vitamin E and 80 mg zinc plus 2 mg copper) is successful in preventing the increase of advanced AMD by 25%, and AREDS-2 contained lutein, zeaxanthin and omega-3 fatty acids in the study of late AMD progression (7).

**Symptoms of age-related macular degeneration can include:**

A-Blurred or "fuzzy" vision.
B-Straight lines, such as sentences on a page, appearing wavy or distorted.
C-Blurry areas on a printed page.
D-Difficulty reading or seeing details in low light levels.
E-Extra sensitivity to glare.

**Risk factors for the development of AMD:** There have been a number of studies examining hazard factors for the growth of AMD. Though, there have been Clashing outcomes for several risk causes in diverse study populations (8). The only regularly positive associations are smoking and a genetic factor

**Smoking:** There is a powerful epidemiological relationship between smoking and the progress of highly developed AMD. Recent smokers have an enhanced hazard of increasing dry and neovascular AMD relative to non-smokers with an odds ratio. Cigarette smoking confers an amplified risk of increasing AMD in adding to known genetic associations (9). The advantage of smoking cessation to prevent second eye disease has not been estimated.

**Genetics:** Both Beaver Dam and Rotterdam studies show an enhanced risk of AMD enlarging in relatives of affected individuals. The OR for a sibling of an affected individual Increasing neovascular AMD later than 5-year follow-up in the Beaver Dam 10.3. In the Rotterdam study, there was an OR of 6.6 for signs of premature AMD in the progeny of affected individuals when compared with progeny of non-affected individuals (10).

Three studies have discovered an relationship between a polymorphism in complement factor *H* (a control protein involved in the regulation of the alternative pathway of the complement cascade) and AMD (11).The relative risk of Increasing AMD with the common polymorphism T → C substitution in exon 9 of the complement factor *H* gene is about 2.3–2.7 for heterozygotes and 3.5–7.4 for homozygotes (12). This discovery has been subsequently supported by discoveries in other population groups (12) .A new member of the complement system, factor B, has also been Proven to have both elevate-risk and protective variants linked with the progress of AMD (13) . A third gene (LOC387715) discovered on chromosome 10, whose gene product has a function however to be fully elucidated, has an independent effect on AMD approximately as strong as that of the Factor H gene (14). Interestingly, both the elevated-risk variants of Factor H and LOC387715 interact with cigarette smoking to confer an amplified risk of developing AMD than each factor alone (9) . .These exciting finding should lead to Progressed understanding of the pathogenesis of AMD and the development of novel therapies.

## SUBJECTS AND METHODS

Selection of participants, recruitment and approval one hundred seven female patients diagnosed of wet age-related macular degeneration, living in the Rewa M.P were selected. This study was performed according to the guidelines laid down in the Declaration of Helsinki and all procedures

involving human subjects/patients were approved. Written informed consent was acquired from all subjects .Wet AMD analysis Wet AMD was diagnosed from a baseline ophthalmic examination. Visual acuity (Snellen chart), slitlamp examination, intraocular pressure, fundus photographs (Canon 60 CFUD, Japan), fluorescein and indocyanine green angiography (HRA, Heidelberg Engineering), and optical coherence tomography, OCT (CirrusTM HD-OCT, Carl Zeiss Meditec, Oberkochen, Germany) were taken. Wet AMD was described by the presence of a subretinal neovascular membrane. Choroidal neovascularitation (CNV) was classified by location into 3 groups: subfoveal, juxta-foveal and extrafoveal, by type into 4: occult, classic, retinal angiomatous proliferation (RAP) and polypoidal choroidal vasculopathy (PCV). Ophthalmic characteristics of participants are summarized in table -1.

**Questionnaires:** During the visit to the hospital, the participants underwent a standardized interview with a trained dietitian based on an overall questionnaire incorpo-rating socio-demographic status and lifestyle factors, two 24-hour recalls and a validated semi-quantitative food frequency questionnaire (15). Socio-demographic variables contained place of residence, place and date of birth, familiar family origin, sex, marital status, home-mates, work situation, and time to residence in Rewa M.P . Information on height, weight, history of cigarette smoking, history of alcohol use, blood pressure level, cholesterol level, history of diabetes mellitus, history of multivitamin utilize, parental history of myocardial infarction, postmenopausal hormone use, and history of an eye exam in the last 2 years. They also offered information about a personal history of AMD.

**Study Design:** The Women's Health Study (WHS) was a randomized, double-blind, placebo-controlled, 2 × 2 factorial trial designed to test whether vitamin E (600 IU ∀-tocopherol [Natural Source Vitamin E Association, Washington, DC] every other day) and low-dose aspirin (Bayer Healthcare, Leverkusen, Germany) (100 mg every other day) could reduce rates of cardiovascular disease and cancer among 107 apparently-healthy female health professionals aged 45 years or older (16). Final results for vitamin E indicated no overall benefit for major cardiovascular events, cancer, or total mortality, but a significant decrease for cardiovascular mortality and venous thromboembolism (17). A third component, beta carotene, was terminated early in January 2018 after a median treatment duration of 2.1 years (18).

**Ascertainment and definition of endpoints:** Women who reported a previous diagnosis of AMD at baseline were excluded. On annual questionnaires, women were asked about new diagnoses in the past year together with “macular degeneration right eye" and “macular degeneration left eye". Women who responded affirmatively were asked to provide the month and year of the diagnosis and to complete a consent form granting permission to study medical records pertaining to the diagnosis. Eye doctors were contacted by mail and asked to complete an AMD questionnaire which requested information on the date of initial diagnosis, the best-corrected visual acuity at the time of diagnosis, and the date when best-corrected visual acuity reached 20/30 or bad (if different from the date of initial diagnosis). The questionnaire also asked about signs of AMD observed (drusen, retinal pigment epithelium [RPE] hypo/hyperpigmentation, geographic atrophy, RPE detachment, subretinal neovascular membrane, or disciform scar) when visual acuity was first noted to be 20/30 or worse, and the date when exudative neovascular disease, if attendance, was first noted (defined by presence of RPE detachment, subretinal neovascular membrane, or disciform scar). If ocular abnormalities were noted that could explain or contribute to vision loss, the eye doctor was enquired to indicate whether the AMD, by itself, was important enough to cause the best-corrected visual acuity to be reduced to 20/30 or worse. Eye doctors could also give the requested information by supplying photocopies of the related medical records. Medical record data were achieved for 85.2% of participants reporting AMD. The primary study endpoint was visually-significant AMD defined as a self-report confirmed by medical record evidence of an initial diagnosis made after randomization but before January 3, 2018, and with best-corrected visual acuity reduced to 20/30 or worse attributable to AMD. Two secondary endpoints were also distinct: advanced AMD, comprised of those cases of exudative neovascular AMD plus cases of geographic atrophy; and AMD with or without vision loss, comprised of all incident cases confirmed in medical record review.

**Data analysis:** We used Cox proportional hazards regression models to estimate the relative risks (RRs) and 95% confidence intervals (95% CIs) of AMD among those assigned to receive vitamin E compared with those assigned to obtain placebo after adjustment for age (years) at baseline and randomized aspirin and beta carotene assignments (19). Statistical significance was put at $P<.05$ using 2-sided tests. Models were also fit individually within three predefined age groups; 45–54, 55–64, 65 years. The proportionality hypothesis was tested by with an interaction term of vitamin E with the logarithm of time in the Cox models. We performed subgroup study by categories of baseline variables that are possible risk factors for AMD.

We looked possible effect modification by Utilizing interaction terms between subgroup indicators and vitamin E assignment, and we tested for trend when subgroup categories were ordinal. Individuals, rather than eyes, were the unit of analysis because eyes were not examined independently, and participants were classified as reporting to the status of the bad eye as explained by disease severity. When the bad eye was excluded for the cause that of visual acuity loss attributed to other ocular abnormalities, the fellow eye was considered for classification.

**Statistics:** Analyses were performed with Statistical Package for the Prism version 2.0. All tests were stratified by age. Significant differences in prevalence were calculated by means of $\chi 2$. Differences between groups means were tested using ANOVA. The level was established for P values $< 0.05$.

**Observation:** The present study entitled - Vitamin E and Age-related Macular Degeneration in a Randomized Testing of Women in Rewa M.P was undertaken in the department of Biochemistry APS University REWA (M.P) .From June 2017 to December 2018.Study samples, including 107 ARMD patients presented inward .Following were the observations.

**Table 1:** Ophthalmic characteristics of women patients.

| | Patients | n = 107 |
|---|---|---|
| | CNV active eye: | N=60 |
| 1 | Right eye | N=16 (26.6%) |
| 2 | Left eye | N=30(50%) |
| 3 | Both eyes | N=14(23.3%) |
| | CNV TYPE | |
| 1 | Classical (or predominant classical membrane) | N=12(20%) |
| 2 | Occult (or predominant occult membrane) | N=20(33.3%) |
| 3 | Retinal Angiomatous Proliferation | N=17(28.3%) |
| 4 | Polypoidal Choroidal Vasculopathy | N=11(18.3%) |
| | CNV LOCATION | |
| 1 | Subfoveal | N=19 (31.6%) |
| 2 | Juxtafoveal | N=16(26.6%) |
| 3 | Extrafoveal | N=25(41.6%) |

CNV: Choroidal neovascularitation.

Table-2 Baseline Characteristics in Randomized Vitamin E and Placebo Treatment Groups in the Women's Health Study.

| Characteristic | | VITAMIN E | | PLACEBO | |
|---|---|---|---|---|---|
| | | Number | Percentage% | Number | Percentage% |
| | Age ,Year | | | | |
| 1 | 45-54 | 13 | 40.6% | 20 | 26.6% |
| 2 | 55-64 | 8 | 25% | 27 | 36% |
| 3 | 65 | 11 | 34.3% | 48 | 64% |
| | Smoking | | | | |
| 1 | Current | 9 | 28.1% | 30 | 40% |
| 2 | Past | 23 | 71.8% | 45 | 60% |
| | Alcohol use | | | | |
| 1 | <1WK | 14 | 43.75% | 35 | 46.6% |
| 2 | >1WK | 18 | 56.2% | 40 | 53.3% |
| | BMI | | | | |
| 1 | <25 | 9 | 28.1% | 19 | 25.3% |
| 2 | 25-29 | 11 | 34.3% | 27 | 36% |
| 3 | >30 | 12 | 37.5% | 29 | 38% |
| | Hypertension | | | | |
| 1 | Yes | 18 | 56.25% | 56 | 74..6% |
| 2 | No | 14 | 43.75% | 19 | 25.3% |
| | Diabetes Mellitus | | | | |

| | | | | | |
|---|---|---|---|---|---|
| 1 | Yes | 15 | 46.8% | 33 | 44% |
| 2 | No | 17 | 53.1% | 42 | 56% |
| | Multivitamin use | | | | |
| 1 | current | 20 | 62.5% | 50 | 66.6% |
| 2 | Past/Never | 12 | 37.5% | 25 | 33.3% |
| | Eye Examination | | | | |
| 1 | Yes | 19 | 59.3% | 40 | 53.3% |
| 2 | No | 13 | 40.6% | 35 | 46.6% |
| | Parental History of MI before 60 yrs of age | | | | |
| 1 | Yes | 11 | 34.3% | 28 | 37.3% |
| 2 | No | 12 | 37.5% | 47 | 62.6% |

Data are given as the percentage of patients, Hypertension was defined as a systolic blood pressure of at least 140 mm Hg, a diastolic blood pressure of at least 90 mm Hg, or self-reported physician-diagnosed hypertension.

Graph -1 Estimation of energy daily intake of women patients.

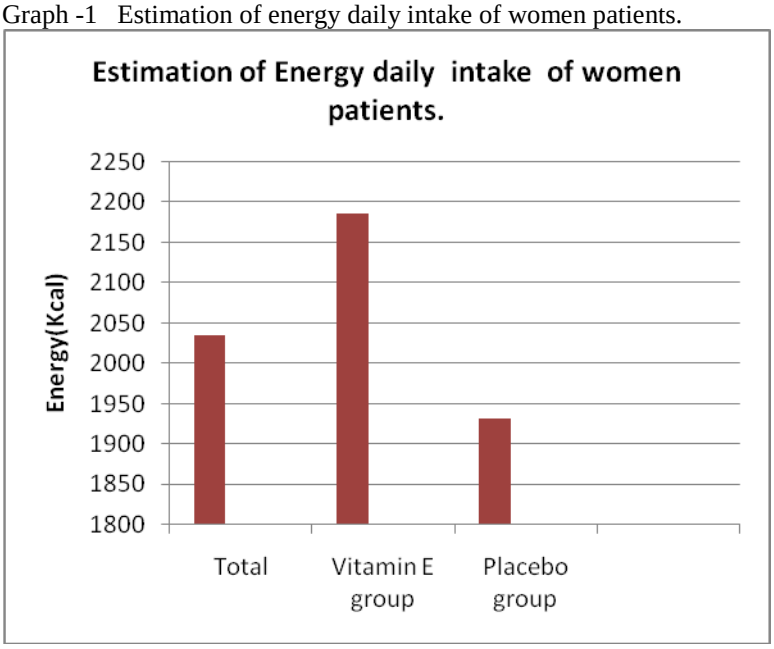



Table-3 Estimation of Macronutrients and Micronutrients daily intake of women patients.

| S.No | Nutrients | Total | | Vitamin E | | Placebo | | P value summary |
|---|---|---|---|---|---|---|---|---|
| | | Mean | S.E | Mean | S.E | Mean | S.E | |
| | Macronutrients | | | | | | | |
| 1 | Carbohydrate (%) | 47.6 | 1.2 | 46.4 | 1.5 | 50.3 | 1.2 | ns |
| 2 | Protein (%) | 15.4 | 0.6 | 16.3 | 0.8 | 15.2 | 0.9 | ns |
| 3 | Fat (%) | 34.5 | 1.3 | 36.7 | 1.4 | 34.2 | 1.4 | ns |
| 4 | Fibre (%) | 20.7 | 1.1 | 19.5 | 1.7 | 21.5 | 1.6 | ns |
| 5 | Alcohol (%) | 8.2 | 1.9 | 13.2 | 3.5 | 4.3 | 1.2 | * |
| 6 | Cholesterol (%) | 271.3 | 25.2 | 317.1 | 52.5 | 241.3 | 22.3 | ns |
| | Micronutrients | | | | | | | |
| 1 | Calcium (mg) | 757.4 | 32.5 | 792.3 | 55.5 | 733.8 | 41.8 | ns |
| 2 | Iron (%) | 20.2 | 1.6 | 21.8 | 2.6 | 19.1 | 2.3 | ns |
| 3 | Magnesium (%) | 298.4 | 13.1 | 305.2 | 19.7 | 292.3 | 17.6 | ns |
| 4 | Sodium (%) | 1720.4 | 115.2 | 1861.3 | 202.6 | 1624.3 | 136.4 | ns |
| 5 | Zinc (%) | 10.3 | 1.2 | 10.3 | 1.4 | 10.2 | 1.5 | ns |
| 6 | Copper (%) | 2.3 | 0.2 | 2.5 | 0.5 | 2.3 | 0.2 | ns |
| 7 | Iodine (%) | 131.5 | 8.4 | 126.3 | 12.2 | 132.1 | 12.6 | ns |

Significant differences between Randomized Vitamin E and Placebo Treatment Groups in the Women's (*P < 0.05; **P < 0.01; NS: not significant) by ANOVA.

## RESULTS

Table-1 Shown that Ophthalmic characteristics of women patients. The sample of 107 patients.60 patients had CNV active eyes, 16 (26.6%) patients had CNV Active right eye, 30 (50%) patients had CNV active left eye, 14 (23.3%) patients had CNV active both eyes. 20 (33.3%) Occult (or predominant occult membrane) type CNV that was more prevalent than other types CNV. 25 (41.6%) Patients had Extrafoveal type CNV Location mostly present than others location.

Table-2 Shown that as expected in this large randomized testing, baseline characteristics were equally distributed between the two treatment groups. During an average of 10 years of treatment and follow-up, a total of 107 cases of visually-significant AMD were confirmed. Most of the ARMD patients belonging to the 45-54 year age in vitamin E 13 (40.6%) and Placebo 20 (26.6%) groups of women. 23 (71.8%) vitamin E group women and 45 (60%) placebo group women were previously smoked. 18 (56.25%) vitamin E group women and 56 (74.6%) placebo group women suffered from Hypertension. 15 (46.8%) vitamin E group women and 33 (44%) placebo group women had Diabetes Mellitus. 20 (62.5%) vitamin E group women and 50 (66.6%) placebo group women currently used Multivitamin.

Table -3 Showed estimation of macro and micronutrient intake stratified by Vitamin E and Placebo Treatment Groups in the Women. There were no differences between Vitamin E and Placebo Treatment Groups for higher protein, phosphorus and Cholesterol intake observed.

## DISCUSSION

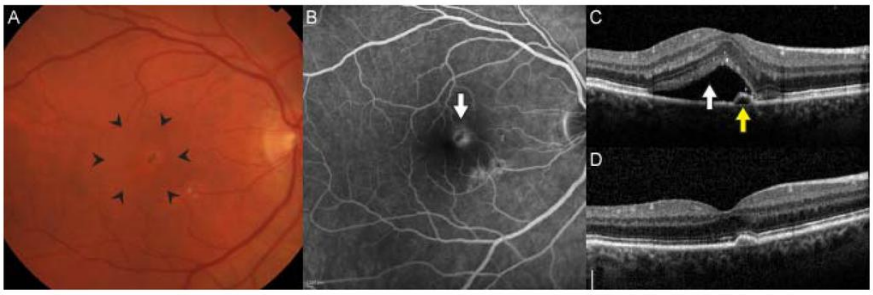
In this huge randomized testing, women assigned to alternate-day treatment with 600 IU of natural-source vitamin E and followed for an natural of 10 years had a non-significant 7% decreased risk of the primary study endpoint of visually-significant AMD. My study shown that left eye 30(50%) patients more affected than right eye and both eyes. Occult (or predominant occult membrane) CNV type 20(33.3%) patients predominately present than other type of CNV active patients .This observation similar to the study of (20) .According to the table 2 Baseline Characteristics in Randomized Vitamin E and Placebo Treatment Groups in the Women's Health Study. Most of the patients belonging to the 45-54 year age groups of women, previously they were smoked ,most of the patients suffered from Hypertension ,some of the patients had Diabetes Mellitus. Most of the patients use Multivitamin. this study similar to the study of (21) .Vitamin E treatment had no significant cause on the secondary endpoints of advanced AMD and total AMD with or without vision loss. The WHS is the highest randomized examination of vitamin E supplementation in AMD to date. Three other trials have observed vitamin E in AMD, but only two were able to evaluate the separate effects of vitamin E supplementation. The Alpha-Tocopherol Beta-Carotene (ATBC) Study was a 2 × 2 factorial trial of vitamin E (50 mg daily) and beta carotene (20 mg daily) performed among more than 29,000 Finnish male smokers aged 50 to 69 years. Median treatment duration was 6.1 years (22).

Estimation of energy, macro and micronutrient intake stratified by vitamin E group women and placebo group women are shown in table III. There were non-significant differences between vitamins and placebo groups of women patients except for alcohol. This study came from a study of (20) in which Estimation of energy, macro and micronutrient intake stratified by sexes. There were no differences between sexes, except for higher protein, phosphorus and alcohol intake observed in men. Our primary endpoint was visually-significant AMD which symbolizes, on average, a less severe stage of disease development than cases meeting the criteria for advanced AMD in AREDS. When we examined the more advanced cases of AMD in our population (defined as the occurrence of exudative neovascular disease or geographic atrophy), we discovered no proof that vitamin E supplementation reduced the risk of advanced AMD. The study of the food source of antioxidant nutrients of participants shows the core dietary contributors of antioxidants. The fat and SFA intake of study participants were larger than the suggested nutritional objectives (23). It has been pointed out that a high dietary intake of fat is related with a higher prevalence or incidence of early or late AMD. These results also agree our findings that most of participants showed a risk of CVD, and hyper-tension, which also maintain the common hypothesis that AMD shares multiple risk factors with cardiovascular disease (24).

## CONCLUSION

These randomized trial data from a large population of healthy women indicate that 10 years of alternate-day treatment with 600 IU of natural source vitamin E only has no material beneficial or harmful effect on AMD occurrence. Whether vitamin E as a component of an antioxidant combination can help to reduce risks of AMD, as suggested by the findings in AREDS, warrants continued analysis.

**Picture**- Choroidal neovascularization is the hallmark of neovascular age-related macular degeneration.

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