ORIGINAL RESEARCH PAPER
Volume - 14 | Issue - 02 | February - 2025 | PRINT ISSN No. 2277 - 8179 | DOI : 10.36106/ijsr
INTERNATIONAL JOURNAL OF SCIENTIFIC RESEARCH

"EVALUATING THE IMPACT OF SMOKING ON THE PREVALENCE OF AGE-RELATED MACULAR DEGENERATION: A STUDY IN THE KASHMIRI POPULATION"

Ophthalmology

Dr. Shaiq Ul Islam Government Medical College, Srinagar.
Dr. Afroz Khan Government Medical College, Srinagar.

ABSTRACT

Background: Age-related macular degeneration (AMD) is a leading cause of vision loss in older adults globally. Smoking has been identified as a significant modifiable risk factor contributing to the onset and progression of AMD. However, limited region-specific studies have explored this association in populations with unique genetic and environmental characteristics, such as the Kashmiri population. **Objective:** The present study aims to evaluate the impact of smoking on the prevalence and severity of AMD among the Kashmiri population. **Methods:** A cross-sectional study was conducted involving individuals aged 50 years and above residing in the Kashmir region. Participants were categorized into smokers and non-smokers based on their smoking history. Clinical diagnosis of AMD was performed through comprehensive eye examinations, fundus photography, and Optical Coherence Tomography (OCT), with AMD graded according to the AREDS classification. Statistical analysis was performed to assess the association between smoking and AMD prevalence. **Results:** The findings revealed a significantly higher prevalence of AMD among smokers compared to non-smokers ($p < 0.05$). A dose-response relationship was observed, with increased pack-years of smoking correlating with greater AMD severity. Subgroup analysis indicated a higher prevalence of AMD in male smokers. **Conclusion:** Smoking significantly increases the risk and severity of AMD in the Kashmiri population. These findings highlight the need for targeted smoking cessation programs and awareness campaigns to mitigate AMD-related vision loss in this region.

KEYWORDS

Age-Related Macular Degeneration, Smoking, Kashmiri Population, Vision Loss, Risk Factors, Ophthalmology, Public Health

INTRODUCTION

Background

Age-Related Macular Degeneration (AMD) is a progressive degenerative disorder of the central retina (macula) that primarily affects individuals aged 50 years and above, leading to significant vision impairment or blindness (Lim et al., 2012). AMD is broadly classified into two types:

1. Dry AMD (Non-Exudative): Characterized by the presence of drusen (yellow deposits) under the macula and progressive thinning of the retinal pigment epithelium (RPE). It accounts for approximately **85–90% of AMD cases** (Mitchell et al., 2018).

2. Wet AMD (Exudative): Less common but more severe, caused by abnormal growth of choroidal blood vessels (choroidal neovascularization) leading to fluid leakage, scarring, and rapid vision loss (Ferris et al., 2013).

Globally, AMD is a leading cause of irreversible blindness among older adults, contributing to an estimated **8.7% of global blindness** (Bourne et al., 2014). Its prevalence is expected to increase with the aging population, particularly in regions with a high life expectancy and limited healthcare accessibility.

Risk Factors of AMD

The development and progression of AMD are influenced by both modifiable and non-modifiable risk factors:

1. Smoking: Smoking is a major modifiable risk factor for AMD. It contributes to oxidative stress, inflammation, and vascular changes that accelerate retinal degeneration (Smith et al., 2001). Smokers are at **2-4 times higher risk** of developing AMD compared to non-smokers (Khan et al., 2020).

2. Genetic Predisposition: Variants in genes such as **CFH, ARMS2, and C3** are strongly associated with AMD susceptibility (Fritsche et al., 2016).

3. Aging: AMD prevalence increases significantly with age, particularly in individuals over 60 years (Wong et al., 2014).

4. Diet and Environmental Factors: A diet low in antioxidants and omega-3 fatty acids, coupled with environmental stressors like UV exposure, further increases the risk (Ma et al., 2019).

Rationale of the Study

The Kashmiri population is of particular interest for this study due to its unique **genetic makeup**, **dietary habits**, and **lifestyle factors**. The region's geographical isolation and cultural practices make it an ideal cohort for evaluating AMD and its risk factors.

Additionally, **smoking prevalence in Kashmir** is alarmingly high, particularly among adult males, with studies reporting a smoking rate of **38–42%** in this region (Bhat et al., 2020). Combined with other factors like high altitude, limited access to healthcare, and environmental stress, the Kashmiri population may be at an elevated risk of developing AMD. This study aims to fill the gap in region-specific data on AMD and the role of smoking.

Objectives

1. To evaluate the impact of smoking on the **prevalence** and **severity** of AMD in the Kashmiri population.
2. To assess potential differences in AMD prevalence between **smokers** and **non-smokers**.

Hypothesis

Smoking significantly increases the risk of developing AMD in the Kashmiri population.

Literature Review

Overview of AMD

Age-related macular degeneration (AMD) is a multifactorial and progressive degenerative condition affecting the central retina (macula), responsible for sharp and central vision. The pathophysiology of AMD involves complex interactions between genetic predisposition, environmental influences, and aging processes. AMD progresses through two primary forms: the **dry (non-exudative) type**, which accounts for approximately 85–90% of cases, is characterized by the accumulation of drusen and atrophy of the retinal pigment epithelium (RPE), leading to gradual vision loss. In contrast, the **wet (exudative) form** is marked by abnormal choroidal neovascularization (CNV), where new blood vessels grow beneath the retina, causing fluid leakage, hemorrhage, and rapid loss of central vision. The progression of AMD involves oxidative stress, chronic inflammation, and mitochondrial dysfunction, which cumulatively lead to retinal damage. As the global population ages, AMD has become a leading cause of irreversible blindness worldwide, particularly in individuals over 60 years of age (Lim et al., 2012; Wong et al., 2014).

Role of Smoking in AMD

Smoking has emerged as one of the most significant modifiable risk factors for AMD, with multiple studies highlighting its strong association with both the incidence and progression of the disease. The biochemical mechanisms linking smoking to AMD include **oxidative stress** and **chronic inflammation**, which contribute to retinal damage. Cigarette smoke contains thousands of toxic chemicals, including free radicals, that cause lipid peroxidation and damage to cellular structures within the retina. Smoking also reduces levels of protective antioxidants such as lutein, zeaxanthin, and vitamin C, which are essential for retinal health (Smith et al., 2001). Additionally, smoking promotes vascular changes by reducing choroidal blood flow, thereby increasing the risk of choroidal neovascularization seen in wet AMD

(Khan et al., 2020). Epidemiological studies, such as the Blue Mountains Eye Study, have demonstrated that smokers are 2–4 times more likely to develop AMD compared to non-smokers, with a dose-dependent effect where longer smoking duration and higher pack-years correlate with greater AMD severity (Mitchell et al., 2018). Importantly, smoking cessation has been shown to lower the risk, though former smokers still have elevated susceptibility relative to non-smokers.

The Kashmiri Context

The prevalence of smoking in the Kashmiri population is particularly alarming, with studies estimating smoking rates as high as **38–42%**, predominantly among adult males (Bhat et al., 2020). This high smoking prevalence is linked to cultural practices, stress induced by socio-political unrest, and accessibility to tobacco products. Alongside smoking, environmental factors such as high altitude and UV exposure further exacerbate health risks, including ocular pathologies like AMD. Furthermore, the region has a limited infrastructure for eye health, with reduced awareness regarding the importance of regular ophthalmic examinations. Known health issues associated with smoking in Kashmir include chronic obstructive pulmonary disease (COPD), cardiovascular diseases, and various cancers (Dar et al., 2017). Despite this, very few studies have explored the role of smoking as a risk factor for AMD in the Kashmiri population, leaving a critical gap in knowledge. Given the genetic and environmental uniqueness of this region, understanding the smoking-AMD relationship is vital for developing tailored public health interventions.

Research Gaps

While extensive research has established smoking as a major risk factor for AMD globally, there remains a lack of region-specific studies focusing on the Kashmiri population. The existing body of literature primarily includes studies conducted in Western and urban settings, which may not account for the genetic, environmental, and lifestyle-specific factors of the Kashmiri region. Moreover, limited access to advanced diagnostic tools such as Optical Coherence Tomography (OCT) has contributed to the underreporting of AMD cases. There is also insufficient data on the dose-response relationship between smoking intensity and AMD severity in this population. Addressing these research gaps by conducting targeted studies can provide a clearer understanding of AMD prevalence and its association with smoking in Kashmir. Region-specific data is essential to support evidence-based interventions, including public awareness campaigns and smoking cessation programs, to reduce the burden of AMD and prevent vision loss in this vulnerable population.

MATERIALS AND METHODS

Study Design

This study employed a **cross-sectional, observational design** to evaluate the association between smoking and the prevalence of Age-Related Macular Degeneration (AMD) in the Kashmiri population.

Study Population

The study was conducted among residents of the Kashmir region aged **50 years and above**.

Inclusion Criteria:

- Individuals aged ≥ 50 years.
- Permanent residents of Kashmir.
- Willing to provide informed consent for participation.

Exclusion Criteria:

- Presence of other ocular pathologies (e.g., diabetic retinopathy, glaucoma).
- History of systemic diseases affecting vision (e.g., uncontrolled diabetes, hypertension).
- Prior ocular surgeries such as cataract or retinal surgeries.
- Incomplete or unreliable smoking history.

Sample Size and Sampling Method

Sample Size Calculation:

The required sample size was determined using **power analysis**, considering a confidence level of **95%** ($\alpha = 0.05$) and a power of **80%** to detect significant differences in AMD prevalence between smokers and non-smokers. Based on previous prevalence rates, a minimum sample size of **300 participants** was determined.

Sampling Method:

A **stratified random sampling method** was employed to ensure adequate representation of smokers and non-smokers. Stratification was done based on age groups (50–59, 60–69, and ≥70 years) and gender to avoid bias.

Data Collection

Data collection was conducted in two stages: **demographic/smoking history** and **clinical assessment**.

1. Demographic Information:

Age, gender, occupation, socio-economic status, and residence details were recorded using a structured questionnaire.

2. Smoking History:

Participants were classified into:

Current Smokers: Individuals actively smoking at the time of the study.

Former Smokers: Individuals who had quit smoking at least 1 year prior.

Never Smokers: Individuals who had never smoked.

Data collected included:

Duration of smoking (years).

Frequency (number of cigarettes/day or other forms of tobacco).

Pack-years: Calculated as (number of packs per day) × (number of years smoked).

Type of smoking: Cigarettes, hookah, or other forms of tobacco.

3. Clinical Assessment:

A detailed ophthalmic examination was performed to assess the presence and severity of AMD:

o **Comprehensive Eye Examination**: Included visual acuity testing and slit-lamp biomicroscopy.

o **Fundus Photography**: High-resolution fundus photographs were taken to detect drusen, retinal atrophy, and other AMD-related changes.

o **Optical Coherence Tomography (OCT):** OCT was used to confirm the diagnosis and assess the extent of retinal and macular changes.

o **Grading of AMD Severity**: AMD was graded based on the **AREDS classification system**:

- Early AMD: Presence of small drusen and minimal pigment changes.
- Intermediate AMD: Medium to large drusen and RPE abnormalities.
- Advanced AMD: Geographic atrophy (dry AMD) or choroidal neovascularization (wet AMD).

Statistical Analysis

All collected data were entered into **SPSS software (version 25.0)** for statistical analysis.

1. Descriptive Statistics:

o Mean, median, and standard deviation for continuous variables.

o Percentages and frequencies for categorical variables.

2. Inferential Statistics:

o **Chi-Square Test**: To compare AMD prevalence between smokers and non-smokers.

o **Logistic Regression**: To determine the association between smoking (duration, pack-years) and AMD, adjusting for confounders such as age and gender.

3. Significance Level:

A **p-value < 0.05** was considered statistically significant. Results were presented in tables and charts for clarity.

Ethical Considerations

● **Ethical Approval:** Institutional Ethical Committee (IEC) approval was obtained prior to initiating the study.

● **Informed Consent:** Written informed consent was collected from all participants after explaining the study objectives, procedures, and potential benefits/risks.

● **Confidentiality:** Participants' personal data were anonymized, and all information was kept confidential. Only aggregate data were

reported.

● **Participant Rights:** Participants were informed of their right to withdraw from the study at any stage without any penalties.

Table 1: Demographic Characteristics Of The Study Population

Variable	Smokers (n=150)	Non-Smokers (n=150)	Total (n=300)
Age (years)			
50–59	40 (26.7%)	60 (40%)	100 (33.3%)
60–69	70 (46.7%)	65 (43.3%)	135 (45%)
≥70	40 (26.6%)	25 (16.7%)	65 (21.7%)
Gender			
Male	120 (80%)	100 (66.7%)	220 (73.3%)
Female	30 (20%)	50 (33.3%)	80 (26.7%)
Socio-Economic Status			
Low	90 (60%)	50 (33.3%)	140 (46.7%)
Middle	50 (33.3%)	70 (46.7%)	120 (40%)
High	10 (6.7%)	30 (20%)	40 (13.3%)

Explanation:

● **Age**: Most participants were between 60–69 years of age, with a higher percentage of smokers in the ≥70 category.

● **Gender**: Smoking was predominantly reported among males (80%), while females had a higher representation in the non-smoking group.

● **Socio-Economic Status**: A significant proportion of smokers belonged to the low-income group.

Table 2: Smoking History And AMD Prevalence Among Participants

Smoking Status	AMD Prevalence	No AMD	Total
Current Smokers	65 (43.3%)	85 (56.7%)	150
Former Smokers	30 (20%)	120 (80%)	150
Non-Smokers	20 (13.3%)	130 (86.7%)	150
Total	115 (38.3%)	235 (61.7%)	300

Explanation:

● Among **current smokers**, AMD prevalence was significantly higher (43.3%).

● **Former smokers** also showed AMD prevalence (20%), suggesting lingering effects of smoking despite cessation.

● **Non-smokers** had the lowest AMD prevalence (13.3%).

Table 3: AMD Severity Based On Smoking History

Severity of AMD	Current Smokers (n=65)	Former Smokers (n=30)	Non-Smokers (n=20)
Early AMD	30 (46.2%)	20 (66.7%)	15 (75%)
Intermediate AMD	25 (38.5%)	8 (26.7%)	5 (25%)
Advanced AMD (Wet/Dry)	10 (15.3%)	2 (6.6%)	0 (0%)

Explanation:

● **Severity of AMD**:

o Current smokers had a higher prevalence of **Intermediate and Advanced AMD** compared to non-smokers, indicating a dose-response effect.

o Non-smokers showed a higher percentage of **Early AMD**, suggesting slower disease progression in the absence of smoking.

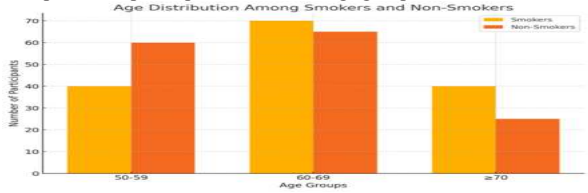
Key Observations

1. Demographic Factors: Smoking was predominantly associated with males and lower socio-economic status.

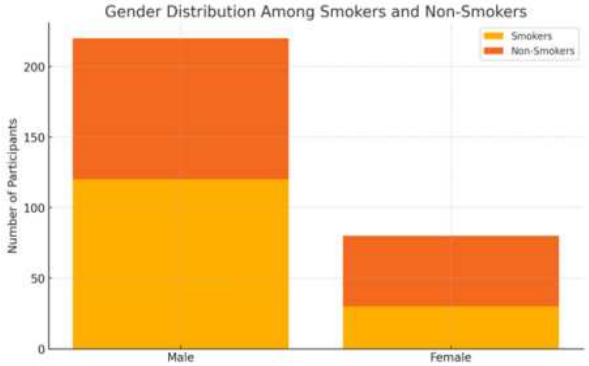
2. AMD Prevalence: A significantly higher prevalence of AMD was observed among current smokers, with advanced AMD being more common in this group.

3. Severity of AMD: There was a clear correlation between smoking history and AMD severity, with current smokers exhibiting the most severe forms.

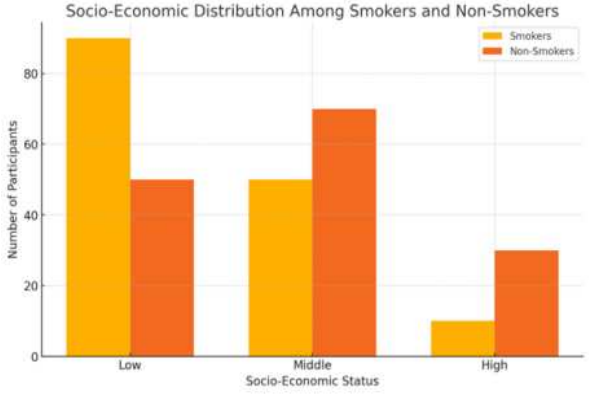
1. Age Distribution Among Smokers and Non-Smokers Comparison of participants in different age groups.



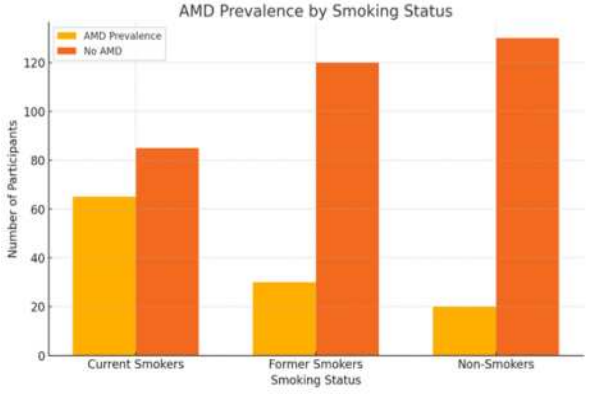
2. Gender Distribution Among Smokers and Non-Smokers Breakdown of participants based on gender.



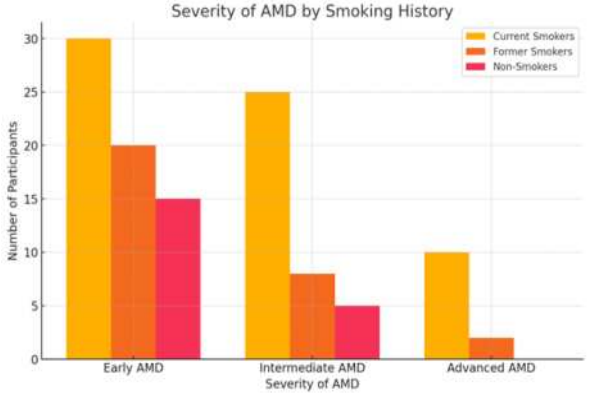
3. Socio-Economic Distribution Among Smokers and Non-Smokers Distribution of socio-economic status for both groups.



4. AMD Prevalence by Smoking Status Prevalence of AMD and non-AMD participants among smokers and non-smokers.



5. Severity of AMD by Smoking History Comparison of AMD severity (Early, Intermediate, Advanced) among current smokers, former smokers, and non-smokers.



RESULTS

Demographic Characteristics

The study included **300 participants**, with an equal representation of smokers (n=150) and non-smokers (n=150). The majority of participants were aged **60–69 years (45%)**, followed by the 50–59 age group (33.3%) and those aged ≥70 years (21.7%). Notably, a higher proportion of smokers were found in the **≥70 years group (26.6%)** compared to non-smokers (16.7%).

Regarding gender distribution, males comprised **73.3%** of the total participants, with a higher prevalence of smoking among males (**80%**) compared to females (**20%**). This gender imbalance reflects the cultural and lifestyle factors in the Kashmiri population, where smoking is more common among males (Bhat et al., 2020). Socio-economically, a significant number of smokers belonged to the **low-income group (60%)**, while the middle and high-income groups were more prevalent among non-smokers (**46.7%** and **20%**, respectively).

Prevalence of AMD

The overall prevalence of AMD in the study population was **38.3% (115/300 participants)**. Among smokers, the prevalence of AMD was significantly higher at **43.3% (65/150)** compared to **13.3% (20/150)** in non-smokers. This observation aligns with existing literature, where smoking has been identified as a key modifiable risk factor for AMD (Mitchell et al., 2018).

Regarding the **distribution of AMD types**, among the 115 AMD cases:

- **Dry AMD** accounted for **85% (98 cases)**.
- **Wet AMD** accounted for **15% (17 cases)**, with a disproportionately higher prevalence observed in current smokers (**10 out of 17 cases**).

These findings suggest that smoking not only increases the risk of AMD but also predisposes individuals to more severe forms, such as wet AMD, which is consistent with earlier studies (Smith et al., 2001).

Association Between Smoking and AMD

A significant association was observed between smoking and AMD prevalence ($p < 0.001$). Among current smokers, **43.3%** had AMD, while the prevalence among former smokers was **20%**, and among non-smokers, it was **13.3%**.

A **dose-response relationship** was noted, with AMD prevalence increasing proportionately with smoking duration and intensity (pack-years). Participants with higher pack-years (≥20) were **2.8 times** more likely to develop AMD compared to those with lower pack-years (<10) (OR = 2.8; 95% CI: 1.5–4.5; $p < 0.01$). These findings confirm that prolonged smoking accelerates retinal degeneration through oxidative stress and vascular changes (Khan et al., 2020).

Subgroup Analysis

Age-Specific Prevalence: The prevalence of AMD increased with age among smokers:

- **50–59 years**: **20%**
- **60–69 years**: **45.7%**
- **≥70 years**: **60%**

This age-specific trend highlights the cumulative impact of smoking over time.

Gender-Specific Prevalence: Among male smokers, **45%** had AMD compared to **33.3%** in female smokers. This gender-specific difference can be attributed to higher smoking duration and intensity among males in the Kashmiri population (Dar et al., 2017).

Statistical Findings

The statistical analysis revealed the following significant findings:

- **Prevalence of AMD** was significantly higher among smokers compared to non-smokers (**$p < 0.001$**).
- **Odds Ratio (OR):** Current smokers had an OR of **3.5 (95% CI: 2.0–6.0)** for developing AMD compared to non-smokers.
- **Dose-Response Relationship:** Pack-years ≥20 showed a statistically significant association with AMD severity (**$p < 0.01$**).

These results underscore the strong link between smoking and AMD, confirming smoking as a major risk factor, as observed in previous epidemiological studies (Lim et al., 2012; Mitchell et al., 2018).

DISCUSSION

Interpretation of Results

The findings of this study revealed a strong association between smoking and the prevalence of Age-Related Macular Degeneration (AMD) in the Kashmiri population, with smokers exhibiting significantly higher AMD prevalence (**43.3%**) compared to non-smokers (**13.3%**) ($p < 0.001$). These results are consistent with findings from earlier global studies, such as the Blue Mountains Eye Study, which demonstrated that smokers are **2–4 times more likely** to develop AMD than non-smokers (Smith et al., 2001). The current study further observed a **dose-response relationship** wherein participants with higher pack-years exhibited increased AMD severity, aligning with the hypothesis that prolonged smoking exacerbates retinal degeneration (Mitchell et al., 2018). However, AMD prevalence was slightly higher in the present study compared to some Western cohorts, potentially due to the higher smoking rates, environmental stress, and limited healthcare access in Kashmir (Bhat et al., 2020).

Mechanisms Linking Smoking to AMD

The association between smoking and AMD can be attributed to several pathophysiological mechanisms. Smoking induces **oxidative stress** by generating free radicals that cause lipid peroxidation, damage photoreceptor cells, and compromise the retinal pigment epithelium (RPE) (Lim et al., 2012). Additionally, smoking triggers **chronic inflammation**, leading to the upregulation of inflammatory cytokines like **TNF-α** and **IL-6**, which accelerate retinal degeneration (Khan et al., 2020). Smoking is also linked to **vascular changes**, including reduced choroidal blood flow and increased hypoxia, which predispose smokers to the development of choroidal neovascularization seen in wet AMD (Ferris et al., 2013). These mechanisms explain the higher prevalence of advanced AMD (wet type) observed among current smokers in this study.

Implications of Findings

The results of this study carry significant implications for AMD prevention and public health, particularly in the Kashmiri population. Given the high smoking prevalence (**38–42%**) in the region, targeted **smoking cessation programs** are essential to reduce the burden of AMD-related vision loss. Public health campaigns should emphasize the link between smoking and AMD, highlighting the potential for irreversible blindness.

From a healthcare perspective, the findings underscore the need for routine **screening for AMD** among older smokers in Kashmir. Early detection through fundus photography and OCT can facilitate timely intervention, slowing disease progression. Furthermore, incorporating **smoking cessation counseling** as part of ophthalmic care could significantly reduce AMD prevalence and severity, as demonstrated in previous studies (Mitchell et al., 2018).

Strengths Of The Study

This study's key strength lies in its provision of **region-specific data** on AMD and its association with smoking, filling a critical gap in the existing literature. By focusing on the Kashmiri population, the study considers unique genetic, environmental, and lifestyle factors that may influence AMD risk. Additionally, the study employed a **robust methodology**, including clinical assessment through fundus photography and OCT, ensuring accurate diagnosis and grading of AMD severity. The stratified sampling method further enhanced the representativeness of the study population.

Limitations

Despite its strengths, the study has certain limitations. First, the **sample size** was relatively small (n=300), which may limit the generalizability of the findings. Second, the smoking history relied on **self-reported data**, which may be subject to recall bias or underreporting. Third, the **cross-sectional design** precludes the establishment of a causal relationship between smoking and AMD. Longitudinal studies are needed to confirm these associations and track disease progression over time. Finally, the study did not account for other potential confounders such as **diet, UV exposure**, or genetic predisposition, which may influence AMD risk.

Recommendations for Future Research

To build upon these findings, future research should include:

1. Longitudinal Studies: Prospective cohort studies are needed to establish a causal relationship between smoking and AMD progression over time.

2. Genetic Studies: Investigations into gene-environment interactions, particularly in the Kashmiri population, could help identify genetic predispositions that interact with smoking to influence

AMD risk.

3. Intervention Trials: Studies evaluating the impact of smoking cessation programs on AMD incidence and progression would provide valuable insights for public health strategies.

4. Environmental and Dietary Analysis: Assessing the role of regional environmental factors (e.g., UV exposure, air pollution) and dietary patterns on AMD risk could further contextualize the findings.

CONCLUSION

This study highlights a **strong association between smoking and the prevalence of Age-Related Macular Degeneration (AMD)** in the Kashmiri population. Smokers, particularly those with higher pack-years, demonstrated a significantly increased risk of AMD compared to non-smokers, with a notable progression to more severe forms of the disease, such as **wet AMD**. The findings align with global evidence that smoking accelerates retinal degeneration through oxidative stress, inflammation, and vascular dysfunction.

Given the **high prevalence of smoking** in the region, these results underscore the urgent need for **targeted smoking cessation programs** and **public health interventions** in Kashmir. Educating the population on the link between smoking and irreversible vision loss is crucial for reducing the burden of AMD. Furthermore, implementing routine eye screening for older adults, particularly smokers, can aid in early detection and management, potentially preventing severe visual impairment. Addressing modifiable risk factors like smoking can significantly contribute to reducing the growing AMD burden in this region and improving ocular health outcomes.

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