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Epidemiology of asteroid hyalosis and associations: the Gutenberg Health Study

Elbaz, H,^{1,2} Schuster AK,¹ Nickels S,¹ Nagler M,³ Ponto KI,¹ Münzel T,⁶ Wild PS,^{3,4, 5} Beutel ME,⁷ Schmidtman I,⁸ Lackner KJ,⁹ Pfeiffer N^{1, *}, Tunde Peto^{10,11 *}

¹ Department of Ophthalmology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany

² Department of Ophthalmology, Otto von Guericke University Magdeburg, Germany

³ Preventive Cardiology and Preventive Medicine, Center for Cardiology, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany

⁴ Center for Thrombosis and Hemostasis, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany;

⁵ DZHK (German Center for Cardiovascular Research), partner site Rhine-Main, Mainz, Germany

⁶ Center for Cardiology, Cardiology I, University Medical Center Mainz, Mainz, Germany

⁷ Department of Psychosomatic Medicine and Psychotherapy, University Medical Center Mainz, Mainz, Germany

⁸ Department of Biomedical Statistics, University Medical Center of the Johannes Gutenberg-University Mainz, Mainz, Germany

⁹ Institute of Clinical Chemistry and Laboratory Medicine, University Medical Center Mainz, Mainz, Germany

¹⁰ NIHR Biomedical Research Centre at Moorfields Eye Hospital NHS Foundation Trust and UCL Institute of Ophthalmology

¹¹ Department of Ophthalmology, Centre for Public Health, Institute of Clinical Sciences, School of Medicine, Queen's University Belfast, Belfast, United Kingdom.

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42 **Corresponding Author and reprint requests:**

43 Dr. med. Hisham Elbaz

44 Email: hisham_elbaz@yahoo.com

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63 Asteroid hyalosis (AH) was first described by Benson in 1894 who called it asteroid hyalitis.
64 The condition is mostly unilateral and rarely impairs vision. It is seen as white, creamy,
65 iridescent particles moving around in the vitreous following eye movement. Within this work,
66 we are reporting on the prevalence, incidence and associations of asteroid hyalosis.

67 The Gutenberg Health Study (GHS) is a population-based, prospective, observational cohort
68 study in the Rhine-Main Region in Germany. The baseline study examined 15,010 subjects
69 aged between 35 and 74 between 2007 and 2012. Of these, 12,423 participants (82.8 % of
70 baseline) attended the 5-year follow-up between 2012 and 2017. The sample was drawn
71 randomly from local governmental registry and the cohort was equally stratified by sex,
72 residence and per each decade of age.^{1,2}

73 All subjects underwent a general medical examination including an analysis of the
74 cardiovascular risk factors as well as an ophthalmological examination including history and
75 other tests including autorefraction, visual acuity and measurement of intraocular pressure.
76 Slitlamp biomicroscopy including fundus examination was conducted. Fundus images were
77 taken with a non-mydriatic fundus camera (Visucam PRO NMTM, Carl Zeiss AG, Jena,
78 Germany) in a darkened room with the pupil's natural width. Three photographs were taken
79 of each eye: at 30° and 45° centred on the optic nerve, and at 30° centred on the macula.

80 The grading of the baseline and five-year follow-up fundus images was based on the
81 detection of creamy white vitreal lesions typical of AH. Incident AH was defined as the first
82 appearance of AH in either eye of subjects who had no sign of AH at the baseline visit in
83 both eyes. Intra-rater and inter-rater reliability showed high agreement.

84 The study protocol and study documents were approved by the local ethics committee of
85 the Medical Chamber of Rhineland-Palatinate in Germany. According to the tenets of the
86 Declaration of Helsinki, written informed consent was obtained from all subjects prior to
87 entering the study.

88 Statistical analysis included quality controls and an estimation of prevalence and incidence
 89 including 95% confidence intervals. Logistic regression analysis with generalized estimating
 90 equations was computed to evaluate whether AH was associated with spherical equivalent,
 91 intraocular pressure and visual acuity adjusted for age and sex. Another model was
 92 computed using logistic regression analysis on person-level (AH in at least one eye) to
 93 evaluate associated systemic diseases and other risk factors including age, sex, arterial
 94 hypertension, diabetes, smoking, alcohol intake and family history of myocardial infarction
 95 and stroke.

96 Baseline fundus photographs were available in 12,779 (85.1%) of 15,010 GHS subjects.
 97 The baseline cohort included 6,398 (50%) men and 6,381 (50%) women. The mean age in
 98 the whole cohort 54.9 ± 11.1 years. The study characteristics is described in supplemental
 99 table 1 available at www.aaojournal.org. AH was seen in 61 (0.48%) participants (74 eyes).
 100 32 subjects had AH in the right eye, 42 in the left eye. 13 subjects (21.3%) had bilateral
 101 lesions, whereas 48 subjects (78.7%) had unilateral involvement. The mean age of the
 102 subjects having AH was 66.2 ± 7.6 years versus 54.9 ± 11.1 years in subjects without AH. The
 103 unweighted prevalence was 0.48% (CI: 0.37% - 0.61%). The systemic associations of AH
 104 are summarized in Table 1: Increased age (OR=1.13 per year, $p < 0.001$), male sex
 105 (OR=1.71, $p = 0.05$), and diabetes (OR = 2.25, $p = 0.007$). The prevalence of AH increased
 106 with age: 0.04% at 35-44 years while 1.3% at 65-74 years (Supplemental table 2 available
 107 at www.aaojournal.org).

108 Of 12,779 baseline participants, 8,176 subjects were followed-up after five years. Incident
 109 AH was identified in 17 participants (19 eyes) with a 5-year cumulative incidence of 0.2%
 110 (95%-CI: 0.11% - 0.32%) which was higher in men 0.27% (95%-CI: 0.13% - 0.47%; $n=11$
 111 subjects) than in women 0.15% (95%-CI: 0.055%, 0.32%, $n=6$ subjects). The incidence
 112 ranged from 0% in the group aged 35-44 years to 0.77% in the group aged 65-74 years. In

113 the 27 subjects with unilateral AH at baseline: 3 unaffected fellow eyes (11%) showed AH
114 within 5 years.

115 The prevalence of AH in the GHS of 0.5% was similar to that reported from the Yonsei Eye
116 Study in South Korea (0.36%; subjects aged ≥ 40 years)³. It was lower than the 1.0%
117 reported in the Blue Mountains Eye study (participants aged 49–97 years)⁴ and the 0.83%
118 from a cross sectional study in the USA (average age 70 years)⁵. However, our age-stratified
119 prevalence values matched the reported data from the Blue Mountains Eye Study⁴ (0% in
120 persons aged <55 years, 0.4% in persons aged 55–64 years, 1.1% in persons aged 65–74
121 years and 2.1% among those aged more than 75 years), compared to 0.39% in persons
122 aged 55–64 years and 1.3% in those aged 65–74 years in our study. Also, age-stratified data
123 from the Yonsei Study³ (0.05% at age 40–49 years, 0.42% at age 50–59 years, 0.89% at age
124 60 to 69 years and 1.18% at age 70 and older) and from the Beaver Dam Eye Study⁶ (about
125 0.2% at age 43–54 years, 1.1% at age 55–64 years, 1.% at age 65 to 74 years) were in line
126 with our results.

127 The association of AH with diabetes mellitus in our study is in line with the positive
128 association reported in previous studies. However, the association between diabetes and
129 AH was substantially attenuated from a univariate OR of 3.88 to an OR of 1.99 [1.12; 3.53]
130 after adjustment for sex and age. Association between AH and diabetes mellitus could be
131 explained by the increased permeability of basal membranes in diabetic eyes which are
132 likely to be the source of phospholipid and calcium needed for asteroid formation⁷.
133 Therefore, testing for diabetes in patients showing AH should be considered.

134 In summary, the prevalence of AH in the GHS is estimated as 0.5% and is associated with
135 advanced age, male sex and diabetes in Europe, while the cumulative 5-year incidence is
136 estimated as 0.2%.

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164 Table 1: Association analysis of baseline asteroid hyalosis with systemic diseases and other
165 potential risk factors. Multivariable logistic regression analysis was conducted. Data from
166 the Gutenberg Health Study (2007-2012; n=12.747)

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168 Supplemental Table 1: Characteristics of the analysis sample. Data from the population-
169 based German Gutenberg Health Study (2007-2012).

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171 Supplemental Table 2: Age-related prevalence and 5-year cumulative incidence of Asteroid
172 Hyalosis

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