# Wet age-related macular degeneration (wet AMD) in rural and urban inhabitants in south-eastern Poland

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### Abstract

**Objective:** Evaluation of the demographic profile of patients from south-eastern Poland treated due to wet age-related macular degeneration.

**Material and methods:** Data concerning 201 patients were analyzed (133 F/ 68 M), aged from 50 -91, (mean age  $76 \pm 8.6$ ), with the wet form of age-related macular degeneration treated by intravitreal injections of vascular endothelial growth factor inhibiting drugs. The significance of the relationships between variables was investigated by means of chi-square test for independence. The differences between the empirical and theoretical sample distribution was examined by means of chi-square goodness-of-fit test. The significance level was set at p=0.05.

**Results:** Analysis did not show any significant differences in the access to treatment with intravitreal injections of vascular endothelial growth factor inhibitors between the rural and urban patients. Urban males and females living in the rural areas received treatment statistically more often (p=0.05). No significant differences were observed with respect to either the waiting time for a visit in a specialist outpatient department, nor the duration of waiting for treatment. Patients from the rural and urban areas presented a similar degree of visual impairment, evidencing the advancement of the pathological process.

**Conclusions:** Place of residence has no effect on obtaining treatment by patients. The lack of significant differences in treatment between the rural and urban inhabitants may indicate a sufficient level of ophthalmological care in the area of south-eastern Poland. An improvement in the awareness of hazards resulting from inadequate diet and life style could exert a positive effect on the state of health of rural and urban inhabitants. At the same time, knowledge of the disease and risk of blindness related with this disease would increase alertness among rural and urban inhabitants, and in consequence, accelerate an early diagnosis and implementation of an effective treatment.

### Key words

age-related macular degeneration, AMD, rural area, urban area, anti-VEGF, VEGF-trap

# **INTRODUCTION**

Age-related macular degeneration (AMD) is the main cause of legal blindness among the elderly in industrialized countries [1]. This concerns the population aged over 45-50, when the incidence is 8%. This incidence then increases with age and among 80-year-olds it is 40% [2]. Also, the advanced form of the disease is considerably more often observed in the elderly aged over 70- in 7.1% of patients, while among those aged 50-0.1% [2].

According to the data by the Main Statistical Office, in 2012, in the Lublin Region people aged 65 and over constituted 14.8% of the total population [3]. Compared to the first half of the year 2011, the number of the elderly increased by 7,300, that of adults (aged 15–64) – by 10,200, and the number of children aged under 14 decreased by 7,100 [3]. This evidences the progressing ageing of society. As many as 53.5% of the population lived

in rural areas. The question arises whether patients from the rural and urban areas have the same possibilities in the access to modern methods of diagnostics and treatment of the wet form of age-related macular degeneration.

# **OBJECTIVE**

The objective of the study was evaluation of the demographic profile of patients from south-eastern Poland who received treatment due to the wet form of age-related macular degeneration (AMD).

### **MATERIAL AND METHODS**

Data were analyzed concerning 201 patients with the wet form of age-related macular degeneration (AMD) qualified for the intravitreal injections of vascular endothelial growth factor inhibiting drugs during the period from January – May 2012 in the Department of Vitreoretinal Surgery and General

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Ophthalmology Department at the Medical University in Lublin. The study group consisted of 133 females and 68 males aged 51–92 (mean age 76±8.6). The diagnosis of AMD was confirmed by clinical examination performed by a retina specialist, based on the presence of fatty deposits, called drusen, changes in the retinal pigment epithelium (RPE), geographic atrophy or an active chorioretinal neovascularisation (CNV) accompanied by haemorrhage or retinal/macular oedema. Fluorescein angiography test was performed in selected cases in order to evaluate the activity of changes. Spectral optical coherence tomography was performed in all patients by Zeiss Cirrus HD-OCT imaging system, using macular cube 512×128 and 5 Line protocols.

Analysis of data. Statistical analyses were carried out by computer software Statistica v. 8. Significance of the relationships between the variables was investigated with the use of chi-square test for independence. The differences between the empirical and theoretical sample distribution was examined by means of chi-square goodness-of-fit test.

In addition, the differences were tested between frequencies of replies in the Tables. Due to the considerable number of tests, the Bonferroni correction was applied. The significance level was set at p=0.05.

# **RESULTS**

Patients were divided into four age groups. Figure 1 presents the percentage distribution of patients in individual age groups. Rural inhabitants constituted 30.8% of the total number of respondents, while urban inhabitants – 69.2%. The largest group were patients aged 70–79 (43.3%).

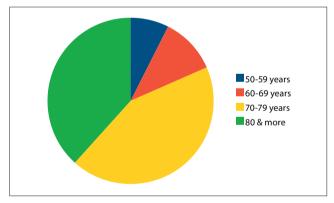


Figure 1. Distribution of patients in four age groups

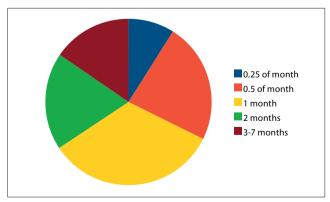


Figure 2. Waiting time for a visit since referral

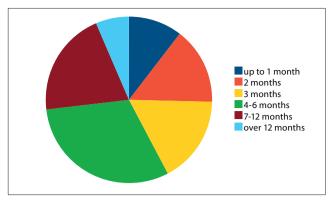


Figure 3. Duration of the deterioration of vision reported by patients

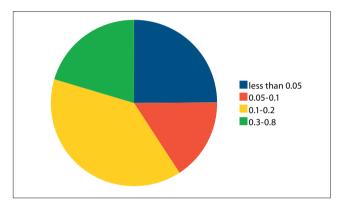


Figure 4. Visual acuity at the moment of qualification for the study

Figures 2–4 demonstrate waiting time for a visit since referral, duration of the deterioration of vision reported by patients, and visual acuity at the moment of qualification for the study.

Table 1 presents the relationship between gender and age of the patients in the study. Table 2 shows the relationships between the patient's place of residence and age, gender, duration of the deterioration of vision reported by the patient, waiting time for a visit, and visual acuity at the moment of qualification for the study.

**Table 1.** Relationship between patients' gender and age.

		Gender (row %)		ala: aaa	_
		Female	Male	— chi-square	р
Age	50-59	53.3	46.7		
	60-69	63.6	36.4		0.054()
	70-79	60.9	39.1	- 4.07	0.254(-)
	80 and more	75.3	24.7	_	

**Table 2.** Relationships between patient's place of residence and age, gender, duration of the deterioration of vision reported by patients, waiting time for a visit, and acuity of vision.

		Place of residence row %		.1.1	
		Urban	Rural	chi-square	р
C	Female	61.7	38.3	10.37	0.001(*)
Gender	Male	83.8	16.2		
	50-59	66.7	33.3	- - 4.07	0.254(-)
Δ	60-69	86.4	13.6		
Age	70-79	64.4	35.6		
	80 and more	70.1	29.9		
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**Table 2** (Continuation). Relationships between patient's place of residence and age, gender, duration of the deterioration of vision reported by patients, waiting time for a visit, and acuity of vision.

	Week	66.7	33.3	- - 2.68	0.612(-)
	2 weeks	78.7	21.3		
Waiting time for a visit	1 month	65.7	34.3		
101 4 11510	2 months	65.8	34.2		
	3-7 months	67.7	32.3		
	Below 0.05	74.4	25.6	- - 0.86 -	0.836(-)
Vienel e enite.	0.05-0.1	63.2	36.8		
Visual acuity	0.1-0.2	68.2	31.8		
	0.3-0.8	69.1	30.9		

### **DISCUSSION**

Age-related macular degeneration (AMD) is the main cause of legal blindness among the population of the elderly in industrialized countries [1]. Two forms of the disease are distinguished: dry and wet. The dry form leads to geographic atrophy of the retinal pigment epithelium (RPE) or accumulation of waste materials in the form of druses. The wet form may be associated with accumulation of the serous fluid under the pigment epithelial detachment (PED) – or the development of choroidal neovascularization (CNV), or retinal angiomatous proliferation (RAP), also defined as retinal-choroidal anastomosis. Both forms lead to damage of photoreceptors, and a considerable visual impairment or loss of central vision. In the wet form, this process takes a more rapid course and in a shorter time may limit the patient's capability for work and independent existence [4].

It is considered that the risk factors of the development of AMD are the aging processes, ischemia, oxidative stress, inflammation, and genetic and environmental factors. As a result, there occurs an accumulation of lipids, especially apolipoproteins in Bruch's membrane, the boundary zone between the choroid and the retina, which causes chronic ischemia and inflammation. Cytokines and growth factors release, including the vascular endothelial growth factor (VEGF), lead to the development of a choroidal neovascular membrane beneath the retina or the retinal pigment epithelial detachment.

Drugs administered intravitreally have become the standard treatment, which has the capability for the binding of VEGF (bevacizumab, ranibizumab, pegaptanib) and protein binding to all isoforms of VEGF-A, and placenthal growth factor (PGF), known as VEGF-Trap (aflibercept). Unfortunately, the treatment has its limitations: it requires the repeating of injections at monthly intervals. Subsequently, the therapy is modified according to the activity of the neovasculaization and acuity of vision evaluated every month during the check-up visits. In the case of the maintenance of an active choroidal neovascularization or its recurrence, the injection is repeated. This procedure is associated with the risk of the development of intraocular infection, with the subsequent procedures. The treatment scheme requires discipline on the part of the patient. This may create greater problems for patients from rural areas who declared the need for assistance with more complex activities, to which, it seems, may be classified a visit to a distant specialist centre [5]. More rare administration of VEGF-Trap at two-month intervals during the first year, and at three-month intervals in the second year allows the reduction in the number of necessary injections in a patient, and decreases the risk of intraocular inflammations.

In many countries, epidemiological studies have been carried out concerning the frequency of occurrence of wet form of AMD [6, 7, 8, 9]. Population studies conducted in Poland, published in 2002, revealed 1,250,000 patients with AMD, including 250,000 individuals with the advanced (late) form of AMD [10]. In 2010, the number of patients in Poland was estimated at 1.2–1.5 million people, including 10–15% of those with the wet form of AMD [2]. The frequency of occurrence of the wet form of AMD in the United Kingdom in 2012 was estimated at 1.2% in patients aged over 50, 25% among those aged over 65, and 6.3% in the group aged over 80 [11].

Age-related macular degeneration (AMD) is the main cause of legal blindness among the population of the elderly in industrialized countries; therefore, an early diagnosis of the disease and the quickest possible implementation of an effective treatment seems to be very important.

According to the data of 2006, large distance and/or problems with transport were not important barriers in reaching the specialist, and created a difficulty for only 19% of respondents. Long waiting time was indicated by 81% respondents [12]. The presented study showed that urban inhabitants usually waited 2 weeks (78.7%) for a visit, whereas the inhabitants of the rural communes – for 1–2 months (34.3–34.2%). Among the respondents, 18 patients (9%) reported to a retina specialist for examination within 1 week from obtaining the referral, 47 patients (23.4%) – within 2 weeks, while 67 (33.3%) – within 1 month. No statistically significant differences were observed between rural and urban patients with respect to waiting time for a visit to a specialist opthalmology department.

In the group examined, 139 patients (69.2%) were urban inhabitants, whereas 62 (30.8%) lived in rural communes. The presented observations are in accordance with the data published in the 'Social Diagnosis' [13]. In 2011, a similar percentage of farmers and inhabitants of cities with a population of more than 100,000 (90% and slightly over 90%) used services of various health care facilities [13]. Also, hospitalizations remained on a similar level among the rural inhabitants and inhabitants of cities with a population of more than 100,000 (25.4% and 23.3–25%, respectively) [13].

However, it is noteworthy that the number of urban patients was twice as large. Possibly, this disproportion is the result of the economic differences between the rural and urban areas. For patients living in rural communes the costs of commuting and the necessity for using the kindness of motorized neighbours may be a certain difficultly. In this, perhaps should be sought the causes for the smaller number of patients from rural areas who reported to a specialist and were qualified for surgical treatment? Studies concerning the smaller independence of the elderly living in rural areas seem to confirm this [5]. Also, according to the analysis by Czapiński and Pank, in 2011, the resignation from the selected types of health services, e.g. purchase of a drug, dental treatment, or a visit to a specialist for financial reasons, more often concerned rural households, compared to urban inhabitants from cities with a population of more than 100,000 (22.6% vs. 15.4-18.1%, 27.3% vs. 20-21.8%; 18.7% vs. 14.4–15.4%, respectively) [13]. While analyzing Małgorzata Latalska, Anna Matysik-Woźniak, Jerzy Bylina, Michał Latalski, Robert Rejdak, Jerzy Mackiewicz, Mirosław J. Jarosz. Wet age-related macular degeneration...

the categories of place of residence, the average expenditures for treatment and examinations were the highest among inhabitants of the largest cities, while the lowest – among the inhabitants of small towns and rural areas [13].

Simultaneously, Poles evaluated their entire life in more positive terms, as many as 80% of respondents declared the feeling of happiness [14], and satisfaction with own state of health also increased [13]. Nevertheless, females continued to evaluate their state of health more negatively, and devoted more attention to its maintenance [13]. Similarly, in the presented study the majority of patients were women. Females from the rural communes were treated statistically more frequently, whereas males who received treatment more often lived in urban areas. This difference was statistically significant (Tab. 2).

In addition, females aged over 80 received treatment most often (75.3%), while among males, younger males aged 50–59 (46.7%) were most frequently treated (Tab.1). In the studies by Zagozdzon et al., urban females consulted a specialist about their complaints more often than rural females (37% vs. 29.7%) [15].

According to the social analysis, the most important factor explaining the general psychological wellbeing of Poles was age [14]. In Poland, a positive relationship is observed between age and depression. The intensity of the symptoms of psychological depression increases with almost every subsequent year [14]. There are studies which confirm a poorer psychological health of women living in rural areas, compared to urban women [15]. The progressing visual impairment caused by the wet age-related macular degeneration also increases the patient's feeling of hopelessness, limits independence and leads to depression [2, 16]. Own observations confirmed a high percentage of the elderly among the patients treated, and the domination of females in the group aged 60 and over.

Physical activity is the factor which is conducive to both physical and psychological health. The positive effect of exercises is considerably higher in females; however, only with a limited number of sports practiced [14]. More than two types of sports activities increase depression rates in females [14]. According to the data by the Main Statistical Office, among the inhabitants of the Lublin Region, in the population group aged over 65, females constituted 18%, while males – 11.4% [3]. In the presented study, women constituted 66.2% of patients who received treatment. Similarly, according to the studies by British researchers, advanced forms of AMD, including the wet form of AMD, were considerably more often observed in females [11].

With age, a decrease is also noted in the efficacy in performing the activities of daily life, more so in individuals who are single [5]. In addition, the elderly from the rural areas of the Rzeszów Region showed a lack of independence and need for assistance from others within walking distances, except for short walks [5]. Usually, they were burdened with one or more disorders, and only approximately 20% of them reported complete efficacy in performing complex activities of daily living [5]. Can this explain the smaller number of patients at an advanced age from the rural areas?

According to own observations, the largest number of rural patients were aged from 70–79 (35.6%), whereas the patients from urban areas were younger, most often aged from 60–69 (86.4%). Patients aged 80 and over were most frequently urban inhabitants. However, rural patients did not

have a worse acuity of vision at referral, which may confirm a similar degree of advancement of the disease (Tab. 2).

Social analyses show that in general, the category of place of residence, socio-occupational status, housing conditions, maintaining children, or cigarette smoking exert a very slight effect on the indicators of psychological wellbeing of Poles [14]. Probably for this reason the differences between the rural and urban inhabitants observed in the presented study were statistically insignificant.

According to the studies by Croatian researchers, exposure to the sun among farmers and fishermen was significantly related with the more frequent occurrence of AMD [17]. In the presented study, respondents from the rural areas constituted a minority – 30.8%. A smaller number of patients with the wet form of AMD from rural areas might have been related with the beneficial effect of a healthier diet, rich in vegetables, and physical effort on the state of the organ of vision. Is this so, for sure? Statistical analyses, which show a high mortality due to cardiovascular diseases among rural inhabitants, seem to contest this hypothesis [3]. In the first half of 2012, in the Lublin Region, 61.1% of the total number of deaths were registered in the rural areas [3]. Mortality among males was higher, and constituted 51.8% of the total number of deaths [3]. In 2010, mortality due to cardiovascular diseases was the highest in the rural areas, and in the Lublin Region [18]. Also, mortality due to accidents, injuries and poisonings was higher in the rural than urban areas [18]. In the light of the presented data, it seems that living in a rural area no longer exerts a protective effect on the health of the inhabitants. This; however, does not explain the smaller number of patients with the wet form of AMD from the rural areas. Economic limitations seem more probable, to which Czapiński and Panek drew attention in 'Social Diagnosis' [13].

## **CONCLUSIONS**

The lack of statistically significant differences between the rural and urban inhabitants receiving treatment allows the belief that opthalmologic care in south-eastern Poland is adequate.

It seems that a higher awareness of the risks resulting from inadequate diet and life style could positively affect the state of health of the rural and urban population. Simultaneously, knowledge of the disease and risk of blindness related with AMD would increase alertness of rural and urban inhabitants, which could facilitate an early diagnosis and implementation of an effective treatment. The goal should be the provision for patients the longest possible useful acuity of vision, which would allow the continuation of occupational activity, and frequently even independent existence.

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