PREVALENCE AND CAUSES OF VISUAL IMPAIRMENT AND BLINDESS IN HUNGARY, TELEMEDICAL SCREENING OF DIABETIC RETINOPATHY

PhD Thesis

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INTRODUCTION

According to the latest WHO (World Health Organization) survey data, 253 million people are visually impaired worldwide, of whom 36 million are blind. The population aged 50 and over represents 82% of blind people. Hungary has also joined the Vision 2020 initiative launched in 1999 by the WHO and IAPB (International Agency for the Prevention of Blindness) with the aim of eliminating avoidable blindness and significantly reducing the number of blind people by 2020. However, due to the lack of reliable epidemiological data, no monitorable changes can be achieved.

For this reason, an internationally accepted standard methodology has been developed to provide a comprehensive, nationally representative population-based epidemiologic data. The Rapid Assessment of Avoidable Blindness (RAAB) survey is relatively inexpensive, it takes a short time as it only includes population over 50 years of age where the prevalence of visual impairment is the highest, and therefore a smaller population sample is required. In many countries, the RAAB survey has been successfully carried out, in Europe only in Moldova and in a region of Russia. We thought it could be an ideal way to replace the missing epidemiological indicators in our country.

In addition, we found it essential to develop a strategy for screening diabetic retinopathy (DR), in order to prevent the progression to severe stages leading to

blindness, as DR is an important cause of avoidable blindness and its prevalence is increasing also in Hungary.

The non-mydriatic (NM) fundus telemedicine system was selected as it has been gaining importance in developed countries since the early 2000s. Its introduction and development eliminated the discomfort and risks due to pupil dilation with good screening results.

Screening for DR does not require comprehensive examination in mydriasis by an ophthalmologist, as digital fundus images can be made without pharmacological dilation of the pupil by trained staff, and the images can be assessed in a distant reading center.

Telemedical screening systems using non-mydriatic fundus cameras have already been implemented successfully in many developed countries worldwide. In England, The NHS Diabetic Eye Screening Programme (NDESP) reached a very high screening coverage, providing free-of-charge fundus photography for diabetic patients older than 12 years.

Several international studies have analysed the cost-effectiveness of DR screening in terms of quality-adjusted life years (QALY). Ophthalmological screening and treating DR is the most effective medical procedure surpassing even coronary bypass surgery or haemodialysis. According to some estimates, based on the average European prevalence of blindness among patients with diabetes, with the implementation of a suitable screening program, the prevalence of diabetic blindness in Europe could be reduced from 3% to 1%.

AIMS

Due to the lack of epidemiological data and the emerging epidemic of DR which were already mentioned in the introduction, the aims of my doctoral work were:

1. To adapt the standard RAAB methodology to Hungarian circumstances. To gain representative epidemiological indicators about visual impairment and blindness.

2. To examine the causes of visual impairment and blindness: to assess the prevalence of avoidable and non-avoidable causes of visual impairment among 50 years or older people.

3. To develop and test a telemedicine model in Hungary, which could significantly reduce the prevalence of avoidable blindness.

4. To test a telemedical screening system in the field of ophthalmology, representing a starting point of an extended countrywide retinopathy screening program.

PATIENTS AND METHODS

1. RAAB+DR survey

The internationally accepted RAAB standard protocol was used for our survey to gain reliable epidemiological data in relatively short period of time.

A representative sample size of 3675 was selected with the help of the RAAB software in 105 census enumeration areas (EA) countrywide used in the national census of 2011 by the Hungarian Central Statistical Office.

The fieldwork was conducted between April and July 2015 by five survey teams with the approval of the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (TUKEB 234/2014). The survey teams included an ophthalmologist, an ophthalmic assistant, a nurse, plus a driver and a local helper in every survey area.

A 5-day-long training programme was organised before the fieldwork by Dr. Hans Limburg (ICEH, International Centre for Eye Health — Consultant) at the Department of Ophthalmology Semmelweis University with the participation of the survey teams, and at the end of the course, inter-observer variation (IOV) assessments were conducted until good to excellent agreement was achieved for visual acuity test, lens assessment, main cause of visual impairment and DR grading. The aim of the training was to achieve at least 75% IOV Kappa.

A total of 3523 participants were examined in their own households in the previously selected 105 EAs. Within each selected EAs, eligible households were selected using compact segment sampling (a special method of random sample selection).

Visual acuity (VA) was measured by using a simplified, portable Snellen tumbling E-chart with the available correction, and pinhole vision was also measured for eyes presenting VA less than 0.5.

Participants were categorised according to the VA in the better eye with the available correction (PVA, Presenting visual acuity) using the classification of visual impairment in accordance with the International Classification of Diseases (ICD-10) and the revision proposed by WHO: normal vision is considered if PVA $\geq$ 0.5, early visual impairment (EVI) refers to PVA < 0.5-0.3, moderate visual impairment (MVI) refers to PVA < 0.3-0.1, severe visual impairment (SVI) refers to PVA < 0.1-0.05 and blind refers to VA < 0.05.

Examination of the anterior segment, the lens, and the fundus was performed without pupil dilation using direct ophthalmoscope. All of the participants underwent a finger-prick random blood glucose (RBG) test using digital glucose meter, and were classified as having diabetes if they had a previous diagnosis of this condition, if they received diabetic medication or if they had RBG level of 200 mg/dl or more. Participants assessed with diabetes underwent dilated eye examination at the household in a darkened room with direct and indirect ophthalmoscope using a 20 D lens. The Scottish DR grading system was used for classification.

A survey record form was filled in for each participant during the fieldwork, which were reviewed and cross-checked at the end of the day and these data were uploaded to the RAAB software.

2. *Telemedicine model - pilot study*

   a. <u>Fundus photography with non-mydriatic fundus camera</u>

   A pilot study was carried out in cooperation between the Department of Ophthalmology, Semmelweis University and the 2nd Department of Internal Medicine, Semmmelweis University in order to evaluate the feasibility of the NM fundus camera in non-ophthalmological settings in Hungary.
   A total of 502 eyes of 251 patients with diabetes were photographed using the Topcon TRC-NW200 NM fundus camera installed at the 2nd Department of Internal Medicine, and the images were transmitted to the Department of Ophthalmology for grading via safe network.
   Detailed medical history was obtained by filling in a table with anamnestic data before the fundus photography.
   Fifty-nine patients with type 1 diabetes (T1DM) and 192 patients with type 2 diabetes (T2DM) were examined in our pilot study (108 male, 143 female) with a mean age of 57.1 ± 14.9 years (mean $\pm$ SD).

We examined inpatient internal medicine patients with diabetes at the 2nd Department of Internal Medicine who gave their written consent to participate in the study. The study was approved by the Semmelweis University Regional and Institutional Committee of Science and Research Ethics (TUKEB 41/2008). Three-field 45° non-stereoscopic images per eye were taken of the central, nasal and superotemporal areas of the retina in accordance with several international recommendations (NM method).

b. <u>Examination in mydriasis</u>

After non-mydriatic photography (NM group), 28 randomly selected patients were also examined for a comparative study in mydriasis by an ophthalmologist (O group) and were photographed in mydriasis (M group) with a fundus camera at the Department of Ophthalmology as well.

The results of each method were evaluated by two independent graders, ophthalmologist specialists (A- and B grader). Diabetes-related lesions of the fundus and the presence of diabetic retinopathy were assessed.

Results of the ophthalmic examination were also transferred back to the Diabetes Centre via safe internet network, and the patient received a report by mail.

The stage of retinopathy, therapeutic suggestion, the date of next control and the need for additional diagnostic tests were determined in accordance with the International (Preferred Practice Pattern of American Academy of Ophthalmology) and the Hungarian ophthalmological recommendations based on the fundus

photos, the stage of retinopathy, the presence of maculopathy and the duration of diabetes mellitus. Patients with abnormal fundus images or ungradable images (e.g. cataract, myopia) were called back for conventional ophthalmic examination in pupil dilation at the Department of Ophthalmology.

3. *Hungarian telemedical DR screening*

At the launch of the DR screening system, Topcon TRC-NW300 non-mydriatic cameras were installed and operated in twelve optical stores countrywide, and fundus images are taken by trained staff without pharmacological dilation of the pupil. The Hungarian telemedical DR screening program was launched at the Semmelweis University in collaboration with the Hungarian Diabetes Association and the First Hungarian Opticians Ltd.

Fundus photographs made in optical stores are being transmitted over a web-based safe network to the Reading Center based in the Department of Ophthalmology, where the two-level assessment of the fundus images is based on UK NSC (National Screening Committee) retinopathy grading standard. Assessment of the images can be carried out on tablets with retina display after connection to a suitable Internet network anywhere in the world.

Results are sent back via the same network to the optical stores. Photographs are saved and archived for 10 years in the system, so during the evaluation, the graders can monitor the changes, the possible progression of the retinopathy.

A total of 2100 examination of 1830 diabetic patients have been conducted so far, with a mean age of 53.6 ± 14.4 years (mean $\pm$ SD) and with a mean diabetes duration of 10.3 ± 8.5 (mean $\pm$ SD) years.

4. *Statistical analysis*

During the RAAB+DR survey, the special RAAB software (version 6) was used for automatic data analysis and generation of reports.

SPSS Statistics and Statsoft Statistica were used for running the statistical tests. For the data analysis we used both parametric and non-parametric tests, based on the Shapiro-Wilk tests needed to establish normalities. We used Student's T-test, chi-square test, Mann-Whitney U, Kruskal-Wallis test, and correlation analyses.

Intermethod and intergrader agreements were determined using Kappa statistics.

RESULTS

1. RAAB+DR survey

We successfully examined 3523 of the previously planned 3675 eligible participants. Seventy-one people were absent (1.9%), 80 refused to participate (2.2%), and one was not able to do the tests because of his physical condition. Compared with the 2011 census data, the age group 50-59 was slightly underrepresented in our study sample, while the age group 70-79 was minimally over-represented.

The standardized prevalence rate of bilateral blindness was 0.9% (0.9% in males and 1.0% in females). The prevalence of severe visual impairment (SVI), moderate visual impairment (MVI) and early visual impairment (EVI) were 0.5%, 5.6% and 7.5%, respectively. Statistically significant difference between the sexes was found only in the category of MVI, namely the prevalence of MVI was significantly higher in females than in males (6.5 vs. 4.0%).

The prevalence of visual impairment and blindness increased exponentially with age: it was the lowest (2.3%) in the age group 50-59 (2.0% MVI, 0.1% SVI and 0.2% blind), which increased by age group 60-69 (2.3% MVI, 0.0% SVI and 0.8% blind) to 3.1%, and by age group 70-79to 8% (7.2% MVI, 0.2% SVI and 0.6% blind). The age group 80+ had the highest prevalence of blindness and visual impairment, 17.2% (10.6% MVI, 3.2% SVI, and 3.4% blind).

The main causes of blindness among people aged 50 years or older were age-related macular degeneration and 'other posterior segment diseases' (both with 27.3%), followed by cataract (21.2%), glaucoma (12.1%) and DR (6.1%). That is, posterior segment eye diseases were responsible for 72.7% of bilateral blindness.

Cataract was the leading cause in all of the visual impairment categories (EVI: 35.3%, MVI: 49.7% SVI: 42.6%). Uncorrected or poorly corrected refractive errors were responsible for 23.9% of MVI cases and 40.7% of EVI cases.
45.5% of bilateral blindness and visual impairment was considered avoidable, of which 21.2% could be treated and 24.2% could be prevented by appropriate prevention. Cataract Surgical Coverage (CSC) for eyes was 90.7%.

2. Telemedicine model - pilot study

Evaluating the fundus images of 502 eyes of 251 diabetic patients, no retinopathy was found in 74.5% and DR was detected in 15.5% of cases: 13.55% mild/moderate non-proliferative, 0.59% severe non-proliferative DR, and 1.39% proliferative DR. The rate of ungradable fundus photos was 10.1%.

After the screening, 37 patients (25%) were referred to the Department of Ophthalmology for a comprehensive eye examination for either DR and/or non-gradable photographs.
In most of the cases referred because of the presence of DR, there were no differences in diagnoses, one stage

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lower DR was assessed in only three cases. Eight eyes (1.59%) required laser treatment, and five cases needed vitrectomy (0.99%).

Comparing the results of the examinations carried out with the three different methods (NM-, M-, O method), we found maximal agreement between NM and M method assessed by both graders (kappa=1.0). Intergrader agreement with NM method was also high with kappa=1.0. Based on the results of the traditional ophthalmological fundus examination in mydriasis (O method), there were no misdiagnosed cases nor with the NM-, neither with the M method.

3.   *Hungarian telemedical DR screening*

A total of 1830 patients underwent 2100 examinations using NM fundus cameras located in optical stores. 91.1% of the images were gradable and 8.9% of them were ungradable.

With NM imaging, no retinopathy was found in 67.6%, DR was detected in 32.4%: 28.3% mild non-proliferative, 3.3% moderate/severe and 0.8% proliferative DR. Among the diabetic patients, 5.5% had maculopathy.

CONCLUSIONS

Our study is the first comprehensive population-based, visual impairment related ophthalmic survey performed in Hungary.

We have successfully adapted the RAAB methodology to Hungarian relations, and proved that after appropriate preparations, this survey can be carried out in developed industrialised countries, either.

Based on our results, the age and sex adjusted prevalences were lower than expected based on earlier WHO estimates, but higher than prevalences of blindness, SVI, MVI found in high-income countries.

The leading causes of blindness and visual impairment were AMD and other posterior segment diseases, and DR was also one of the most common causes. These results are consistent with trends in developed countries,that is, posterior segment diseases are likely to grow in importance as causes of visual impairment and blindness. This should be taken into account in the future planning and developing of ophthalmic care services.

According to our results, 45.5% of blindness was avoidable, which makes it urgent to develop secondary preventive eye care services in Hungary.

The high CSC indicates that the Hungarian cataract surgical care is adequate and most of the cases requiring surgery are detected and delivered in a timely manner. The number of cataract surgeries still has to be further

increased, as cataracts remained the leading cause of visual impairment (SVI, MVI, EVI) in all three categories.

The high prevalence of DR found in our RAAB survey and in our pilot study justifies the need to implement a nationwide telemedical DR screening system in Hungary.

Our study is the first pilot telemedical system carried out in the field of ophthalmology. After testing the network using a NM fundus camera in a clinical setting, we found it ideal for telemedical screening of the Hungarian diabetic population.
Based on our results we can conclude that the telemedical DR model is a suitable starting point for a countrywide DR screening system, which is essential to develop because of the constant increase in the number of people with diabetes and the demographic changes.

By establishing a screening system with an extensive countrywide coverage, the regular ophthalmic control of diabetic patients could be available, and with the necessary treatment options, effective prevention could be ensured with relieving of the ophthalmological society.

LIST OF PUBLICATIONS

1. Publications related to the thesis

Szabó, D., Sándor, GL., Tóth, G., Pék, A., Lukács, R., Szalai, I., Tóth, GZs., Papp, A., Nagy, ZZs., Limburg, H., Németh, J.. Visual impairment and blindness in Hungary. Acta Ophthalmol. 2018 Mar;96(2):168-173. doi: 10.1111/aos.13542. Epub 2017 Aug 21.

IF: 3.324

Szabó, D., Fiedler, O., Somogyi, A., Somfai, GM., Bíró, Zs., Ölvedy, V., Hargitai, Zs., Németh, J. Telemedical diabetic retinopathy screening in Hungary: a pilot programme. J Telemed Telecare, 2015. 21(3) p. 167-73.

IF: 1.377

2. Publications not related to the thesis

Németh, J., Szabó, D., Tóth, G., Sándor, G. L., Lukács, R., Pék, A., Szalai, I., Papp, A., Resnikoff, S., Limburg, H. Feasibility of the rapid assessment of avoidable blindness with diabetic retinopathy module (RAAB+DR) in industrialised countries: challenges and lessons learned in Hungary. Ophthalmic Epidemiology, 2018: p. 1-7.

IF: 1.297

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Tóth, G., Szabó, D., Sándor, G. L., Szalai, I., Lukács, R., Pék, A, Tóth, GZs., Papp, A., Nagy, ZZs., Limburg, H., Németh, J.. Regional disparities in the prevalence of diabetes and diabetic retinopathy in Hungary in people aged 50 years and older. [Cukorbetegség és retinopátia diabetica regionális egyenlőtlenségei Magyarországon az 50 éves és idősebb korú lakosság körében. Orvosi Hetilap.] Medical Weekly (Hung.) 2017. 158(10): p. 362-367.

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