Regional analysis of diabetic retinopathy and co-existing social and demographic factors in the overall population of Poland

Type
Research paper

Keywords
diabetes mellitus, epidemiology, diabetic retinopathy, public health, Moran's I statistics

Abstract
Introduction
The aim of our study was to analyze the regional differences in diabetic retinopathy (DR) prevalence and its co-existing social and demographic factors in the overall population of Poland in the year 2017.

Material and methods
Data from all levels of healthcare services at public and private institutions recorded in the National Health Fund database were evaluated. International Classification of Diseases codes were used to identify patients with type 1 and type 2 diabetes mellitus (DM) and with DR. Moran's I statistics and Spatial Autoregressive (SAR) model allowed to understand the distribution of DR prevalence, and its possible association with environmental and demographic exposures.

Results
In total, 310,815 individuals with diabetic retinopathy (DR) were diagnosed in the year 2017 in Poland. Of them, 174,384 (56.11%) were women; 221,144 (71.15%) lived in urban areas; 40,231 (12.94%) and 270,584 (87.06%) had type 1 and type 2 DM, respectively. The analysis of the SAR model showed a higher level of average income and a higher number of ophthalmologic consultations per 10 000 adults in the particular county were the significant factors for the occurrence of DR in the counties.

Conclusions
The analyses of social, demographic, and systemic factors co-existing with DR revealed that the level of income and the access to the ophthalmologic and diabetic service are crucial in DR prevalence in Poland.
Abstract

Introduction: The aim of our study was to analyze the regional differences in diabetic retinopathy (DR) prevalence and its co-existing social and demographic factors in the overall population of Poland in the year 2017.

Material and methods: Data from all levels of healthcare services at public and private institutions recorded in the National Health Fund database were evaluated. International Classification of Diseases codes were used to identify patients with type 1 and type 2 diabetes mellitus (DM) and with DR. Moran’s I statistics and Spatial Autoregressive (SAR) model allowed to understand the distribution of DR prevalence, and its possible association with environmental and demographic exposures.

Results: In total, 310,815 individuals with diabetic retinopathy (DR) were diagnosed in the year 2017 in Poland. Of them, 174,384 (56.11%) were women; 221,144 (71.15%) lived in urban areas; 40,231 (12.94%) and 270,584 (87.06%) had type 1 and type 2 DM, respectively. The analysis of the SAR model showed a higher level of average income and a higher number of ophthalmologic consultations per 10 000 adults in the particular county were the significant factors for the occurrence of DR in the counties.

Conclusions: The analyses of social, demographic, and systemic factors co-existing with DR revealed that the level of income and the access to the ophthalmologic and diabetic service are crucial in DR prevalence in Poland.

Key words: diabetic retinopathy, diabetes mellitus, epidemiology, public health, Moran’s I statistics
Introduction

According to International Diabetes Federation (IDF) the global population with diabetes mellitus (DM) has reached 451 million in the year 2017 (age 18-99) and it is estimated that in the year 2045 this number will increase to 693 million people around the world [1]. We divide complications of DM into macro- and micro-vascular related e.g. macro-vascular- coronary heart disease (CHD), myocardial infarction, peripheral arterial disease (PAD), and stroke; micro-vascular- diabetic retinopathy (DR), and nephropathy [2,3,4]. There are also diabetes induced syndromes like diabetic foot syndrome, which recently has been associated with adverse effects on brain function [5,6]. The incidence of DR is falling probably owing to better management of glucose levels, lipid abnormalities, and hypertension. Nonetheless, DR is still the most vision-threatening complication and the crude prevalence (at all ages) of visual impairment and blindness caused by DR increased significantly between the years 1990 and 2015 with respect to the global population [7,8,9]. Although, there is a massive number of articles concerning prevalence, developing factors, and current treatment strategies of DR, the geographical analysis with advanced statistical methods could result in new interesting conclusions in terms of the origin of the disease and the organization of the healthcare system. And the number of studies showing the geographical analysis of the DR prevalence and co-existing social and demographic factors is limited [10,11,12].

The logic behind using geography to study disease or health care comes from the realization of factors resulting in non-uniformity of disease distribution [13,14,15]. These factors include social, economic, environmental, and genetic ones. All these factors may have spatial distributions influencing the incidence of a disease. Geographic information systems with spatial analytical methods are helpful in the study of health status and health care delivery [16]. That approach is extremely useful in the case of analyzing the outbreaks of contagious diseases like malaria or mumps [17,18]. However, the literature review covers the large use of such methods in case of noncontiguous diseases e.g. leukemia [19]. This approach allows to statistically verify the regions of either extremely high or low prevalence of diseases. In addition, the knowledge of spatial properties and disease patterns allows planning a health care service in a rational manner and meets the needs of patients.

The aim of our study was to analyze the regional differences in diabetic retinopathy prevalence and its co-existing social and demographic factors in the overall population of Poland in the year 2017.
Material and Methods

The present study was co-financed by the European Union funds through the European Social Fund under the Operational Program of Knowledge Education and Development and was a part of the Polish Ministry of Health project “Maps of Healthcare Needs - Database of Systemic and Implementation Analyses” [20,21]. The study design was a nation-wide survey. The Republic of Poland is the largest Central European country with a population of 38,422,346 people (in the year 2017), mostly of middle socio-economic status [22]. The area of Poland is 312,679 square kilometers and Poland is divided into 16 voivodships and 380 counties in terms of administrative division. The population data and socio-demographic information of the counties for the year 2017 were obtained from the Central Statistical Office of Poland [22]. For the purpose of this study, the Polish National Health Fund (NHF) database, the only public insurer in Poland, was retrospectively analyzed [23]. The NHF database records data from all levels of healthcare services at public and private institutions in Poland and compiles both medical and personal data including age, sex, place of living, and identification number (PESEL) of each individual patient. The medical data include diagnoses coded according to the International Classification of Diseases, 10th Revision (ICD10) and unique NHF codes. The NHF database also contains the records of all medications purchased by the Polish patients in pharmacies that were reimbursed by NHF. In the first part of the study, for each individual patient in the years 2013-2017, diabetes mellitus (DM) type 1 and type 2 was identified with ICD-10 codes E10 and E11, respectively. All diagnoses were then confirmed if the patient purchased antidiabetic drugs (and/or insulin) during the study period. Following that, diabetic retinopathy (DR) was identified in DM patients using the ICD-10 codes H36.0, H36.8, and H35.8 during 2013-2017. The overall prevalence of DR and DM in Poland in 2017 was the total number of individuals who were alive on 31st of December 2017 and occurred in the NHF database during 2013-2017 with DR and DM, respectively.

For statistical analysis, the socio-demographic data of all patients including age, sex, and place of residence were anonymously recorded. In the first part of the statistical analysis, the spatial analysis has been conducted. That approach provides opportunities to understand the spatial distribution of diseases, and the possible association between its environmental and demographic exposures [13,17,18,19]. There are numerous methods for testing clustering in data. The method, which is widely used by epidemiologists was
the one developed by Patrick Alfred Pierce Moran [11]. Moran’s Index is a weighted correlation coefficient that is used to measure deviation from spatial randomness and has a form as below:

\[ I = \frac{N}{\sum_i \sum_j w_{ij}} \sum_i \sum_j w_{ij} (x_i - \bar{x})(x_j - \bar{x}) \]

\[ \sum_i (x_i - \bar{x})^2 \]

where N is a number of spatial units, in this study denotes a number of counties (380); \( x_i, x_j \) are values of a variable of interest (retinopathy prevalence per 10 k population) for \( i, j=1,\ldots, 380 \), \( \bar{x} \) is a mean of variable of interest, \( w_{ij} \) denotes an element of spatial weights matrix. \( w_{ij} \) is zero either when \( i = j \) or two counties \( i, j \) are totally separated in terms of the common border (queen neighbourhood). When two counties share a border, the weight is equal to 1. The values of \( I \) range from -1 (perfect dispersion) to +1 (perfect clustering) [24,25,26].

The next part of the statistical analysis was to identify the variables explaining the differences in retinopathy prevalence values among counties. It was important to consider a spatial approach because the assumption of observation’s independence is no longer valid. Due to this argument Spatial Autoregressive (SAR) model has been used. The SAR model is an OLS (Ordinary least squares) method with correction related to autocorrelation defined by the spatial weights matrix [19]. The factors used to explain the differences in the prevalence in diabetic retinopathy in the counties of Poland were grouped into 3 categories: epidemiological, sociodemographic, and accessibility/quality. All details of the factors used to explain the differences in the prevalence of diabetic retinopathy in the counties of Poland are presented in Table I. To build the model, each variable has been transformed i.e. divided by the median value of the variable. That modification enables to interpret the results of the model in terms of median values, what is especially useful, in particular when the factors are in different scale. Before model building the normality of the dependent variable has been verified. Box-Cox transformation and Shapiro-Wilk test (p value=0.08) revealed that the logarithmic transformation met the assumptions of normality. In addition, the collinearity of explanatory variables has been verified. The value of Variance Inflation Factor (VIF) was of value up to 3 for each variable that indicated the lack of collinearity. The adjusted \( R^2 \) has been used to validate the goodness of the model. R statistical software V. 3.5.2, including package spdep [19], was used for all analyses. The study adhered to the tenets of the Declaration of Helsinki for research involving human
Results

In total, 310,815 individuals with diabetic retinopathy (DR) were diagnosed in the year 2017 in Poland. Of them, 174,384 (56.11%) were women; 221,144 (71.15%) lived or had lived in urban areas; 40,231 (12.94%) and 270,584 (87.06%) had type 1 and type 2 DM, respectively. Since, 99.8% of individuals in DM population were adults, all presented statistics were calculated per adult population in Poland. Figure 1 shows the diabetic retinopathy (DR) prevalence per 10 thousand population in the counties of Poland in the year 2017.

There are groups of counties of either high or low value of retinopathy prevalence in Poland in terms of quantiles values. The spatial dependence between the counties has been statistically verified with Moran Index I (Figure 2). The I value equals 0.18 and is statistically significant (p<0.001). The ‘hot spot’ (the counties of high retinopathy prevalence are surrounded by counties of high retinopathy prevalence) and ‘low spots’ (groups of counties of low retinopathy prevalence) indicate that the distribution of DR is not random in Poland. The highest DR prevalence occurred in the south-west part of Poland and in many counties of the north and east of Poland. The lowest DR prevalence occurred mainly in the center of Poland.

DM prevalence in Poland also is demonstrated on the map in Figure 1.

Relatively lower values of DM prevalence were found in the eastern part of the country in comparison to the western part. To evaluate the factors of retinopathy occurrence in the counties the SAR model has been built. The descriptive statistics of each variable used in the model are presented in Table II and indicate the differentiation among counties’ values.

The median number of subjects with DM and DR per county was 823.39 and 72.67, respectively. The median of average earnings among counties was about 3146.48 PLN (804.27 USD), whereas the difference between the richest and the poorest county revealed to be of value about 3825.64 PLN (977.86 USD). The median of the number of diabetic and ophthalmologic consultations per 10 k adults were 2736.09 and 713.85, relatively. In addition, access to ophthalmologic and diabetic specialist (measured as a number of
consultations per adult population) varied among counties (Figure 3). The analysis of the SAR model showed that average earnings were a significant factor for the occurrence of DR in the counties (Table III). The increment of income by 10% in relation to the income median increases retinopathy prevalence by 10.9% in relation to the retinopathy median. In terms of absolute values, the increase of income of about 300 PLN (76.73 USD) in counties causes the increase of DR prevalence by 8 per 10 000 adults. DR prevalence in the county was also highly influenced by DM prevalence (82 per 10 000 adult people higher DM prevalence in the county causes 7 per 10 000 adult people higher DR retinopathy). Furthermore, the accessibility to medical services proved to be statistically significant. The increase in the number of ophthalmologic consultations founded by NHF database per 10 000 adults in a county of 10% of median (273) resulted in the increase of 2.2% of DR prevalence median (1.6 per 10 000 adults). On the other hand, the limited access to the diabetic service has the effect of the decreased occurrence of DR in the counties. The goodness of the model has been verified with $R^2$ which was equal to 0.21.

**Discussion**

The vascular (micro and macroangiopathy) complications of DM are the main cause of morbidity and mortality of DM population. These complications like blindness, chronic renal insufficiency, and amputation of the lower limb lead to increased mortality rates. In addition, DM is an important risk factor for the onset of Alzheimer’s disease, cognitive functional decline and reduced health related quality of life [5,6]. The application of spatial analytical methods is wildly common among studies concerning the distribution of occurrence of both, contiguous and noncontiguous diseases [13,17,18,19 ]. However, the authors did not find any study focusing on spatial analysis of diabetic retinopathy on the national level. This study is based on the overall population of Poland in the year 2017 and presents the geographical characteristics of the prevalence of diabetic retinopathy and co-existing social, demographic, and systemic factors on the county level. The given score of Moran Index (0.18, p-value<0.01) indicates that the null hypothesis of complete randomness of the distribution of DR prevalence in Poland is rejected, and it suggests the presence of cluster patterns. The high DR prevalence occurred in the south-west part of Poland, where hotspot counties have been noticed. The low DR prevalence occurred mainly in the center of Poland. The SAR model analyses revealed that the most influential factor on DR prevalence in the counties was
DM prevalence, which in Poland is not random as well (I= 0.21, p-value < 0.01). In addition, in 2017, relatively lower values of DM prevalence were in the eastern part of the country in comparison to the western part. The analysis of SAR model also showed that the average income was the most significant socioeconomic factor for the occurrence of DR in the counties. A higher level of average income resulted in a higher prevalence of DR in the counties of Poland. In contrast, the results of the study from the United Kingdom showed socioeconomic deprivation was associated with the increased DR prevalence in patients with type 1 DM. However, this association was not confirmed in patients with type 2 DM [27]. The results of other studies from Europe showed in Spain socioeconomic status was not significantly associated with DR [28]. But the multicenter EURODIAB IDDM Complications study showed a higher prevalence of proliferative DR in men with lower educational qualifications compared with those with a higher level of education [29].

The analysis of the socioeconomic status and global diabetes prevalence showed that diabetes prevalence rises with increasing socioeconomic status in developing countries, and this is reversed in developed countries [30]. However, Poland is a middle-income country [31], our pattern of DR and DM prevalence is similar to that found in developing countries. In our study, DR prevalence in the counties was not significantly associated with place of residence, which was in agreement with the results of the study from the United Kingdom, which showed that distance to medical services was not associated with attendance in DR screening [32]. When it comes to the variables describing the access to the medical service, the higher number of ophthalmological consultations have the effect of the increased occurrence of DR in the counties. The regions with a greater number of ophthalmologic consultations per population are characterized by a greater number of ophthalmologists. This, in turn, indicates the DR diagnoses are less often in counties with limited access to ophthalmologists, which agrees with the results of previous studies from the United Kingdom [27]. However, the higher number of consultations in diabetes specialists influences the decreased DR prevalence, the number of diabetic consultations in General Practitioners (GPs) does not affect the DR occurrence in the counties. It shows the differences in the effectiveness of diabetic care in GPs and in diabetic specialists. In Poland, there are counties where the number of diabetic consultations is exceptionally low and high, which indicates the great inequalities in diabetic healthcare in the country. Knowing the hotspot and lowspot locations of DR prevalence could influence the prevention program of DR. One of the possible actions which can improve the access of DM patients to ophthalmologists is the introduction of telemedicine. In the aspect of DR, telemedicine-based screening of
DM patients incorporating artificial intelligence technology has the potential to facilitate more widespread and cost-effective screening, particularly in low- and middle-income countries. Early results showed high diagnostic sensitivity and specificity of such systems in DR screening programs in many countries. [33,34,35]

Limitations of the study concern mostly data used. NHF’s data include data provided to all insured people in Poland (in 2017 approx. 89% of the whole population). The data does not include information about medical services and drugs purchased by not-insured people and finances out of pocket. However, such mistakes likely had only a minor impact on the study findings, because not-insured people are rather poor and do not purchase a lot of medical services in Poland. The population size and national recruitment are the most important strengths of the present study.

Conclusions

In summary, geographic information systems with spatial analytical methods are helpful in the study of health status and health care delivery. All social, economic, environmental, and genetic factors may have spatial distributions influencing the prevalence of a particular disease. Our study showed statistically significant differences in the prevalence of DR and DM in the overall population of Poland in the years 2013 – 2017 on the regional level. This is the first nationwide study of DR in Central Europe on such a low administrative level. The presented results indicate that the high DR prevalence occurred in the south-west part of Poland and the low DR prevalence occurred mainly in the center of Poland. The analyses of co-existing social, demographic, and systemic factors revealed that the level of income and access to the ophthalmologic and diabetic service are crucial in DR prevalence.
References


**Table 1** The factors used to explain the differences of the prevalence of diabetic retinopathy in the counties of Poland

<table>
<thead>
<tr>
<th>Variable</th>
<th>Description</th>
<th>Category</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRprevalence</td>
<td>DM prevalence per 10 k adults in a county</td>
<td>explanatory variable</td>
</tr>
<tr>
<td>Income</td>
<td>The median of income in a county</td>
<td>socio-demographic</td>
</tr>
<tr>
<td>Age65+</td>
<td>Share of population aged 65 or more in a county</td>
<td>socio-demographic</td>
</tr>
<tr>
<td>UrbanLiving</td>
<td>Share of population living in the urban area in a county</td>
<td>socio-demographic</td>
</tr>
<tr>
<td>DMprevalence</td>
<td>DM prevalence per 10 k adults in a county</td>
<td>epidemiological</td>
</tr>
<tr>
<td>DIABconsultations</td>
<td>The number of diabetes specialist consultations in NHF database per 10 k adults in a county</td>
<td>accessibility/quality</td>
</tr>
<tr>
<td>OPTconsultations</td>
<td>The number of ophthalmological consultations in NHF database per 10 k adults in a county</td>
<td>accessibility/quality</td>
</tr>
<tr>
<td>DIABconsultationsGP</td>
<td>The number of GP’s diabetic consultations per 10 k adults in a county</td>
<td>accessibility/quality</td>
</tr>
<tr>
<td>OPHTdistance</td>
<td>The average distance to ophthalmologist in a county. The distance was defined by the shortest distance between the center of a county of patient’s residence and center of a county of ophthalmological service</td>
<td>accessibility/quality</td>
</tr>
<tr>
<td>DIABdistance</td>
<td>The average distance to diabetes specialist in a county. The distance was defined by the shortest distance between the center of a county of patient’s residence and the center of a county of diabetic service</td>
<td>accessibility/quality</td>
</tr>
</tbody>
</table>
Table II The primary statistics of variables used in the SAR model

<table>
<thead>
<tr>
<th>Variable</th>
<th>Minimum in the counties</th>
<th>Median in the counties</th>
<th>Maximum in the counties</th>
<th>SD in the counties</th>
</tr>
</thead>
<tbody>
<tr>
<td>DRprevalence</td>
<td>10.10</td>
<td>72.67</td>
<td>373.96</td>
<td>64.31</td>
</tr>
<tr>
<td>Income</td>
<td>2487.05</td>
<td>3146.84</td>
<td>6312.69</td>
<td>435.27</td>
</tr>
<tr>
<td>Age65+</td>
<td>0.11</td>
<td>0.16</td>
<td>0.26</td>
<td>0.02</td>
</tr>
<tr>
<td>UrbanLiving</td>
<td>0.00</td>
<td>0.46</td>
<td>1.00</td>
<td>0.27</td>
</tr>
<tr>
<td>DMprevalence</td>
<td>527.98</td>
<td>823.39</td>
<td>1757.17</td>
<td>111.95</td>
</tr>
<tr>
<td>DIABconsultations</td>
<td>45.13</td>
<td>713.85</td>
<td>4154.73</td>
<td>615.13</td>
</tr>
<tr>
<td>OPTconsultations</td>
<td>146.63</td>
<td>2736.09</td>
<td>11055.81</td>
<td>1660.21</td>
</tr>
<tr>
<td>DIABconsultationsGP</td>
<td>435.88</td>
<td>1909.48</td>
<td>5763.62</td>
<td>733.14</td>
</tr>
<tr>
<td>OPTdistance</td>
<td>0.00</td>
<td>10.83</td>
<td>40.74</td>
<td>6.17</td>
</tr>
<tr>
<td>DIABdistance</td>
<td>0.00</td>
<td>11.34</td>
<td>73.97</td>
<td>9.98</td>
</tr>
</tbody>
</table>
Table III SAR model results for diabetic retinopathy social and demographic risk factors in the counties of Poland.

<table>
<thead>
<tr>
<th>Variable</th>
<th>Coefficients estimate</th>
<th>CI 2.5%</th>
<th>CI 97.5%</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>(Intercept)</td>
<td>0.812</td>
<td>0.745</td>
<td>0.886</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>Earnings</td>
<td>1.109</td>
<td>1.041</td>
<td>1.182</td>
<td>0.001*</td>
</tr>
<tr>
<td>Age65+</td>
<td>1.019</td>
<td>0.963</td>
<td>1.080</td>
<td>0.51</td>
</tr>
<tr>
<td>UrbanLiving</td>
<td>1.000</td>
<td>0.983</td>
<td>1.017</td>
<td>0.995</td>
</tr>
<tr>
<td>DMprevalence</td>
<td>1.110</td>
<td>1.047</td>
<td>1.176</td>
<td>&lt;0.001*</td>
</tr>
<tr>
<td>DIAABconsultations</td>
<td>0.988</td>
<td>0.977</td>
<td>1.000</td>
<td>0.041*</td>
</tr>
<tr>
<td>OPTconsultations</td>
<td>1.022</td>
<td>1.006</td>
<td>1.038</td>
<td>0.007*</td>
</tr>
<tr>
<td>DIAABconsultationsGP</td>
<td>1.005</td>
<td>0.986</td>
<td>1.023</td>
<td>0.619</td>
</tr>
<tr>
<td>OPTdistance</td>
<td>0.993</td>
<td>0.975</td>
<td>1.011</td>
<td>0.428</td>
</tr>
<tr>
<td>DIAABdistance</td>
<td>0.991</td>
<td>0.980</td>
<td>1.002</td>
<td>0.098</td>
</tr>
</tbody>
</table>

*statistically significant
Figure 1 The prevalence of diabetic retinopathy (left) and diabetes mellitus (right) per 10 k population in the counties in Poland in 2017
Figure 2 The analysis of spatial dependence between the counties with Moran Index I

The average value of retinopathy prevalence per 10k population in the neighbour counties

Retinopathy prevalence per 10k population in the county
Figure 3 The number of diabetic consultations (left) and ophthalmologic consultations (right) per 10 k adult population in the counties in Poland in 2017.