

A Study on Multi Stages of Diabetic Retinopathy among Diabetic Patients in Puducherry - Using Markov Chain Model Approach

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Abstract

Objective: To find the various stages of DR by using Markov chain analysis approach and to find the transition of DR. **Methods:** *Study Design:* retrospective study. *Study Population:* Type 2 diabetics patients. *Study Period:* May – June 2012. *Study tool:* Pre-designed and pre-tested questionnaire was used. *Study Variables:* Stages of Diabetic Retinopathy. *Study Subjects:* 200 Patients with various stages of DR were included in this study. *Study Method:* Various stages of DR patients were collected in January 2011 and the stages of the same patients in the year January 2012. *Software used:* MS Excel 2007 for data entry and for analysis SPSS 16.0 version was used. *Statistical Analysis:* Markov Chain Model approach was used to find out the transition of DR. **Results:** Out of 200 patients, 126 (63%) were male and 74 (37%) female. The diabetes patients who had type II diabetes for at least five years, a mean age of 58.80 ± 10.53 years and ranged in the age from 27 to 91 years. In one year transition, the probability of an individual in grade-I to move to grade-II is 0.82 which is very high. In the case of the Transition Probability Matrix (TPM) after a period of 5 years it is observed that, the chance of moving from the other lower grades to the final grade is also fairly high. **Conclusion:** In future, to study the transition of diabetic retinopathy should consider a matrix of estimated transition probabilities,

depending on the population, to judge probabilities of transition between states of retinopathy, for the two groups taken up for study and comparison.

Keywords: diabetic retinopathy, multi stages, Markov Chain analysis, Puducherry

Introduction

Diabetes Retinopathy (DR) is a major health problem throughout the world. Diabetic retinopathy is an important cause of visual impairment [1]. DR is caused by changes in the blood vessels of the retina. It is a serious sight-threatening complication of diabetes. Persons with diabetic retinopathy can suffer significant vision loss [2]. DR is also a major micro vascular complication of diabetes, affects 97% of insulin-dependent diabetes patients and 80% of diabetes patients not receiving insulin who have had diabetes for 15 or more years [3]. DR currently is the leading cause of new cases of blindness in people aged 20 to 74 years in the United States [4].

An increasing prevalence of diabetes is occurring throughout the world. In addition, this increase appears to be greater in developing countries [5]. The progression of DR in successive years is a matter of interest. For the purpose of finding the intensity and progression [6] of DR from one state of severity to another state the Markov process is used. The Transition Probability Matrix (TPM) has been formulated using the data collected. The TPM has been formulated taking a time interval of one year and also a period of five years.

Objectives

- To find the various stages of DR by using Markov chain analysis approach and
- To find the transition of DR.

Materials and Methods

Study Area

A retrospective hospital based study was carried out in Aravind Eye Hospital, Thavalakuppam, Puducherry (UT) during April – June 2012. The data collected at two different point of time of the same DR patients.

Data Collection

In this study, total sample size 200 Diabetic Retinopathy patients were collected by using simple random sampling method. Data were collected by using pre-designed and pre-tested questionnaire. DR patients with age 27 years and above were included in this study. At each visit, a retinal specialist graded retinal findings using a modified Airlie House Classification [7]. 200 patients screening in first time in a particular time period ie., January 2011, then second screening for the same patients after one year and find out the stages of their diabetic retinopathy.

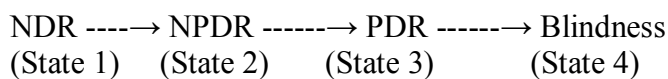
Statistical Analysis:

Two methods of statistical analysis, Markov chains [8] and Markov process [9], were used to determine the Transition Probability Matrix (TPM). The Markov chains [8] is a probability model based on the transition matrix, which can describe the probability of change from one state to another state. In Markov chains, the transition matrix determines the probability of changing from one state to another state using the years. To calculate the transition probabilities for a longer period, then we multiplied the transition matrix by itself as many times as we wanted to predict years in the future. For example, if the transition matrix represents 1 year of transition, we multiply the matrix by itself five times to predict 5 years of transition.

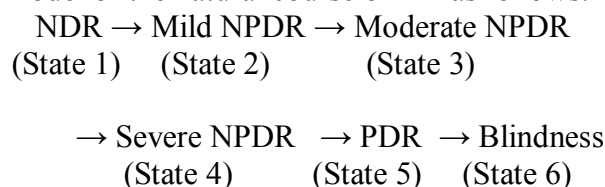
The Markov model, using the Markov process, as described by Kay. R [9], is an extension of Markov chains using the continuous time. This model allows estimation of the transition probability matrix when the data are collected at two different intervals. The Markov process was used to confirm the estimations of the transition matrix initially calculated using discrete times (Markov chains). The term absorbing state is used to refer to a state from which there is no regression. Which is denoted by the stages 5 and 6. The grading of retinal findings was done by a retinal specialist in the retinal center on each visit in a masked fashion without knowledge of the previous retinal classification or other clinical parameters of the modified Airlie House classification system [7] for the worst eye initially. As per the above classification: grade I indicates no retinopathy; grade II indicates micro aneurysms only; grades III and IV indicate intermediate stages of background retinopathy, and grades V and VI indicate pre-proliferative and proliferative retinopathy, respectively[10].

Model for the Natural Course of Diabetic Retinopathy:

In the present study, the four-state Markov chain model for the natural course of DR among type 2 diabetics following the pathway of the proliferative phase was mapped as follows:



Markov model follows a time-homogeneous distribution, using the method of estimating transition probabilities (the probability of progressing from one state to another) described by Kalbfleisch and Lawless [11], and the algebra for transition probabilities referred to by Chen et al. [12]. In this study, we also mapped a six-state Markov chain model of the natural course of DR as follows:



Similarly, we could calculate the transition rate matrix and transition probability matrix for the six-state model of DR. The data was entered in MS Excel 2007 and analyzed by using statistical software SPSS 16.0 version. To predict the probability

of developing DR in a person for one year and for five year by forming a transition matrix and Transition Probability Matrix (TPM).

Results

Out 200 patients, 126 (63%) were male and 74 (37%) female. Among two hundred patients, who had type II diabetes for at least five years, a mean age of 58.80 ± 10.53 years and ranged in the age from 27 to 91 years where seen at the Aravind Eye Hospital, Thavalakuppam, Puducherry (UT). South India.

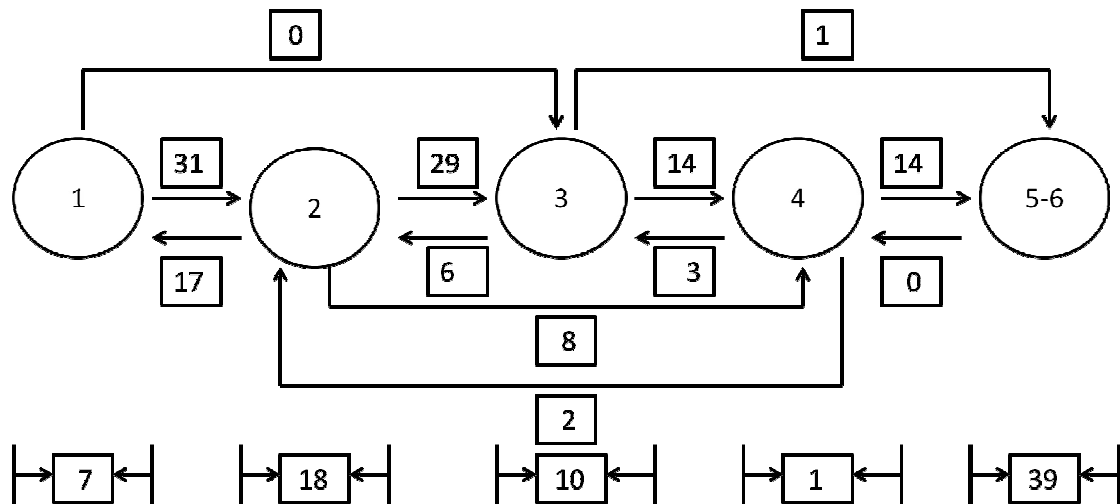


Figure: 1 The numbers in the circles indicate the grade of Diabetic Retinopathy; solid bars with arrows to the right, progression; and solid bars with arrows to the left, regression. Bottom, Number of subject observations per year with no change in grade.

A transition matrix for changes between grades of retinopathy as shown in [Table 1]. It can be seen in [Figure-1] and in the transition probability matrix for one year as shown in [Table 2] that 31 (81.57%) of 38 observations showed progression from grade 1 to 2, and 17 (23.61%) of 72 observations showed regression from grade 2 to 1. Approximately 11 (21.56%) of 51 observations for subjects with grades 3 or 4 retinopathy changed for the better during the year between examinations.

Table: 1 One – Year Transition (Data) Matrix

Severity Grade of Retinopathy at Start	No. of Observations					
	Severity Grade of Retinopathy After 1 Year					
	1	2	3	4	5-6	Total
1	7	31	0	0	0	38
2	17	18	29	8	0	72
3	0	6	10	14	1	31
4	0	2	3	1	14	20
5-6	0	0	0	0	39	39
Total	24	57	42	30	47	200

Table: 2 One – Year Transition Probability Matrix

Severity Grade of Retinopathy at Start	Probability of Observations				
	Severity Grade of Retinopathy After 1 Year				
	1	2	3	4	5-6
1	0.18	0.82	0	0	0
2	0.24	0.25	0.40	0.11	0
3	0	0.19	0.32	0.45	0.03
4	0	0.10	0.15	0.05	0.70
5-6	0	0	0	0	1.00

Discussion

The Transition Probability Matrix (TPM) relating to the transition of individuals from one grade of severity of Diabetic Retinopathy to the other grades after a period of one year. The following observations can be made: The probability of an individual in grade-I to move to grade-II is 0.82 which is very high. But, probability of a person move from grade-I to grade-II was very less after one year by Garg SK et al [3]. It implies that, the chance of the severity of the DR at start is very high. Similarly, the probability of a transition from grade-II to grade-III is 0.40 and from III to IV is 0.45. Again, the probability of transition from grade-IV to the most severe state ie., grade: 5–6 is 0.70 [Table:2]. Therefore, initially the chance of the increase in severity and similarly the chance of an increase at a more developed state were very high. Moreover, the Probability of moving from the other lower states to higher is fairly high. In the case of the Transition Probability Matrix (TPM) after a period of 5 years it is observed that, the chance of moving from the other lower grades to the final grade is fairly high [Table: 3]. Therefore, it can be observed that with the passage of time, the severity of the DR increases.

Table: 3 Five – Year Transition Probability Matrix

Severity Grade of Retinopathy at Start	Probability of Observations				
	Severity Grade of Retinopathy After 5 Year				
	1	2	3	4	5-6
1	0.06	0.19	0.19	0.13	0.32
2	0.04	0.14	0.15	0.10	0.45
3	0.02	0.08	0.09	0.06	0.65
4	0.01	0.03	0.03	0.02	0.86
5-6	0	0	0	0	1.00

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Conclusion

To introduce the preventive strategies such as: control of sugar level, blood pressure, and medical intervention for every year to arrest the progress of DR, it will be worthwhile to have a comparative study on the differences in the progression of intensity of DR for persons under treatment which forms the treatment group and the other one which is the control group. In future, to study the transition of diabetic retinopathy should consider a matrix of estimated transition probabilities, depending on the population, to judge probabilities of transition between states of retinopathy, for the two groups taken up for study and comparison.

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