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Estimating transition probability of different states of type 2 diabetes and its associated factors using Markov model

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ABSTRACT

Aims: Type 2 diabetes is a chronic metabolic disorder and one of the most common non-contagious diseases which is on the rise all over the world. The present study aims to assess the trend of change in fasting blood sugar (FBS) and factors associated with the progression and regression of type 2 diabetes. Moreover, this study estimates transition intensities and transition probabilities among various states using the multi-state Markov model.

Methods: In this study Multi-Ethnic Study of Atherosclerosis (MESA) dataset, from a longitudinal study, was used. The study, at the beginning, included 6814 individuals who were followed during the five phases of the study. FBS, serving as the criterion to assess the progression of diabetes, was classified into four states including (a) normal (FBS < 100 mg/dl), (b) impaired fasting glucose I (IFG I) (100 mg/dl < FBS < 110 mg/dl), (c) impaired fasting glucose II (IFG II) (110 mg/dl < FBS < 126 mg/dl), and (d) diabetes status (FBS > 126 mg/dl). A continuous-time Markov process was used to describe the evaluation of disease changes over the four states. The model estimated the mean sojourn time for each state.

Abbreviations: IGT, impaired glucose tolerance; WHO, World Health Organization; ADA, American Diabetes Association; FBS, fasting blood sugar; IDF, International Diabetes Federation; BMI, body mass index; WHR, waist-to-hip ratio; TG, triglyceride; LDL, low-density cholesterol; TC, total cholesterol; IFG I, impaired fasting glucose I; IFG II, impaired fasting glucose II; MESA, Multi-Ethnic Study of Atherosclerosis; NHLBI, National Heart Lung and Blood Institute; CES-D, Center for Epidemiology studies — Depression scale; PR model, progression and regression model; SD, standard deviation; CI, confidence interval; OR, odds ratio; WC, waist circumference; AIC, Akaike information criteria; MET, Metabolic Equivalent of Task.

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Results: Based on the results obtained from fitting the Markov model, the transition probability for a normal individual to remain in the same status over a 10-year period was 0.63, while the probability for a person in the diabetes state was 0.40. The mean sojourn time for the normal and diabetic individuals aged 45–84 years was 6.26 and 5.20 respectively. The covariates of age, race, body mass index (BMI), physical activity, waist-to-hip ratio (WHR) and blood pressure, significantly affected the progression and regression of diabetes.
Conclusion: An increase in physical activity could be the most important factor in the regression of diabetes, while an increase in WHR and BMI could be the most significant factors in progression of the disease.
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1. Introduction

Type 2 diabetes is nowadays one of the major health threats which is on the rise globally. Type 2 diabetes, as a chronic metabolic disorder, is also known as non-insulin-dependent or adult-onset diabetes resulting from a combination of genetic factors, environmental influences, unhealthy lifestyle and high-risk behaviors. In long term, diabetics are susceptible to cardiovascular diseases, blood pressure, diabetic retinopathy, diabetic nephropathy, eclipse of the vessels; in acute cases they might die earlier than usual [1,2].

The pathophysiology of type 2 diabetes is specified by peripheral insulin resistance, reducing β-cell function and eventually leading to panceratic β-cell dysfuction. Insulin resistance and hyperinsulinemia finally result in impaired glucose tolerance (IGT) [3]. When the β-cell could not secret enough insulin to domination insulin resistance, IGT precede type 2 diabetes [4]. Most individuals with type 2 diabetes exhibit intra-abdominal obesity which plays an important role in the pathophysiology of insulin resistance. Obesity is a strong risk factor for hypertension and dyslipidemia [5,6].

Type 2 diabetes symptoms are often like type 1 diabetes but usually with fewer clinical symptoms. Individuals before the onset of diabetes are in a state called “pre-diabetes” in which the individual’s blood sugar is higher than normal level, but it is not high enough to be diagnosed as diabetes. The fasting blood glucose level of pre-diabetic patients is based on World Health Organization (WHO) (mg/dl 110–126 mg/dl) as well as the American Diabetes Association (ADA) (mg/dl 100–126 mg/dl) [7]. The latency period of the disease varies from 9 to 12 years before the clinical symptoms of the disease appear [8]. Hence, about 33% of people with type 2 diabetes remain unaware of their disease, thereby receiving no particular treatment. About 25% of type 2 diabetics have capillary problems at the time of diagnosis indicating a history of the disease for more than 5 years before diagnosis. The main challenge in treating this disease is difficulty is achieving early diagnosis and control of fasting blood sugar (FBS) [1,9].

According to the International Diabetes Federation (IDF), 366 million people were diagnosed as diabetes in 2011. Further, according to WHO, 422 million young people were diagnosed as diabetes in 2014, and the number of diabetic people in the world is expected to reach 522 million by 2030, of whom 439 million will have type 2 diabetes [1,10].

Some factors under investigation in the current study which might account for diabetes trend include gender, age, race, body mass index (BMI), physical activity, waist-to-hip ratio (WHR), blood pressure, triglyceride (TG), low-density cholesterol (LDL), total cholesterol (TC) level, depression, and smoking. Added to these is patients’ health insurance which can indirectly affect the disease [8–15].

As a chronic disease, diabetes may take different states during its progression over time, although just a specific state of the disease at a particular period might be observed. Besides, given that many individuals do not have a proper schedule for regular check-ups, the precise time of change in the state of the disease might remain undetected [16,17].

In diabetes studies carried out thus far, Cox proportional hazard model and logistic regression have been used to assess factors accounting for the progression of type 2 diabetes only from normal to pre-diabetes and then to diabetes state; also, the maximum number of response categories considered in these models was just based on the normal, pre-diabetes and diabetes state [8,9,14,15]. Nonetheless, the implementation of multi-state Markov model with continuous-time process could yield better results for modeling of diabetes because, by considering the time intervals between the changes in the disease states, the model could provide a more comprehensive vision of the processes involved in the disease [16,18,19].

As an attempt to overcome some of the previous studies’ limitations, the current study used Markov model to identify the key factors affecting the trend of change in diabetes based on FBS levels. As such, the responses were classified into four states including the normal, the impaired fasting glucose I (IFG I), the impaired fasting glucose II (IFG II) and the diabetes.

2. Methodology

The data were taken from a longitudinal study called Multi-Ethnic Study of Atherosclerosis (MESA). A total of 6814 people from the United States participated at the beginning of the study and their data were collected in 6 research institutes in different regions of the United States. The total number of observations in 5 phases was 34,070. The study continued from July 2000 to December 2015, during five phases with time intervals of 24, 18, 18, 21, and 21 months, respectively. Goals and design of the study have already been published elsewhere [20,21].

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