Research Paper

Association between major Non-Communicable Diseases Risk Factors and Fasting Blood Glucose in Iran: Comparison of two techniques, with and without dichotomizing the response

Raziyeh Bidhendi Yarandi[1], Mehdi Rahgozar[2], Jalil Koohpayehzadeh[3], Ali Rafei[4], Fereshteh Asgari[6], Enayatollah Bakhshi[2*]

[1] Student Research Committee, Department of Biostatistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

[2] Department of Biostatistics, University of Social Welfare and Rehabilitation Sciences, Tehran, Iran.

[3] Head of NCD Surveillance Office, Center for Disease Control, Ministry of Health and Medical Education, Tehran, Iran.

[4] Research assistant at Non-Communicable Diseases Risk Factors Surveillance office, Center for Diseases Control, Ministry of Health and Medical Education, Tehran, Iran.

[5] Center for Diseases Control, Ministry of Health and Medical Education, Tehran, Iran.

[*] **Corresponding author**: Enayatollah Bakhshi

Address: Koudakyar Street, Evin, Tehran, Iran.

E-mail: Bakhshi@razi.tums.ac.ir

Abstract

Background: Dichotomizing a continuous outcome variable is a common approach to estimate the odds ratio (OR) as a measure of association. In the present study we aimed to compare a non-dichotomizing technique with logistic regression which exploits dichotomizing the response for estimating OR.

Method: Data including a total of 17,152 Iranian individuals aged 25–65 years were derived from the third national survey of non-communicable Diseases Risk Factors in Iran. To measure the associations between fasting blood glucose and attributed risk factors two distinct techniques were used. Using a non-dichotomizing technique, an approach proposed by B. K.Moser and L.Coombs (2004) was employed to estimate odds ratios and associated 95% confidence intervals (CI_s); A binary logistic regression model was also applied to fit the data as a common dichotomizing approach. Finally the results of two models were compared by use of relative efficiencies and relative length of CI_s.

Results: The odds ratios provided by both approaches are approximately the same, but relative efficiencies and relative length of CIs are greater than 2 which reflected better results for the technique used a non-dichotomizing technique compared to Logistic Regression Model.

Conclusions: Dichotomizing continues outcome variable is not necessary to estimate ORs, especially when there is no pre-specified optimal cut-off point for the response variable.

Keywords: Dichotomizing, Logistic Regression Model, Odds Ratio

Introduction

As the 21th century unfolds, Diabetes mellitus (DM) has remained as a vital area of concern to public health throughout the world. DM is currently ranked among the top twelfth leading causes of death worldwide by undertaking 1.9% of the Global Burden of Diseases. Moreover, it is estimated 1.1 million people die annually due to DM in which 80% of them belong to developing countries(1). According to the International Diabetes Federation (IDF), 366 million people suffered from DM in 2011 and expected to reach 552 million by 2030(2). In Iran DM is the seventh cause of mortality by killing 7 individuals per 100,000(3). Along with the global trend, DM is dramatically growing in Iran. As within just two years, one percent increase was detected from 7.7% in 2005 to 8.7% in 2007 (4, 5). In addition Type 2 Diabetes Mellitus (T2DM) consumes more than 8.69% of total health expenditure in Iran(6). Although the causes of DM are complicated, the number of risk factors have been recognized to be highly associated with it. Unhealthy diet; physical inactivity, overweight and obesity are taking into account as major causes of diabetes. The phenomena of urbanization and alteration of age pattern are real concerns. With the aging of the baby-boom generation and increases in life expectancy Iranian population is growing older. Aging is associated with adverse changes in glucose tolerance and increased risk of diabetes; the increasing prevalence of diabetes among older adults suggests a clear need for effective diabetes prevention approaches for this population(7). Family history of diabetes plays a significant role in suffering from diabetes; it has long been known that T2DM is partly inherited. Family studies have disclosed that first degree relatives of individuals with T2DM are about 3 times more likely to develop the disease than individuals without a positive family history of the disease(8). Blood lipids especially cholesterol, has been detected as the one of T2DM risk factors(9). Diabetes and hypertension frequently coexist. It is a common risk factor in patients with diabetes, and occurs in 75% of patients with the more prevalent form of T2DM(10).

Most of the clinical response variables are continuous such as blood glucose, blood pressure, body mass index and so on.to study these variables a common statistical method is to determine a cut-off point and categorizing original data to implement logistic regression. There are several reasons to do this, such as easer interpretation of odds ratios, better representation of the phenomenon under study by dichotomizing the outcome variable in two or more categories and specific clinical definition of the range of continuous outcome variable

(e.g., fasting blood glucose over 126 mg/dl is treated as an at risk diabetes). Despite these advantages, using this method arouses some statistical controversies (11-18). Determining a proper cut-off point is a great challenge for clinicians in a way that most of the time this is a subjective choice not an objective one. It is proved that the statistical power and the magnitude of Odds Ratio (OR) depend on the cut-off point which provoke potential biases and different results due to subjective choice of cut-off point (19). Practically by dichotomizing original data we discard some information, on the other hand it is necessary to increase sample size to reach to the pre-specific power which increase the cost of experiments. Also loss of statistical efficiency happens in the process of dichotomizing. Misclassification of data and borderlines could be misleading to over evaluate associations between factors under study.

In the present study we aimed to compare an alternative non-dichotomizing technique with logistic regression which exploits dichotomizing the response for estimating OR_s.

Materials and Methods

Data source

Data for the present study were derived from the third round of the survey of Non-Communicable Diseases Risk Factors Surveillance in Iran (20). This population-based cross-sectional study was conducted in 2007 by Iran Center for Diseases Control (CDC) based on the STEPwise approach of WHO (9, 21). A total sample of 24,000 non-institutionalized Iranian adults aged between 25 to 64 years was taken through a stratified cluster random sampling scheme. Participants were eventually interviewed at their homes by trained healthcare workers from 43 medical schools and a blood sample was taken after receiving a verbal informed consent. After excluding pregnant women, controlled diabetics who care their Fasting Blood Glucose (FBG<126 mg/dl) by taking drug, and those with missing information, analysis was performed on a sample of 17,152 Iranian adults.

Measurements and variables

Interview phase of the study was performed using a standard questionnaire measuring demographic, behavioral and physical risk factors proposed by WHO. Biochemical risk factors including FBG and total cholesterol was recorded in the subsequent phase. FBG (mg/dl) was treated as the main response variable of the study. Age (year), residential area (rural/urban),

hypercholesteremia (total cholesterol ≥200 mg/dl), hypertension (systolic blood pressure ≥140 and), low level of physical activity (total physical activity ≤600 MET-Minute per week), vigorous level of physical activity (total physical activity ≥1,600 MET-Minute per week) , it is calculated according to WHO guide lines, MET (Metabolic Equivalent) values are applied to vigorous and moderate intensity variables in the work, transport and recreation domains. These have been calculated using an average of the typical types of activity undertaken. Calculating total physical activity and different types of activities have been grouped together and given a MET value based on the intensity of the activity, waist circumference (cm), vegetable intake (servings per day), family history of diabetes were considered as independent variables.

Overview of without dichotomizing method proposed by B.K.Moser and L.Coombs (WDICH)

According to the method proposed by Moser and Coombs(22), it is assumed that a random sample of observations $(Y_1, Y_2, .., Y_n)'$ where Y_i, X_i and β are related through the regression equation

$$Y_i = \beta X'_i + E_i \quad (1)$$

for i=1,2,…,n and where the P×1 vector of explanatory variable $X_i = (1, X_{1i}, X_{2i}, \dots, X_{i,p-1})'$ and E_i are independent and identically distributed logistic random variable with mean 0 and variance $\sigma^2 > 0$.Moser and Coombs supposed that the random E_i terms follow a logistic distribution and explanatory variables X_i follow a discrete uniform distribution. They provided an estimate of the same odds ratio Parameter as the logistic method, but without discarding information (23).An estimated of odds ratio parameter O_j is given by

$$O_j = \exp\left(\frac{\lambda\hat{\beta}}{\hat{\sigma}}\right) \quad (2)$$

Where

$$\hat{\beta} = \left(\widehat{\beta_0}, \dots, \widehat{\beta_j}, \dots, \widehat{\beta_{p-1}}\right)' = (X'X)^{-1}X'Y \quad (3) \quad \text{for j=0,…, p-1} \quad \text{and}$$

$$\hat{\sigma}^2 = \sqrt{\frac{Y'AY}{n-p}} \quad (4)$$

Where the n×n matrix $A = I_n - (X'X)^{-1}X' \quad (5)$

Relative efficiency of OR by using WDICH approach represent as

$$r.e.(OR_{WDICH}, OR_{LRM}) = \frac{Var(OR_{jLRM})}{Var(OR_{jWDICH})} = \frac{\hat{\sigma}^2{}_{\theta_j}}{\lambda^2 \delta_j} \quad (6)$$

Where $\hat{\sigma}^2{}_{\theta_j}$ is the estimation of variance of j+1 st coefficient by LRM $\lambda \approx 1.8138$, δ_j is the j+1 st diagonal element of $(X'X)^{-1}$.

Statistical analysis

Fasting Blood Glucose (FBG) was treated as a continuous outcome variable. we fitted a linear regression model proposed by Moser then by the use of equation (2) we transfer estimated coefficients to the estimated odds ratio corresponding to β_j.In other words the odds ratios as the measures of association between diabetes and age, Place of residence, waist circumference, cholesterol, hypertension, vegetable intake, physical activity and family history of diabetes were estimated by using WDICH method. Moreover, the common logistic Regression Model (LRM) was implemented to obtain ORs by dichotomizing FBG at 126 mg/dl as the cut-off point. Analyses results were obtained using R (Version 2.14.1)

Results

Distributions of covariates are shown in tables 1 and 2 to make the data presentation complete.

Our results showed that nearly 56.5% of population was urban citizens. It was illustrated that nearly 36.7% and 23.7% and 39.6% of people had low, moderate and vigorous level of physical activity, respectively. Nearly 21% of participants had family history of diabetes and approximately 21.6% of participant had systolic blood pressure more than 140 mg/dl and 38.3% had cholesterol level more than 200mg/dl. This study was conducted among Iranian adults with means of 41.71 years for age, 90.17 cm for waist circumference and 1.96 servings per day for vegetable intake.

Results in Table 3 draw a comparison with two regression approaches, with and without dichotomizing. Generally we found shorter CI for WDICH approach and Relative efficiency greater than 2 for all covariates. More clearly we had smaller estimated variances for each covariates, which represented statistically better results for WDICH approach.

It is illustrated that age was directly associated with diabetes (OR= 1.022 , 95% Cl: 1.019- 1.024), urban residence had significantly higher odds of diabetes than their rural counterparts (OR=1.196, 95% CI: 1.217- 1.265), a positive association between diabetes and hypertensive participants was detected (OR=1.307,95% CI:1.209-1.403), cholesterol was found as a significant factor for diabetes (OR=1.347,95% CI:1.268 - 1.424) ,waist circumference (WC) as the measure of obesity had a significant relationship with diabetes (OR=1.011, 95% CI: 1.009 - 1.013), having family history of diabetes had a profound influence on diabetes (OR=1.840, 95 %CI: 1.719- 1.970), the odds ratio of vegetable intake for diabetes was reported (OR= .998 , 95 %CI: .983- 1.0129). Finally, there was an association between physical activity and diabetes. By using low as the reference group, diabetes odds ratios were 0.949 (95% CI: .884-1.020) and 0.859 (95 % CI: .807-.9158) for the moderate and vigorous levels, respectively.

Discussion

Dichotomizing a continuous outcome variable arouse statistical challenges, it could prove costly by discarding information and increasing sample size. In this study we showed that WDICH approach produce better results from statistics point of view, the other study demonstrated the same results (23, 24). We obtained approximately the same estimation of OR for both LRM and WDICH, but relative length of CI showed shorter CI for OR, also relative efficiency found smaller variance for OR estimation by implementing WDICH method, which statistically speaking showed the superiority of this approach.

Drastic demographic changes in Iranian population open a new gate of study on health area. By 2050, it is estimated that 21.7% of the Iranian population will be aged 60 and above, compared to 5.2% in 2000(25). Many studies has shown that aging increases the risk of diabetes(7)we detected this positive association in Iranian population too. The urbanization phenomenon as the consequence of industrialization by the migration of people from rural to urban areas may account in part for the increasing prevalence of type 2 diabetes mellitus in developing countries. Positive association was found in this study too. our result was consistent with the other studies(26). Lifestyle modification seems to be making obesity a severe common problem in the country. It increases the risk of developing T2DM.(27). We used waist circumference as a measure of obesity to show this relationship .Our result also detected that increasing of WC has a

significant association with T2DM which was similar to previous studies (28-30).

Vegetable intake may have an inverse association with diabetes in Iran, with (OR=0.998, 95 %CI: .983-1.013). Unfortunately low vegetable intake has been detected in Iranian population compare with some other developing and most of the developed nations, About 87·5% of Iranian adults consumed less than the WHO-recommended daily intake which is defined as intake of less than five servings of fruit and/or vegetable daily (88·4% of men and 86·6% of women)(31). Education which could be effective on income and socioeconomic status has been shown to have one of the strongest influences on fruit and vegetable intake. Studies in the United States and France among adults declare this(32). Low level of education can affect vegetable intake due to the adoption of inadequate dietary habits. In addition, low socioeconomic groups generally have a more restrictive food budget, and prefer more energy dense and satisfying foods. As in many developing countries, Iran is facing rapid nutritional transition. Taking high caloric and low fiber foods has been prevalent in our community since the last decade (33) .Then, fruit and vegetable consumption will decrease more and more in future(34). Furthermore, our findings indicate a significant inverse association between physical activity and diabetes which were consistent with some other studies (35, 36). For communities in a transition phase of lifestyle, industrialization and sedentary lifestyle, could be the major threads; lifestyle modification by encouraging physical activity may help to prevent diabetes and its adverse consequences(37). The trend of unhealthy lifestyle leads to high intake of fatty foods and it would be the main cause of cholesterol disorders, diabetes was clearly associated with high cholesterol(38).Family history of diabetes plays a significant role in suffering from diabetes; it has long been known that T2DM is, in part, inherited. Family studies have revealed that first degree relatives of individuals with T2DM are about 3 times more likely to develop the disease than individuals without a positive family history of the disease(8).We estimated a positive association between family history of diabetes and diabetes in Iranian population. Metabolic factors like hypertension and high cholesterol level, which are prevalent among all nations, are the challenging NCDs issues by themselves. Beside the genetic reasons the new trend of lifestyle would be the root of them. Consequently there should be mutual relationship between these metabolic factors and Diabetes (39-41). Diabetes and hypertension frequently coexist, leading to additive increases in the risk of life-threatening

cardiovascular events. Hypertension is a common comorbid condition in patients with diabetes when compared with the general population, and occurs in 75% of patients with the more prevalent form of T2DM. Prevalent hypertension among diabetics is approximately double that of non-diabetics. It is well-known that hypertension accelerates the course of microvascular and macrovascular complications of diabetes and that hypertension often precedes type 2 diabetes and vice versa(10, 42).In addition, we detected the positive association between hypertension and diabetes in Iranian adults too. The advantages of this study include a large sample size representative of the nation, using a standardized international questionnaire whereas the main limitation of our study was its cross-sectional nature which did not allow us to assess causal relationships. This limitation also prevented any measure of temporal changes in prevalence of diabetes and factors associated with it. Longitudinal studies would complement the present study to determine causality and directional effect of the factors.

Conclusion

Dichotomizing continues outcome variable is not necessary to estimate ORs, especially when there is no pre-specified optimal cut-off point for the response variable. WDICH method could be an appropriate alternative for binary logistic regression model when the response variable is continuous. By implementing this method not only we have advantages of logistic regression such as estimating OR but also we discard its disadvantages.

Abbreviations

DM: Diabetes Mellitus
IDF: International Diabetes Federation
NCD: Non-Communicable Disease
T2DM: Type 2 Diabetes Mellitus
WC: Waist Circumference
MET: Metabolic Equivalent
SuRFNCD: The National SUrveillance of Risk Factors of Non-Communicable Diseases
KDM: Known Diabetes Mellitus
WDICH: Without Dichotomizing Method
CDC: Center for Disease Control of Iran
FBG: Fasting Blood Glucose

Conflict of interest

The authors have no conflicts of interest.

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Table 1 : Descriptive characteristics of categorical variables for (SuRFNCD-2007)

Factor	Number	Percentage
Residential Area		
Rural	7,453	43.5
Urban	9,699	56.5
Physical Activity		
Low	6,296	36.7
Moderate	4,067	23.7
Vigorous	6,789	39.6
Family History		
No	13,627	79.4
Yes	3,525	20.6
Blood Pressure		
Normal	13,447	78.4
Hypertensive	3,705	21.6
Cholesterol		
Normal	10,557	61.3
Hypercholesteremic	6,575	38.7

Table 2 : Descriptive characteristics of continuous variables for (SuRFNCD-2007)

Factor	Mean	SD
Age		
Men	44.86	11.44
Women	44.58	11.15
Total	44.71	11.29
Waist Circumference		
Men	89.63	12.84
Women	90.51	13.98
Total	90.17	13.45
Vegetable Intake		
Men	1.98	1.97
Women	1.94	1.67
Total	1.96	1.82

450 Table3: Odds ratios for diabetes and their CI using two approaches for (SuRFNCD-2007)

Variables	LRM[1]		WDICHM[2]		Relative Efficiency	Relative length of CI(LRM/ WDICHM)
	OR[3]	95%CI[4]	OR	95%CI		
Age	1.05	1.043-1.057	1.022	1.019-1.025	2.33	2.33
Residential area						
Rural	1	----	1	----	----	----
Urban	1.35	1.188-1.538	1.196	1.215- 1.265	9	7
Hypertension						
Normal	1	----	1	----	----	----
Hypertensive	1.561	1.367- 1.781	1.307	1.209-1.403	3.5	2.13
Cholesterol						
Normal	1	----	1	----	----	----
Hypercholesteremia	1.506	1.333- 1.703	1.344	1.268- 1.424	4.27	2.65
Waist Circumference	1.024	1.019-1.028	1.011	1.009-1.013	4	2.25
Family History of Diabetes						
No	1	----	1	----	----	----
Yes	3.163	2.792 -3.582	1.840	1.719-1.970	4.4	3.15
Physical Activity						
Low	1	----	1	----	----	----
Moderate	0.890	0.765- 1.035	0.950	0.884 -1.020	4	1.99
Vigorous	0.760	0.660- 0.876	0.860	0.807 - 0.916	5.4	1.98
Vegetable Intake	0.983	0.945-1.016	0.998	0.983 - 1.013	5.1	2.37

451 [1]Logistic Regression
452 [2]Without DICHotomizing Method
453 [3]Odds Ratio
454 [4]95% Confidence Interval
455