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Clinical scoring for early detection of Prediabetes in Egyptian Population

By

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- Prediabetes
- HbA1C
- Risk factors
- Scoring system
- BMI
- Smoking habit
- Physical activity.

Abstract

Background: Prediabetes is a wide spread condition where blood glucose is above normal, but it does not measure up to the criteria of diabetes mellitus. Yet there is no national scoring system for prediabetes according to the potential risk factors. **Methods:** A case-control study has been carried out in Mansoura Specialized Hospital. Subjects have been recruited from out-patients clinic in the period from October 2018 to August 2019. Those with prediabetes had been assigned to be the case group whereas control subjects were those who had a normal HbA1C. A scoring system was based on risk factors of prediabetes by use demographics data including information about age and sex. **Results:** In the current study participants with obesity have 4.9 times higher odds to exhibit prediabetes (a score of 16 points is assigned to those with obesity). Participants who are current smokers have 3 times higher odds to exhibit prediabetes (a score of 11 points is assigned to current smokers). Participants with lack of moderate physical activity have 2.6 times higher odds to exhibit prediabetes (a score of 10 points is assigned to those who lack moderate physical activity). Binary logistic regression was run to assess the performance of Egyptian Prediabetes risk score in predicting the likelihood of prediabetes in Egyptian patients. The model is statistically significant ($\chi^2 [1] = 60.684, P < 0.001$), and it correctly classified 75% of cases. The model has sensitivity, and positive predictive value of 74%, and specificity, and negative predictive value of 76%.

INTRODUCTION

Diabetes is one of the most common chronic diseases found throughout the world, where the prevalence continues to grow significantly. According to the International Diabetes Foundation, in 2013 there were approximately 382 million people with diabetes worldwide, and this is expected to rise to 592 million by 2035 [1].

Prediabetes is a condition where blood glucose is above normal, but it does not measure up to the criteria of diabetes mellitus. Conditions included in prediabetes are impaired glucose tolerance (IGT), impaired fasting glucose (IFG), or both. For patients who carry both IGT and IFG, cumulative incidence of diabetes in the period of 6 years is 65%, compared with the person with normal blood glucose level [2] and an annualized conversion rate of 5%–10% [3]. Thus, identifying those individuals with prediabetes becomes crucial and cost-effective [4].

Observational evidence suggests association between prediabetes and complications of diabetes such early nephropathy, small fiber neuropathy, early retinopathy and risk of macrovascular disease [5].

The traditional diabetes screening methods, including the fasting plasma glucose (FPG), the 2-h oral glucose tolerance test (OGTT) or HbA1c test, are invasive, inconvenient, and expensive, especially for large populations. This is one of the important reasons why there are a large number of diabetic patients remaining undiagnosed. Seeking a simple, reliable, and cost-effective screening method, such as a prediabetes risk score that can be easily conducted in clinical or community settings becomes necessary[1].

Subjects and methods

Study design, setting and recruitment of patients

A case-control study has been carried out in Mansoura Specialized Hospital. Subjects have been recruited from out-patients clinic in the period from October 2018 to August 2019.

Subjects

All the included subjects were above 21 years old. Those with prediabetes had been assigned to be the case group whereas control subjects were those who had a normal HbA1C. Prediabetes was diagnosed with HbA1c ratio more than or equal to 5.7 and less than 6.4.

Exclusion criteria

Subjects known to be diabetics, chronic depleting diseases, endocrinal disorders that affect blood glucose levels, pregnancy, and those who are taking drugs known to influence blood glucose levels e.g. metformin, thiazolidinediones and steroids.

Sample size calculation

The sample size calculated according to the following Equation with reference to the results of [1]:

$$(1.96)^2 \times \text{anticipated specificity} (1 - \text{anticipated specificity}) \times \text{anticipated prevalence} / d^2 = 1.96 \times 1.96 \times 0.67 \times 0.23 \times 0.40 / 0.0025 = 94.7 \approx 100 \text{ per each group}$$

Clinical scoring tool description

Scoring system is based on risk factors of prediabetes by use demographics data including information about age and sex.

Family history of diabetes was restricted to first relatives only, such as father, mother, or siblings. History of gestational diabetes in female subjects has been also reported in women included in this study. In addition, subjects were classified into smoking categories of smokers and nonsmokers by self-report.

Based on physical activity, subjects is considered physically active if having at least 5 days or more with total active duration of 150 min in 1 week. Sedentary activity is the behavior of a sitting or lying everyday both in the workplace, at home, on the go/transport, but not including bedtime, with cutoff point <3 h/day, 3–5.9 and ≥ 6 h/day for risky behavior [1]. Acanthosis nigricans is characterized by dark, coarse, thickened skin with a velvety texture, usually asymptomatic, but occasionally, it can be pruritic. The lesions are symmetrically distributed and affect back and sides of neck, axillae, groin, and ante-cubital and popliteal area [6].

Classification for body mass index (BMI) was calculated in this study using WHO classification where 18.5– 24.9 kg/m² defined as normal, 25.0–29.9 kg/m² as overweight, and 30.0 kg/m² and above as obese. Measuring of waist circumference (WC) with WC equal to or more than 102 cm in males and WC equal to or more than 88 cm in females are considered as risk factor for prediabetes [7].

Normal weight is defined as BMI 18.5 to 25 kg/m², overweight 25 to ≤ 30 kg/m², obese

(class I and II) 30–40 kg/m², and obese (class III) ≥ 40 kg/m² [8].

Subjects have been diagnosed and reported as hypertensive if they are documented to have hypertension diagnosed by a physician or if they are taking anti-hypertensive medication, or diagnosed as hypertensive based on JNC-VIII classification for hypertension [systolic blood pressure (SBP) ≥ 140 mmHg or diastolic blood pressure (DBP) ≥ 90 mmHg] [9].

The score has been calculated and interpreted according to the method described by Mehta et al. (2016) [1]. Our mainstay proposed modification would be adding acanthosis nigricans and waist circumference as a higher supposed risk factor than educational level and considering HbA1C as a laboratory diagnostic factor. Laboratory parameters, HbA1c test based on ADA standards. Prediabetes is diagnosed with HbA1c ratio more than or equal to 5.7 and less than 6.4.

Statistical analysis

The data collected have been coded, computed, tabulated, analyzed statistically using statistical software package (SPSS). The receiver operating characteristic (ROC) curve has been constructed.

Results

A. Developing Egyptian Prediabetes risk score:

The results of univariate binary logistic regression analysis to predict prediabetes displayed that the following 10 variables were statistically significant predictors of prediabetes: age ≥ 35 years, current smoking, lack of moderate physical activity, sedentary lifestyle ≥ 3 hours, dietary fiber intake of <3 servings / day, high WC (≥ 102 cm in male, and ≥ 88 cm in female), obesity, high BMI (≥ 29.7 kg / m²), BP >120 /80 mmHg, and mean arterial pressure ≥ 98 mmHg tables 1,2.

Table (1): Univariate analysis of the predictors of prediabetes (from history taking)

Predictor variable	P value	COR	95% CI of COR
Gestational DM (female)	0.182		
No		R	R
Yes		1.95	0.73 – 5.20
DM in 1 st degree relative	0.174		
No		R	R
Yes		1.6	0.81 – 3.15
Sex	0.777		
Male		R	R
Female		1.1	0.62 – 1.88
Age (years)	0.027		
<35		R	R
≥35		2.2	1.09 – 4.44
Current Smoking	0.002		
No		R	R
Yes		3.6	1.56 – 8.04
Moderate physical activity	<0.001		
Yes		R	R
No		6.9	3.52 – 13.61
Sedentary life (hours)	0.022		
<3		R	R
≥3		1.95	1.1 – 3.46
Dietary fiber daily servings	0.001		
≥3		R	R
<3		4	2.21 – 7.21
Education level			
High	R	R	R
Low	0.654	0.81	0.33 – 1.97
Non-education	0.875	0.95	0.52 – 1.72

Notes: COR = Crude odds ratio CI = Confidence interval. R = Reference category.

Table (2): Univariate analysis of the predictors of prediabetes (from physical exam)

Predictor variable	P value	COR	95% CI of COR
Waist circumference (cm)	<0.001		
<102 (male), <88 (female)		R	R
≥102 (male), ≥88 (female)		7.3	3.92 – 13.73
Obesity	<0.001		
Normal / overweight		R	R
Obese		9.01	4.75 – 17.1
BMI (kg/m ²)	<0.001		
<29.7		R	R
≥29.7		8.61	4.58 – 16.3
Blood pressure	<0.001		
≤ 120/80 mmHg		R	R
> 120/80 mmHg		4.37	2.3 – 8.33
Mean arterial pressure (mmHg)	0.001		
<98		R	R
≥98		5.06	2.76 – 9.27

Notes: COR = Crude odds ratio CI = Confidence interval. R = Reference category.

The results of binary logistic regression analysis with backward conditional method to ascertain the effects of the significant predictors on

univariate analysis on the likelihood that participants will exhibit prediabetes was shown in table 3.

Table (3): Multivariate analysis of the predictors of prediabetes

Predictor	B	SE	Wald	P value	OR	95% CI of OR
Obesity Normal / overweight	1.587	0.402	15.589	<0.001	R 4.9	R 2.22 – 10.75
Obese Current Smoking	1.099	0.473	5.395	0.020	R 3	R 1.87 – 7.58
No Yes Moderate physical activity	0.966	0.437	4.891	0.027	R 2.6	R 1.12 – 6.19
Yes No						

Notes: B = Binary logistic regression coefficient. SE = Standard error. OR = Odds ratio. CI = Confidence interval. R = Reference category. Test of significance is binary logistic regression (Backward conditional method).

The model was statistically significant (χ^2 [3] = 62.240, $P < 0.001$). The model correctly classified 75% of cases. The model has sensitivity, and positive predictive value of 74%, and specificity, and negative predictive value of 76%. Participants with obesity have 4.9 times higher odds to exhibit prediabetes (a score of 16 points is assigned to those with obesity).

Participants who are current smokers have 3 times higher odds to exhibit prediabetes (a score of 11 points is assigned to current smokers). Participants with lack of moderate physical activity have 2.6 times higher odds to exhibit prediabetes (a score of 10 points is assigned to those who lack moderate physical activity).

Table (4): Egyptian prediabetes risk factors

Risk category (score)	Control	Prediabetes	P value
Active / Non-smoker / Not obese (Zero)	68 a	18 b	<0.001
Lack of moderate activity / non-smoker / not obese (10)	2 a	3 a	
Smoker / active / not obese (11)	6 a	5 a	
Obese / active / non-smoker (16)	9 a	15 a	
Lack of moderate activity / non-smoker / Obese (26)	12 a	38 b	
Obese / active / Smoker (27)	2 a	7 a	
Lack of moderate activity / Smoker / Obese (37)	1 a	14 b	

Notes: Data are N. Test of significance is Fisher's exact test. Comparisons of column proportions are shown as different letters if difference is statistically significant.

There was a statistically significant difference in the distribution of risk categories in prediabetes vs. control table 4. Those who are Active, non-smoker and not obese are statistically

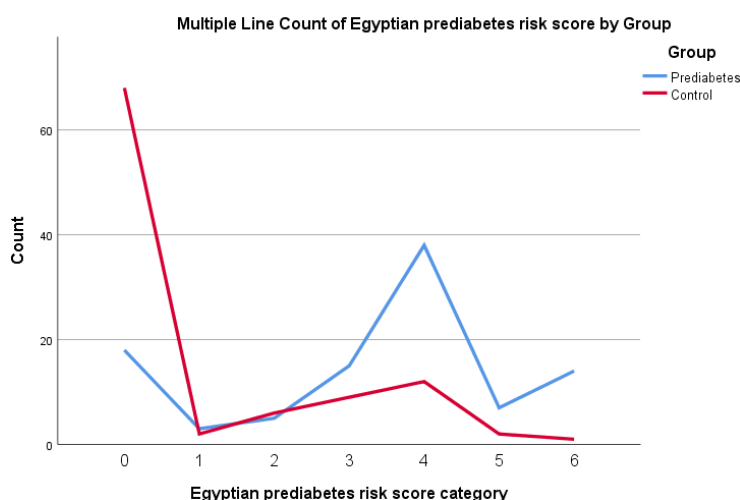
significantly more in control group while those who are inactive and obese whether smoker or non-smoker statistically significantly more in prediabetes group.

Cochran Armitage Trend test:

This test was run to assess the association between Egyptian prediabetes risk score (ordinal) and occurrence of prediabetes (dichotomous). There was statistically significant correlation between Egyptian prediabetes risk score and occurrence of prediabetes ($P < 0.001$), i.e., as risk score increases, the proportion of prediabetes

increases. This is shown in figure 1. In this figure, based on assigned scores, risk score categories are classified from category ‘0’ who are active/non-smoker/non-obese with the lowest risk to have prediabetes to category ‘6’ who are inactive/smoker/ obese with the highest risk to have prediabetes.

Figure (1): Egyptian prediabetes risk score categories (0-6) in Egyptian prediabetics vs. control.



Predicting the likelihood of prediabetes by Egyptian Prediabetes risk score:

Binary logistic regression was run to assess the performance of Egyptian Prediabetes risk score in predicting the likelihood of prediabetes in Egyptian patients. The model is statistically significant ($\chi^2 [1] = 60.684, P < 0.001$),

and it correctly classified 75% of cases. The model has sensitivity, and positive predictive value of 74%, and specificity, and negative predictive value of 76%. For every increase in risk score by one unit (one category), there is 1.6-times increase in the likelihood that participant will exhibit prediabetes as shown in table 5.

Table (5): The likelihood that participant will exhibit prediabetes in Egyptian population

Predictor	B	SE	Wald	df	P value	OR	95% CI for OR
Risk score	0.497	0.072	47.058	1	<0.001	1.640	1.42 – 1.89
Constant	-1.215	0.236	26.500	1			

Discussion

In the current study we developed our scoring system based on regression coefficients multiplied by 10 and rounded to the nearest integer to derive weights of the scores. This was according to what previously reported in literature [10]. This

scoring system then performed in a questionnaire form that can be used easily by health personnel in clinics and primary care centers.

Our multivariate analysis of the predictors of prediabetes showed that obesity (OR = 4.9; 95%–CI: 2.22 – 10.75; $p < 0.001$), current smoking

(OR = 3 ; 95%–CI: 1.87 – 7.58; p= 0.020) and lack of moderate physical activity were the most significant risk factors for predicting prediabetes (OR = 2.6 ; 95%–CI: 1.12 – 6.19; p=0.027).

A number of risk assessment tools based on readily available clinical variables have been developed to predict the incidence of new diabetes cases in various countries. These are derived from European [11, 12]; American [13-17], Australian [18], and Asian [19] [20] [21] studies. Nonetheless up to our knowledge there was no scoring for predication of diabetes in Egypt or another Arab nation as differences in territories, ethnicities, and lifestyles may limit the application of some of these effective risk scores to the other population [22].

By applying this to our data, the smoking habit assigned a score of 11, obesity was assigned a score of 16 and finally the lack of moderate physical activity was given as score of 10. Therefore a total score of 37 was assigned to subjects of this study.

Men and women who have a BMI ≥ 30 kg/m² are considered obese and are generally at higher risk for adverse health events than are those who are considered overweight (BMI between 25.0 and 29.9 kg/m²) or lean (BMI between 18.5 and 24.9 kg/m²) [7]. Current ADA guidelines recommend screening for all overweight subjects with BMI ≥ 25 kg/m² of any age who have one or more T2DM risk factors, whereas the European Association for the Study of Diabetes and the International Diabetes Federation recommend the use of a risk score questionnaire [23].

Low physical activity (PA), or sedentary lifestyle, is associated with the development of

several chronic diseases. A previous study showed that the prevalence of sedentariness is 32.3% for men and 39% for women. Sex differences are principally distinguished at early and older ages. Sedentary individuals have higher BMI (28 vs. 27 kg/m²) and obesity prevalence (37 vs. 26%) [24]. Lack of physical activity predisposes to T2DM and makes its management more difficult. Conversely, engaging in regular physical activity can not only prevent the development of T2DM, but can also potentiate the effects of anti-diabetic drug therapy, thereby improving glycaemic control [25].

Physical inactivity and obesity are both risk factors for T2D. Since they are strongly associated, it has been suggested that they might interact. Both interact on an additive scale. This means that prevention of either obesity or physical inactivity, not only decreases the risk of diabetes by taking away the independent effect of this factor, but also by preventing the cases that are caused by the interaction between both factors [26].

Our system also assigned smoking habit a score of 11 based on its data as a risk factor. Despite the growing evidence demonstrating strong epidemiologic and mechanistic associations between cigarette smoking, hyperglycemia, and the development of T2D, tobacco abuse has not been uniformly recognized as a modifiable risk factor in diabetes prevention or screening strategies [27]. Nonetheless, there is accumulating evidence that regular smokers are at risk of developing incident diabetes. Since the prevalence rates of smoking in patients with diabetes are relatively similar to those of the general population, it is essential to address the main

modifiable risk factor of smoking to prevent the onset of diabetes and delay the development of its complications [28].

Conclusion

In the current study the obesity, smoking habit and lack of moderate physical activity high were the strongest risk factors respectively for developing prediabetes. Therefore they were assigned the highest score in the current study in a descending order. Yet it is recommended to apply this score on a wide scale national study that include thousands of Egyptians in order to standardize a simple clinical tool for prediction of prediabetes in Egyptian population.

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Compliance with ethical standards

Approval of this work was obtained from IRB of Mansoura College of Medicine College of Medicine Ethical Committee.

Conflict of interest

There is no conflict of interest.

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