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Research Article

Frequency of Type 2 Diabetes According to Optimal Cut-points for Body Mass Index in Saudi Population

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Abstract

Background and Objective: The prevalence of type 2 diabetes mellitus (T2DM) are increasing worldwide. Body mass index (BMI) cut-off for T2DM can vary. The objective of this study is to identify the optimal BMI cut-off that is associated with T2DM.

Methods: For the present study, we analyzed participants who are equal to or older than 18 years old. A total of 5498 were analyzed at the present study. Patients were recruited from the population of the primary health and diabetic Centres at King Fahad Armed Forces Hospital. T2DM was defined according to self-report, clinical reports, use of antidiabetic agents and HbA1c (≥ 6.5). We collected data personal interview and electronic medical chart review. Physician and nurse interviewers measured the weight (kg) and height (cm) of the participants and BMI was calculated. Receiver operating characteristic curve analysis was used to obtain the optimal sensitivity and specificity using different BMI cut-off values to predict the presence of diabetes.

Main Results: Of the 5498 participants analyzed, 2049 (37.3%) were male and 3449 (62.7%) were female with female to male ratio 1.7:1. Age was 42.7 ± 15.8 (minimum 18 and maximum 105 years) and males were older compared to females (45.3 ± 16.6 vs. 41.1 ± 15.1 respectively, $p < 0.0001$). BMI was 29.6 ± 6.9Vwhere females were having higher as compared to males (30.1 ± 7.5 vs. 28.8 ± 5.5 respectively, $p < 0.0001$). T2DM was present in 1873 (34.1%), 743 (39.7%) were male and 1130 (60.3%) were female with female to male ratio 1.5:1. BMI values ranged from 28.50 to 29.50 in total population, 27.50 to 28.50 in men and from 28.50 to 29.50 in women. The area under curve was 0.588 (95% CI,0.563 - 0.613) in men and 0.673 (95% CI,0.654 - 0.692) in women. Regression analysis showed that the risk of T2DM was significantly increased at BMI values as low as 12 to 14 and increased progressively as BMI increased. Applying this criterion to identify the cut-off values resulted in improvements in sensitivity, false negative rate and worsening in specificity and false positive rate. A very small false negative rate ranging from 0.01 to 0.02 was found after using these lower BMI cut-offs. A significant positive association was observed with BMI values starting at 12 to 14 for females and at 17 and increasing progressively with higher BMI values for both genders.

Conclusion: In defining obesity, the usefulness of diagnostic of BMI alone is limited among men and women Saudi adults.

Keywords: *Diabetes; Body Mass Index*

Introduction

Diabetes mellitus (DM) is associated with increased mortality risk and significant long-term morbidity [1-4]. 90%-95% of all diabetes cases are type 2 diabetes mellitus (T2DM) and data showed steadily increasing in worldwide prevalence [5-7]. T2DM is projected to increase to 592 million in 2035, with Asia having the highest number of individuals with T2DM globally and importantly, with the prevalence increasing at a much faster rate than in Western countries [8].

The most commonly used indicator to evaluate excess body fat and measurement of the degree of obesity is body mass index (BMI). As a known risk factor of T2DM, high BMI (> 30 kg/m^2) is associated with 3 - 10 times greater risk of developing T2DM compared to low BMI (< 25 kg/m^2) [9-14]. Although this index has advantages in clinical and epidemiological practice, as a non-invasive and low-cost method, its predictive value for chronic diseases has been questioned, especially when applied to certain population groups [15-17].

Epidemiologic studies have demonstrated an appropriate BMI cut-off for DM can vary by race and ethnicity. [18,19] Experts explain that this is largely because the associations between BMI, proportion of body fat, and body fat distribution pattern differ across populations [18]. Furthermore, because the cutoffs for BMI used to define obesity or overweight are different for Asian populations [20,21]. Earlier research examined BMI cut-offs associated with DM in various Asian populations. For South Asians, evidence suggests that diabetes is associated with a BMI between 22.0 kg/m^2 and 24.0 kg/m^2 [19,22-25]. As observed in Caucasians, among both male and female Japanese-Brazilians, the associations between BMI and DM were statistically significant with BMI ≥ 25 kg/m^2, a value that WHO sets as the upper limit for normal weight [26]. There is an increased risk of diabetes relative to BMI, as low as 21 kg/m^2, in Saudi population [27]. One study from Oman was conducted in Omani adult subjects showed the optimal BMI cut-off points for men and women were 23.2 and 26.8 respectively [28,29]. Two large cross-sectional studies of diabetes from Indian cities reported BMI cut-offs of 23.1 kg/m^2 for males and 23.8 kg/m^2 for females in one study and 23.0 kg/m^2 for both sexes in the other [22,24]. A nationwide population-based cross-sectional study conducted in Pakistan found that diabetes was associated with BMI cut-offs of 22.1 kg/m^2 for males and 22.9 kg/m^2 for females [23]. A prospective cohort study from Canada found that a BMI cut-off of 24.0 kg/m^2 was appropriate for Asians [19]. 50% of the cases of diabetes incidence involved underweight or normal weight participants, and the risk for diabetes incidence increased progressively from a BMI of 20 kg/m^2. [30] The risk of T2DM is known to increase as the BMI increases among Asians [31].

Identifying individuals likely to be affected by T2DM using a simple indicator such as BMI is an important step toward reducing the burden of diabetes in Saudi communities. It has not been investigated whether a BMI cut-off lower than 25 kg/m^2 is feasible to indicate elevated likelihood of having T2DM in population of Saudi Arabia. The objective of this study is to identify the optimal BMI cut-off that is associated with T2DM.

Methods

We analysed 5498 participants who are equal to or older than 18 years old. All cases were from the population of the primary health and diabetic Centres at King Fahad Armed Forces Hospital. T2DM cases were defined according to self-report, clinical reports, use of anti-diabetic therapies and HbA1c (≥6.5) [32]. All data were collected by personal interview and on the basis of a review of electronic medical records. Physician and nurse interviewers measured and recorded weight (kg) and height (cm).

Statistical Analysis

Unpaired t-test analysis and Chi square (X^2) test (categorical data comparison) were used between variables to estimate the significance of different between groups for demographic and clinical laboratory. were used for. The optimal sensitivity and specificity using different BMI cut-off values to predict the presence of diabetes were examined by receiver operating characteristic curve (ROC) analysis. A greater area under the curve (AUC) indicates better predictive capability. An AUC = 0.5 indicates that the test performs no better than chance, and an AUC=1.0 indicates perfect discrimination. An ideal test is one that reaches the upper left corner of the graph (100% true positives and no false positives). To determine the optimal BMI cut off points, we computed and searched for the shortest distance between any point on the curve and the top left corner on the y-axis. Distance was estimated at each one-half unit of BMI according to the equation: Distance in ROC curve = $(1\text{-sensitivity})^2 + (1\text{-specificity})^2$ [33,34]. Additional criteria were also used to select cut-offs, including the greater sum of sensitivity and specificity, the smallest misclassification rate, and the significant associations between BMI and risk factors based on the logistic regression. Diagnostic performance of BMI in predicting diabetes was assessed by calculating AUC, sensitivity, specificity, likelihood ratios, false positive, false negative and the total misclassification rate. All results are presented as mean ± standard deviation or percentage, where applicable. Data analysis was performed in each gender separately. BMI was stratified in unit of 0.5 for both gender. We consider a BMI < 15.0 as the reference. The independent relationship between the stratified BMI and the odds ratio of having diabetes were analysed using logistic regression. All statistical analyses were performed using SPSS Version 22.0. The difference between groups was considered significant when P < 0.05.

Results

Of the 5498 participants analyzed, 2049 (37.3%) were male and 3449 (62.7%) were female with female to male ratio 1.7:1. Age was 42.7 ± 15.8 (minimum 18 years and maximum 105 years) and males were significantly older than females (45.3 ± 16.6 vs. 41.1 ± 15.1 respectively, p < 0.0001). BMI was 29.6 ± 6.9Vwhere females had higher BMI than males (30.1 ± 7.5 vs. 28.8 ± 5.5 respectively, p < 0.0001), Table 1. T2DM was present in 1873 (34.1%), 743 (39.7%) were male and 1130 (60.3%) were female with female to male ratio 1.5:1.

Parameters	Total	Male	Female	P value
n (%)	5498	2049 (37.2)	3449 (62.7)	
Age (years)	42.7 ± 15.8	45.3 ± 16.6	41.1 ± 15.1	< 0.0001
Body mass index (kg/m^2)	29.6 ± 6.9	28.8 ± 5.5	30.1 ± 7.5	< 0.0001
Diabetes	1873 (34.1)	743 (39.7)	1130 (60.3)	0.008

Table 1: *Population characteristics (means ± SD or number (%)).*

Table 2 displays details of the diagnostic performance of BMI in detecting T2DM using optimal BMI cut-off values based on the shortest distance in ROC curve. Values ranged from 28.50 to 29.50 in total population, 27.50 to 28.50 in male and from 28.50 to 29.50 in female. The AUC was 0.588 (95% CI,0.563-0.613) in male and 0.673 (95% CI,0.654-0.692) in female, Figure. These values were statistically significantly higher than that would be expected by chance alone (*P* < 0.0001).

Parameters	Area under curve (95% CI)	Cut-offs BMI kg/m^2	Sensitivity	Specificity	False positive rate	False negative rate	Positive likelihood ratio	Negative likelihood ratio	Misclassification rate
Total	0.640 (0.625-0.655)	29.0	0.59	0.58	0.42	0.41	1.02	0.71	0.83
Male	0.588 (0.563-0.613)	28.5	0.55	0.56	0.44	0.45	0.98	0.8	0.89
Female	0.673 (0.654-0.692)	29.5	0.63	0.64	0.36	0.37	0.98	0.58	0.73

Table 2: *Diagnostic performance of BMI in detecting diabetes using optimal BMI cut-off values based on the shortest distance in ROC curves in Saudi adults.*

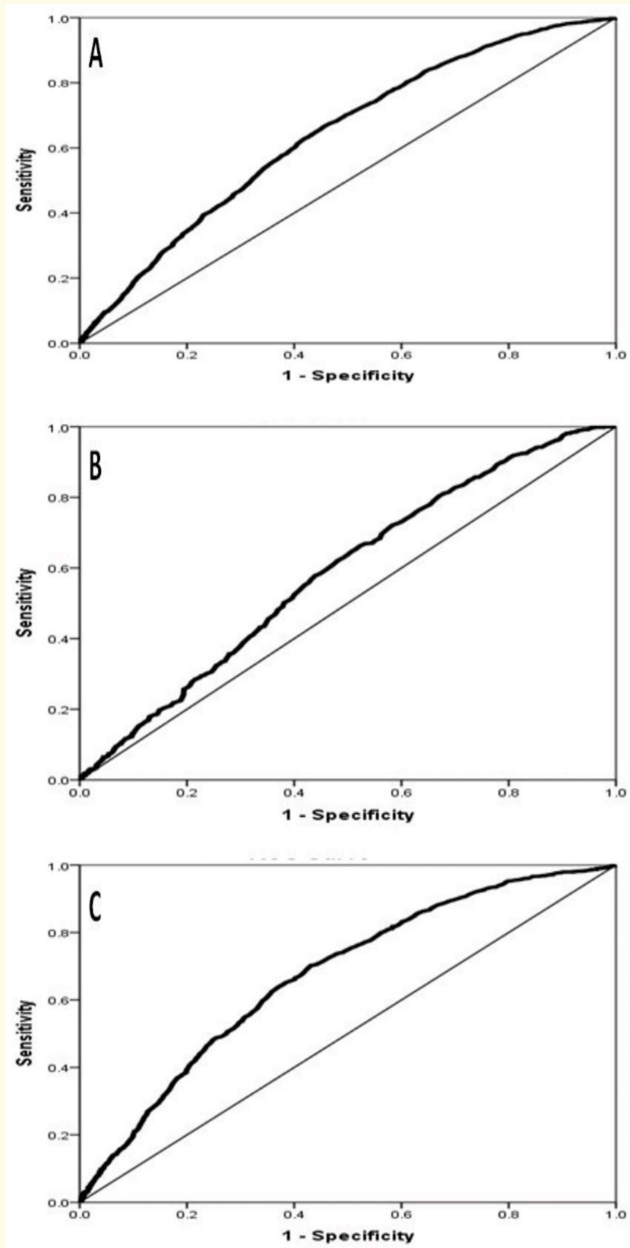

Figure: *ROC curve showing the performance of BMI in predicting diabetes (A: diabetes in total population, B: diabetes in male, C: diabetes in female).*

Table 3 shows the predictive value of BMI in detecting T2DM using BMI cut-off values based on the lowest significant association between BMI and the risk factors from the logistic regression analysis. Regression analysis showed that the risk of T2DM was significantly increased at BMI values as low as 12 to 14 and increased progressively as BMI increased. Applying this criterion to identify the cut-off values resulted in improvements in sensitivity, false negative rate and worsening in specificity and false positive rate. A very small false negative rate ranging from 0.01 to 0.02 resulted by using these lower BMI cut-offs.

Parameters	Area under curve (95% CI)	Cut-offs BMI kg/m^2	Sensitivity	Specificity	False positive rate	False negative rate	Positive likelihood ratio	Negative likelihood ratio	Misclassification rate
Total	0.640 (0.625-0.655)	16.0	0.996	0.012	0.988	0.004	1.01	0.33	0.99
Male	0.588 (0.563-0.613)	18.0	0.999	0.030	0.970	0.001	1.03	0.03	0.97
Female	0.673 (0.654-0.692)	19.0	0.982	0.064	0.936	0.018	1.05	0.28	0.95

Table 3: *Diagnostic performance of BMI in detecting diabetes using optimal BMI cut-off values based on the significant association using logistic regression in Saudi adults.*

Table 4 shows the odds ratios of the association between diabetes and BMI in male and female. A significant positive association was observed with BMI values starting at 12 to 14 for females and at 17 and increasing progressively with higher BMI values for both genders.

	Total		Male		Female	
BMI (kg/m^2)	**Odd ratio (95% C I)**	**P**	**Odd ratio (95% C I)**	**P**	**Odd ratio (95% C I)**	**P**
< 15.0	6.8 (1.5-30.8)	< 0.0001	-	-	6.6 (1.5-30.0)	0.02
15.0-15.9	5.5 (2.1-14.6)	0.001	-	-	4.8 (1.8-13.1)	0.002
16.0-16.9	13.7 (4.2-45.1)	< 0.0001	-	-	10.6 (3.2-35.6)	< 0.0001
17.0-17.9	8.4 (3.5-20.2)	< 0.0001	15.6 (1.9-125.6)	0.01	6.4 (2.4-16.9)	< 0.0001
18.0-18.9	12.8 (5.2-29.0)	< 0.0001	18.9 (2.4-150.7)	0.006	10.3 (4.0-26.7)	< 0.0001
19.0-19.9	10.6 (5.2-21.8)	< 0.0001	4.8 (1.7-13.4)	0.003	20.5 (6.3-67.0)	< 0.0001
20.0-20.9	8.4 (4.8-14.8)	< 0.0001	3.8 (1.4-10.8)	0.01	11.0 (5.5-21.9)	< 0.0001
21.0-21.9	4.2 (2.7-6.4)	< 0.0001	1.7 (0.8-3.6)	0.2	8.3 (4.4-15.9)	< 0.0001
22.0-22.9	4.9 (3.2-7.6)	< 0.0001	2.6 (1.2-5.5)	0.01	7.6 (4.1-14.2)	< 0.0001
23.0-23.9	3.6 (2.5-5.2)	< 0.0001	2.1 (1.0-4.4)	0.04	4.5 (2.9-7.1)	< 0.0001
24.0-24.9	3.0 (2.1-4.2)	< 0.0001	1.6 (0.8-3.2)	0.2	4.0 (2.6-6.0)	< 0.0001
25.0-25.9	2.7 (1.9-3.8)	< 0.0001	1.8 (0.9-3.4)	0.1	3.2 (2.1-4.9)	< 0.0001
26.0-26.9	2.3 (1.7-3.2)	< 0.0001	1.5 (0.8-2.9)	0.2	2.8 (1.8-4.2)	< 0.0001
27.0-27.9	2.2 (1.6-3.0)	< 0.0001	1.5 (0.8-2.6)	0.2	2.7 (1.9-4.0)	< 0.0001
28.0-28.9	2.3 (1.3-3.22)	< 0.0001	1.3 (0.7-2.5)	0.4	3.1 (2.1-4.6)	< 0.0001
29.0-29.9	1.8 (1.3-2.4)	< 0.0001	1.0 (0.85-1.9)	0.9	2.4 (1.7-3.5)	< 0.0001
30.0-30.9	1.6 (1.2-2.1)	0.004	1.0 (0.5-1.9)	0.9	1.9 (1.3-2.8)	0.001
31.0-31.9	1.4 (1.1-2.0)	0.02	1.2 (0.6-2.3)	0.6	1.5 (1.0-2.1)	0.04
32.0-32.9	1.7 (1.3-2.4)	0.001	1.0 (0.5-2.0)	0.9	2.1 (1.4-3.1)	< 0.0001
33.0-33.9	1.5 (1.1-2.0)	0.02	1.4 (0.7-2.7)	0.3	1.3 (0.9-2.0)	0.1
34.0-34.9	1.2 (0.9-1.7)	0.2	1.2 (0.6-2.4)	0.6	1.2 (0.8-1.7)	0.4
35.0-35.9	1.3 (0.9-1.8)	0.2	1.0 (0.5-2.3)	0.9	1.3 (0.8-1.9)	0.2
36.0-36.9	1.1 (0.7-1.6)	0.7	0.9 (0.4-2.0)	0.8	1.1 (0.7-1.7)	0.7
37.0-37.9	1.1 (0.7-1.7)	0.6	1.7 (0.7-4.2)	0.2	0.9 (0.5-1.5)	0.7
38.0-38.9	1.1 (0.7-1.7)	0.7	0.8 (0.3-2.0)	0.7	1.1 (0.7-1.9)	0.6
39.0-39.9	1.8 (1.2-2.9)	0.01	13 (0.5-3.8)	0.6	2.0 (1.2-3.3)	0.01

Table 4: *Risk of diabetes associated with increasing BMI in Saudi adults based on regression analysis.*

Discussion

In this hospital-based cohort of Saudi adults, we showed that lower BMI was associated with an increased frequency of T2DM. Individuals with a BMI of < 21 kg/m^2 have been significantly at higher risk of developing T2DM. Obesity has been shown to be associated with diabetes in Caucasians and Middle Eastern people, including Saudis [37-40]. The use of BMI with optimal cut-off points for diagnosis of obesity is important to establish consequent public health policies, treatment protocols and to determine the correct optimal cut-off points of BMI for each population.

T2DM is characterized by both insulin resistance and dysfunctional insulin secretion. High BMI is a strong risk factor for insulin resistance and T2DM. However, impaired insulin secretion also increases the risk for T2DM, particularly in Asians and may cause T2DM at low BMI values [41-43]. The relative insulin deficiency may impair glucose utilization in muscle and adipose tissues as occurs in type 1 diabetes [44].

The risk of T2DM associated with each BMI level was estimated, adjusting for other covariates. To assess the impact of the other covariates, we estimated an unadjusted logistic regression model (with BMI level as the only covariate). The Odd Ratios (OR), which approximate the relative risks in the nested case-control analysis, are listed in Table 4. BMI cut-off of 16.0 kg/m^2 was associated with the highest unadjusted and adjusted prevalence ratio. The unadjusted ORs were slightly higher than the adjusted ORs. This implies that some factors, such as age and gender, are associated with both increased BMI and increased risk of T2DM, but the impact of these factors on the association between BMI and risk of T2DM is limited. Moreover, BMI values were clinically measured in the current study, compared with BMI calculated from self-reported height and weight in those earlier studies. Self-reported weight and height considerably underestimate the individuals' measured BMI and may thus have weakened the association between obesity and risk of T2DM and/or biased the estimated results [45,46]. Self-reported diabetes has high specificity and positive predictive value but low sensitivity [47]. This may explain the higher OR associated with BMI levels in the current study compared to other report [48]. Adults with early diagnosed diabetes were more obese and more likely to be female than adults with a later onset of type 2 diabetes [49]. We have shown using regression models unadjusted for baseline characteristics that the frequency of diabetes increased progressively starting at BMI of 16.0 kg/m^2 particularly in females. Jung., *et al.* showed that among the 103,063 cases of incident diabetes, 47,713 (46.3%) occurred in normal weight or underweight participants (BMI, 16.0-24.9 kg/m^2). Cox regression models adjusted for baseline characteristics showed that the incidence of diabetes increased progressively as the baseline BMI increased irrespective of sex [50].

Pre-specified anthropometric cut-points serve to standardize comparisons of obesity within and between populations [51]. However, the currently used cut-points are derived from studies among subjects of European ancestry and may not be applicable to other ethnic groups such as Asians, including Saudis [26]. A recent consultation by a World health organization expert group reviewed the scientific evidence for appropriate cut points for BMI in Asians and suggested that Asians have different associations between BMI, percentage of body fat, health risk of T2DM compared to European populations [18]. In this study, ROC curve analysis and associated sensitivity and specificity showed that, among Saudi men and women respectively, BMI values of 28.5 to 29.5 kg/m^2, best characterize individuals' optimal cut-points. Alternatively, the differences in cut-points may reflect real underlying differences in body fat percentages corresponding to a given BMI value between Saudis and Asians or Europe ethnic groups. Thus, the proposed cut-points need to be validated in other Arab populations of the Middle East. Studies among Asians living in Asia have documented similar or lower cut-points for BMI (27 in Hong Kong, Indonesia and Singapore; in rural Thailand; and 29 kg/m^2 in Japan) [52]. For Chinese and South Asians living in Canada, the optimal BMI ranged from 20.6 to 28.8 kg/m^2 [53,54]. Two large cross-sectional studies of diabetes from Indian cities reported BMI cut-offs of 23.1 kg/m^2 for males and 23.8 kg/m^2 for females in one study, and 23.0 kg/m^2 for both sexes in the other [22,24]. A nationwide population-based cross-sectional study conducted in Pakistan found that diabetes was associated with BMI cut-offs of 22.1 kg/m^2 for males and 22.9 kg/m^2 for females [23]. A prospective cohort study from Canada, which analysed diabetes incidence rates using Cox proportional hazards models, found that a BMI cut-off of 24.0 kg/m^2 was appropriate for South Asians [19].

The overall performance of the ROC curve can be quantified by estimating the AUC which ranged from 0.59 to 0.69, Table 3. An area of 1.0 is perfect and an area < 0.5 is considered non-informative. Our results indicated that the ROC analysis was close to a non-informative test as shown in the Figure. ROC curve analysis showed that the corresponding sensitivities and specificities were poor (< 0.63 and < 0.62, respectively). This indicates that the percentage of people identified as having the risk factors and the percentage of people who were identified as not being at risk were less than 63% of total population. Both positive likelihood ratio and negative likelihood ratio were close to 1.0, indicating a minimal increase in the likelihood of the presence of the risk factor if the test is positive and a minimal decrease in the likelihood if the test is negative. The false positive and false negative rates were high and close to each other in both women and men. Several reasons may explain the weakness of BMI as a tool to classify obesity in the Saudi Arabian population. First, BMI does not reflect fatness uniformly in all populations and different ethnic groups [55]. This may suggest the importance of including a measure of abdominal obesity in classifying obesity in Saudi populations. Second, the short stature of Saudi women could be limiting the usefulness of BMI in this population [27].

The overall misclassification was high and exceeded 80% of the total population across all the selected BMI cut-off points. Most of the other previous studies that have been conducted in non-Caucasian populations did not assess the misclassification rate [28,29,42,56-60]. However, one study conducted in Asian Indians indicated a high overall misclassification rate, particularly in women [55]. Those authors concluded that the BMI did not accurately predict overweight in that population. This is not the first study to suggest the presence of a significantly increased risk of T2DM at BMI values less than 25. However, the use of such low cut-offs would lead to large misclassification of healthy people as being at risk, as indicted by the high values of sensitivities and false positive rates. This fact that could cause unnecessary and costly diagnostic testing. Overall the total misclassification rate was unacceptably high, even with the use of different BMI cut off points. These findings illustrate the significant limitations in using BMI alone for obesity diagnosis in the Saudi Arabian population.

Our results should be interpreted in light of the study's limitations. First, and foremost, the use of a retrospective cohort design prevented us from understanding the causal effect of BMI on the risk of developing T2DM. Selection bias due to the healthy volunteer effect may have affected this study. Another limitation of the present study was having considered only overall obesity (assessed by BMI) and not abdominal obesity (measured by waist circumference), which is known to bear a close relationship with the target diseases. Prospective studies should be done to identify the causes of the incidence of these diseases and explain the role of genetic, nutritional, and/or metabolic factors in the appearance of these diseases in Saudis. Our data on diagnosed diabetes was based on self-report. The accuracy of self-reporting for diabetes is reasonably high in population surveys; self-reported diabetes has high specificity and positive predictive value but low sensitivity. Several authors point out that self-reported data could underestimate diabetes prevalence [47]. Although this underestimation is possible, other authors have confirmed that self-reported diabetes is a reasonably reliable surrogate for diagnosed diabetes, based on their studies of the accuracy of patients' self-reports compared with medical records. Our sample was drawn from a hospital-based patient; therefore, this study may not be comparable to other population studies and cannot strictly be generalized to the whole older Saudi population. Finally, generalization of these findings is limited, because the data are predominantly from those of Jeddah ancestry. Considering the goal population, a larger cohort would have probably provided a greater power of the statistical analyses.

Conclusion

The diagnostic usefulness of BMI alone in defining obesity is limited in this large population of among men and women Saudi adults.

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Volume 3 Issue 3 August 2018