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RESEARCH ARTICLE

Elevated HbA1c levels in individuals not diagnosed with type 2 diabetes in Qatar: a pilot study

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ABSTRACT

Background: The prevalence of type 2 diabetes (T2D) in Qatar and the Middle East is one of the highest in the world. It is estimated that about one quarter of the individuals with T2D are undiagnosed. Elevated HbA1c levels are an indicator of T2D or a pre-diabetic state. In this study we set out to examine which factors, such as anthropometric and socio-demographic risk factors, are associated with elevated HbA1c levels in a population without T2D.
Methods: We examined 191 subjects with no record of T2D. Anthropometrics and HbA1c were measured. Socio-demographic (age, gender, ethnicity and educational level) and health information were assessed through questionnaires. Elevated HbA1c levels were defined as $>6.0\%$ (>42 mmol/mol). Individual risk factors were examined in relationship to having elevated HbA1c levels using logistic regression.
Results: Thirty-eight (20%) study participants had elevated HbA1c levels. Participants from South Asian and Filipino descent were more likely to present with elevated HbA1c levels than Arab participants (adjusted odds ratios (OR): 13.30 (95% confidence interval (CI): 4.24, 41.79), $p < 0.001$ for South Asian and 4.54 (95% CI: 1.04, 19.83), $p = 0.04$ for Filipinos). A body mass index of above 30 kg/m^2 was associated with elevated HbA1c levels (adjusted OR: 2.90 (95% CI: 1.29, 6.51), $p = 0.01$). Neither gender nor educational level was associated with elevated HbA1c levels.
Conclusions: Elevated HbA1c levels in individuals not diagnosed with diabetes were most frequently found in the South Asian and Filipino immigrant population. Special attention should therefore be given to the early identification of T2D in these subjects.

Keywords: HbA1c, undiagnosed type 2 diabetes, public health, pre-diabetes, ethnic differences

Table 1. Subject characteristics.

	HbA1c ≤ 6.0% (≤ 42 mmol/mol)	HbA1c > 6.0 (> 42 mmol/mol)
	N = 153	N = 38
	Mean (standard deviation) or number of participants (%)	
Ethnicity		
Arab*	102 (67%)	17 (45%)
South Asian**	27 (18%)	17 (45%)
Filipino	18 (12%)	4 (10%)
Other or mixed	6 (4%)	0 (0%)
Age (Years)	39.0 (12.2)	49.5 (9.0)
Gender		
Male	67 (44%)	18 (47%)
Female	86 (56%)	20 (53%)
Highest educational level		
No schooling or primary school	15 (10%)	3 (8%)
Intermediate or high school	51 (34%)	13 (35%)
College or university	83 (56%)	21 (57%)
Weight (kg)	76.9 (15.7)	82.1 (16.5)
Height (cm)	164.5 (8.8)	161.6 (9.3)
Body mass index (kg/m^2)	28.4 (5.1)	31.7 (7.2)
Waist circumference (cm)	94.4 (12.5)	104.9 (14.6)
HbA1c (%)	5.4 (0.4)	6.4 (0.5)
HbA1c (mmol/mol)	35.8 (3.8)	46.4 (5.6)

* Arab: Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates and Yemen.
** South Asian: Bangladesh, India, Nepal, Pakistan and Sri Lanka.

INTRODUCTION

The prevalence of type 2 diabetes (T2D) in Qatar is estimated to be 23% and is one of the highest in the world.[1] In 1990, the prevalence was estimated at 6%, thus showing an exceptionally high rate of increase over the past decades. Furthermore, it is estimated that about a quarter of individuals with T2D in Qatar are still undiagnosed.[1] With this rate of increase, T2D has become an increasing burden on the Qatari society.

It has become a growing public health challenge to identify those individuals that are at risk for developing T2D. Primary preventive strategies are focused on recognizing risk factors and when possible intervening, while screening strategies are aimed at identifying individuals with undiagnosed T2D. For example, elevated HbA1c levels are known to be predictive for the later development of T2D. Furthermore, an abundance of studies have shown that characteristics such as a high waist-hip ratio, lower socio-economic status, dark skin-color, fewer years of education and higher BMI are associated with elevated HbA1c levels.[2–4]

Qatar is a rapidly growing economy with a free nationalized healthcare program, which is accessible to all residents regardless of ethnic or social background. Many of the preventive strategies are based on research that was performed outside of Qatar, often in Western societies.[5] Also Qatar, like many other countries around the Gulf region, has a unique and dynamic socio-demographic structure with a stable native population and a rapidly growing expatriate population. Therefore, preventive strategies for T2D should be based on up-to-date studies from the region, and they also need to be stratified by population type. Thus, in this pilot study we set out to examine what anthropometric and

Table 2. Associated factors for elevated HbA1c levels among participants without T2D.

Ethnicity	HbA1c ≤ 6.0% (≤42 mmol/mol)	HbA1c > 6.0% (>42 mmol/mol)	Odds Ratios		
			Model 1	Model 2	Model 3
Arab	102 (66.7%)	17 (44.7%)	Reference -0-	Reference -0-	Reference 0-
South Asian	27 (17.6%)	17 (44.7%)	3.78 (1.71, 8.37) **p = 0.001**	5.40 (2.14, 13.63) **p < 0.001**	13.30 (4.24, 41.79) **p < 0.001**
Filipino	18 (11.8%)	4 (10.5%)	1.33 (0.40, 4.42) p = 0.64	2.16 (0.59, 7.94) p = 0.25	4.54 (1.04, 19.83) **p = 0.04**
Age	HbA1c ≤ 6.0% (≤42 mmol/mol)	HbA1c > 6.0% (>42 mmol/mol)	Odds Ratios		
			Model 1	Model 2*	Model 3*
<40 years	91 (59.5%)	8 (21.1%)	Reference -0-	Reference -0-	Reference -0-
40–49 years	33 (21.6%)	9 (23.7%)	3.10 (1.11, 8.71) **p = 0.03**	3.14 (1.12, 8.84) **p = 0.03**	3.52 (1.18, 10.46) **p = 0.02**
50–59 years	20 (13.1%)	18 (47.4%)	10.24 (3.91, 26.83) **p < 0.001**	10.61 (3.98, 28.26) **p < 0.001**	12.58 (4.44, 35.68) **p < 0.001**
>60 years	9 (5.9%)	3 (7.9%)	3.79 (0.85, 16.88) p = 0.08	3.87 (0.87, 17.30) p = 0.08	3.59 (0.74, 17.34) p = 0.11
Gender	HbA1c ≤ 6.0% (≤42 mmol/mol)	HbA1c > 6.0% (>42 mmol/mol)	Odds Ratios		
			Model 1	Model 2**	Model 3**
Female	86 (56.2%)	20 (52.6%)	Reference -0-	Reference -0-	Reference -0-
Male	67 (43.8%)	18 (47.4%)	1.16 (0.57, 2.36) p = 0.69	0.82 (0.38, 1.78) p = 0.82	1.26 (0.54, 2.96) p = 0.60
Highest educational level	HbA1c ≤ 6.0% (≤42 mmol/mol)	HbA1c > 6.0% (>42 mmol/mol)	Odds Ratios		
			Model 1	Model 2	Model 3
No schooling or primary school	15 (10.1%)	3 (8.1%)	Reference -0-	Reference -0-	Reference -0-
Intermediate or high school	51 (34.2%)	13 (35.1%)	1.28 (0.32, 5.07) p = 0.73	2.01 (0.46, 8.89) p = 0.36	1.91 (0.41, 9.02) p = 0.41
College or university	83 (55.7%)	21 (56.8%)	1.27 (0.34, 4.78) p = 0.73	2.35 (0.55, 10.03) p = 0.25	2.14 (0.47, 9.81) p = 0.33

Body Mass Index	HbA1c ≤ 6.0% (≤ 42 mmol/mol)	HbA1c > 6.0% (> 42 mmol/mol)	Odds Ratios		
			Model 1	Model 2	Model 3
Non-obese (< 30 kg/m^2)	103 (67.3%)	16 (42.1%)	Reference	Reference	N/A
			-0-	-0-	
Obese (> 30 kg/m^2)	50 (32.7%)	22 (57.9%)	2.83 (1.37, 5.86)	2.90 (1.29, 6.51)	N/A
			p = 0.005	p = 0.01	
Waist circumference	HbA1c ≤ 6.0% (≤ 42 mmol/mol)	HbA1c > 6.0% (> 42 mmol/mol)	Odds Ratios		
			Model 1	Model 2	Model 3
Normal	42 (28.0%)	5 (13.2%)	Reference	Reference	Reference
			-0-	-0-	-0-
High	108 (72.0%)	33 (86.8%)	2.57 (0.94, 7.02)	2.36 (0.79, 7.08)	1.39 (0.42, 4.62)
			p = 0.07	p = 0.13	p = 0.59

Cut-off for normal/high waist circumference were based on cut-off of the International Diabetes Federation (10).
Arab: Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates and Yemen.
South Asian: Bangladesh, India, Nepal, Pakistan and Sri Lanka.
Model 1: Unadjusted
Model 2: Adjusted for age and gender
Model 3: Adjusted for age, gender and body mass index
* Model not adjusted for age
** Model not adjusted for gender

socio-demographic risk factors are associated with elevated HbA1c levels in a population without T2D.

METHODS

Study design and enrolment

This study was embedded in the Qatar Metabolomics Study on Diabetes (QMDiab),[6] a larger collaborative effort between the Dermatology Department of Hamad Medical Corporation (HMC) in Doha, Qatar and Weill Cornell Medical College – Qatar (WCMC-Q). Subjects were recruited through the Dermatology Department at Rumailah Hospital. All patients, visiting the dermatologist, were asked to participate in the study. Subjects were enrolled between February and July 2012. All subjects needed to be above 18 years of age and have no record of T2D. All participants gave written informed consent. Ethical approval was obtained from the Institutional Review Board from both HMC and WCMC-Q.

Population for analysis

In total, 191 subjects without T2D were enrolled, based on absence of self-reported T2D. Furthermore, we confirmed that the subjects were not taking oral glucose lowering drugs by questionnaire. Elevated HbA1c levels was based on the standard clinical cut-offs of > 6.0% (> 42 mmol/mol).[7] This cut-off has also been approved by the American Diabetes Association (ADA) as a diagnostic cut-off for pre-diabetes.[7] Also, in several other populations, HbA1c has been shown to be a reliable alternative to fasting plasma glucose to detect diabetes.[8,9] In total, 38 participants (19.9%) had an elevated HbA1c level. Subject characteristics are shown in Table 1.

Data collection

Data regarding sex, age, ethnicity and highest educational qualification were obtained through questionnaire. Ethnicity was determined based on the birthplace of the participant, both parents and four grandparents. The Arab population consisted of subjects from Bahrain, Egypt, Iraq, Jordan, Kuwait, Lebanon, Morocco, Oman, Palestine, Qatar, Saudi Arabia, Somalia, Sudan, Syria, Tunisia, United Arab Emirates and Yemen. The South Asian subjects were from Bangladesh, India, Nepal, Pakistan and Sri Lanka.

Using standardized protocols trained researchers performed all measurements. Weight was measured lightly clothed to the nearest decimal with an electronic scale (SECA Scale 813, Hamburg,

Germany). Height was measured without shoes and to the nearest decimal using a stadiometer (SECA Mobile Stadiometer 217, Hamburg, Germany). Waist circumference was measured with SECA 201 Ergonomic Circumference Measuring Tape (SECA, Hamburg, Germany) and a high waist circumference was based on ethnic specific cut-offs.[10] For Arabs, a high waist circumference was defined as ≥ 94 cm for males and ≥ 80 cm for females. For South Asians and Filipinos, these cut-offs were ≥ 90 cm and ≥ 80 cm, respectively.[10] Using standardized protocols, venous blood samples were collected by venipuncture in 4.0 ml EDTA tubes and stored at 7°C prior to processing. Blood samples were taken under non-fasting conditions. Automated analyses of HbA1c levels were performed within four hours of blood collection at the Department of Laboratory Medicine and Pathology of HMC with the cobas® 6000 (Roche Diagnostics, Basel, Switzerland).

Statistical analyses

Individual risk factors were examined in relationship to having elevated HbA1c levels using logistic regression. Since the age distribution was different between the two groups, we used an unadjusted model (model 1), an age- and gender-adjusted model (model 2), and an age-, gender- and body mass index-adjusted model (model 3). Body mass index was calculated as weight divided by height squared (kg/m^2). Effect estimates for the risk of increased HbA1c levels for each individual risk factor are presented using odds ratios and their 95% confidence interval (95% CI). A p-value lower than 0.05 was considered statistically significant. All statistical analyses were performed using the IBM Statistical Package for the Social Sciences Version 20.0 (SPSS Inc., Chicago, IL, USA).

RESULTS

Table 2 shows the odds ratios for the risk of having elevated HbA1c levels according to various risk factors. Of the participants from South Asian descent, 39% had HbA1c levels higher than 6.0%.
The unadjusted odds ratio for elevated HbA1c among South Asians was 3.78 (95% CI: 1.71, 8.37, $p = 0.001$). After adjusting for age and gender, the risk for South Asians to have elevated HbA1c levels was over five times higher than for Arabs (odds ratio: 5.40 (95% CI: 2.14, 13.63), $p < 0.001$). When we additionally adjusted the model for BMI the odds ratios increased (13.30 (95% CI: 4.24, 41.79), $p < 0.001$ for South Asians and 4.54 (95% CI: 1.04, 19.83), $p = 0.04$ for Filipinos). Obese (BMI > 30 kg/m^2) subjects were more likely to have elevated HbA1c levels (odds ratio: 2.90 (95% CI: 1.29, 6.51), $p = 0.01$). Subjects with an increased waist circumference had higher HbA1c levels, but this association was not significant (odds ratio: 2.36 (95% CI: 0.79, 7.08, $p = 0.13$). However, when examining the waist circumference as a continuous variable, the odds ratios (per cm increase) for an increased HbA1c were 1.06 (95% CI: 1.03, 1.09), $p < 0.001$ (for both models: unadjusted and adjusted for age and gender). There was no significant difference between males and females, nor was there an association between educational level and HbA1c levels.

DISCUSSION

In this study we set out to examine which factors are related to having elevated HbA1c levels in a population without T2D in Qatar. We found more than a 13-fold increased chance of having high HbA1c levels among South Asians in comparison to Arabs and a 4.5-fold increased chance among Filipinos compared to Arabs. Moreover, of all participants from South Asian descent who did not have T2D, 38% had HbA1c levels above 6.0% which is indicative of undiagnosed impaired glucose metabolism or T2D.

Some methodological issues need to be considered. Most importantly, we consider this study to be a pilot due to the relatively low number of participants. Previous studies performed on undiagnosed diabetes in other populations are generally larger.[9,11–13] For a number of the risk factors such as gender and education levels that we investigated, the absence of association may be due to lack of statistical power. Secondly, subjects were recruited through the Dermatology Department, which potentially may have led to selection bias. Some of the individuals may use topical steroids, which increases the risk of developing insulin resistance. Nonetheless, this risk would be increased in all ethnicities and therefore this is unlikely to have influenced our effect estimates. Finally, we used the known clinical cut-off of HbA1c levels above 6.0% (42 mmol/mol). This cut-off is generally accepted by the American Diabetes Association.[7] For impaired glucose metabolism and pre-diabetes, however, there has been some recent discussion whether the cut-off should be lowered to 5.7% (39 mmol/mol) instead of 6.0%.[14] Using a 5.7% cut-off also gave an increased risk for having high

HbA1c levels amongst South Asians and Filipinos (odds ratios: 3.90 (95% CI: 1.73, 8.77), p = 0.001, and 4.43 (95% CI: 1.60, 12.26), p = 0.004, respectively). These results indicate that our findings are robust and not dependent of the clinical cut-offs.

The concentration of HbA1c in plasma reflects glucose metabolism over the past two-three months. Positive associations have been found between the risk of T2D or hyperglycemia and total fat intake.[15–18] Dietary fat intake may have an effect on glycaemia, and subsequently high HbA1c. High fat intake may also be related to obesity, which is in turn associated with insulin resistance.[19–21] The racial and ethnic differences in HbA1c have been recognized for many years but have generally been attributed to differences in access to medical care or quality of care.[22] However, various studies have now shown that despite adjustment for socio-demographic characteristics, access to care, quality of care, and self-management behaviors, racial and ethnic differences in HbA1c remain.[23–25] In this study, the BMI correction for HbA1c in the various ethnicities made the differences in HbA1c in Arabs compared to South Asian larger. The Arabs in our study had a markedly higher BMI and waist circumference than the South Asians and Filipinos. Therefore, one would expect a higher HbA1c level in the Arabs compared to the South Asians. However, the opposite is true, which emphasizes the important role of ethnicity in relation to HbA1c in Arabs and South Asians.

Qatar has one of the fastest growing economies worldwide, with an equally rapidly increasing population. In our study almost 20% had an elevated HbA1c, which is similar to a screening pilot study that was recently performed in Saudi Arabia.[26] Like many other Gulf countries, the size of the local population has been relatively stable over the past decade, while the population growth has come from a huge surge of immigrants. Most of these immigrants are native to South Asia (India, Pakistan, Nepal, Sri Lanka and Bangladesh) and the Philippines. Our data suggests that these immigrant populations have a large increased risk of having undiagnosed T2D.

CONCLUSION

In this study we found large ethnic differences in the HbA1c levels amongst subjects without T2D in Qatar. Larger epidemiological studies are necessary to examine these differences and other risk factors in Qatar and the entire Gulf region. The ADA already recommends screening for T2D in all asymptomatic adults above 45 years old.[27] However, regarding this study, the screening and focus on the early detection of T2D should particularly be performed among the South Asian and Filipino populations in Qatar.

AUTHOR DISCLOSURE STATEMENT

All authors have no conflict of interest to disclose.

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