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Complete List of Authors:	Regmi, Dybesh; University of Toronto Faculty of Medicine, Department of Family and Community Medicine Al-Shamsi, Saif; UAE University College of Medicine and Health Sciences, Department of Internal Medicine Govender, Romona; UAE University College of Medicine and Health Sciences, Department of Family Medicine Al-Kaabi, Juma; UAE University College of Medicine and Health Sciences, Department of Internal Medicine
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Incidence and risk factors of type-2 diabetes mellitus in an overweight and obese population: a long-term study from a Gulf State

Dybesh Regmi[1], Saif Al-Shamsi[2*], Romona D. Govender[3], Juma Al Kaabi[2]

[1]Department of Family and Community Medicine, University of Toronto, Toronto, Canada

[2]Department of Internal Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

[3]Department of Family Medicine, College of Medicine and Health Sciences, Al Ain, United Arab Emirates University, United Arab Emirates

*Corresponding author:

Saif Al-Shamsi

Department of Internal Medicine, College of Medicine & Health Sciences, United Arab Emirates University, PO Box 17666, Al Ain, United Arab Emirates

Phone: +971 3 713 7439

Fax: +971 3 767 2995

E-mail address: salshamsi@uaeu.ac.ae (SAS)

Abstract

Objectives: A high body mass index (BMI) is associated with a risk for type-2 diabetes mellitus (DM). The United Arab Emirates (UAE) is experiencing a marked increase in obesity. Data on the incidence of type-2 DM in this high-risk adult UAE population is unavailable. This study aimed to evaluate the incidence and risk of developing type-2 DM among individuals with above-normal BMI in the UAE.

Design: A retrospective cohort study.

Setting: Outpatient clinics at a tertiary care centre in Al Ain, UAE.

Participants: 362 overweight or obese adult UAE nationals who visited outpatient clinics between April 2008 and December 2008.

Primary outcome measure: Patients with type-2 DM were identified based on diagnosis established by a physician or glycated hemoglobin (HbA1c) levels ≥ 6.5% during the follow-up period (until April 2018).

Results: The overall incidence rate of type-2 DM during the median follow-up time of 8.7 years was 16.3 (95% CI: 12.1–21.4) cases per 1000 person-years. Incidence rates in males and females were 17.7 (95% CI: 1.14–2.60) and 15.0 (95% CI: 0.99–2.35), respectively. Using multivariable Cox proportional hazard analysis, older age and obesity in females and HbA1c levels in males were determined to be independent risk factors for developing type-2 DM.

Conclusions: The incidence rate of type-2 DM in overweight and obese UAE nationals is high. In addition to screening, current strategies should strongly emphasize lifestyle modifications that decrease HbA1c and BMI levels in this high-risk population.

Article Summary

Strengths and limitations of this study

- A long-term (9-years) study that utilizes anthropometric and laboratory data to accurately quantify previously unknown incidence rate of type-2 DM in a high-risk group in the United Arab Emirates.
- In doing so, the results demonstrate different independent risk factors that influence the development of type-2 DM in males and females suggesting unique focused gender based strategies to be incorporated into the current preventative program.
- The study results provide a baseline to assess effectiveness of national diabetes preventative programs in obese and overweight individuals while allowing epidemiologists to benchmark the incidence rates globally.
- The usual limitations of a retrospective study apply here as well. A prospective study would probably also allow capturing data on physical activity, and changes in weight, both of which can influence development of type-2 DM.
- Another limitation of this study is missing baseline data on family history and history of Gestational diabetes both of which are well-known risk factors for developing type 2-DM. Their contribution if any to the development of new onset type-2 DM in our study population is not accounted for.

Keywords: incidence; obesity; risk factors; type-2 diabetes mellitus; United Arab Emirates

INTRODUCTION

There has been a rapid increase in the prevalence of obesity and type-2 diabetes mellitus (DM) globally. The United Arab Emirates (UAE) is one of the epicenters of this epidemic. Among UAE nationals, the crude prevalence of obesity and type-2 DM is 37%[1] and 29%[2], respectively and the number of people with type-2 DM in the country is estimated to reach over 2 million by 2040.[3]

Obesity, defined as a body mass index (BMI) ≥30 kg/m[2,4], is a known risk factor for type-2 DM[5] while lifestyle interventions such as weight loss in obese individuals with impaired glucose tolerance have been shown to reduce the risk for type-2 DM.[6] There has been significant attention and effort over the last decade in the UAE to curb the prevalence of overweight and obesity, as well as to decrease the incidence of associated diseases.

The *Weqaya,* a population-wide CVD screening program, was initiated in 2008[7] to enable individuals and healthcare providers to implement preventative measures. Epidemiological studies on type-2 DM in the UAE have primarily focused on its prevalence in the general population.[8] A decade after the implementation of the preventive program, data on the incidence of type-2 DM among obese and overweight UAE nationals remain unknown.

In this retrospective longitudinal cohort study, we aimed to determine the incidence of DM and elucidate the effect of BMI on type-2 DM risk in overweight and obese adult UAE nationals.

METHODS

Study setting

A retrospective electronic medical record review of adult patients who presented to outpatient clinics at Tawam hospital in Al Ain, UAE between April 1st, and December 31st 2008 was

performed. The tertiary care hospital is one of two governmental hospitals in the city and serves an estimated population of 650,000 patients, of which 30% are UAE nationals.[9] Tawam Hospital and the UAE University research and ethics board granted ethical approval for this study (CRD239/13). Informed consent was waived because patient records and information were anonymized and de-identified prior to analysis.

Subjects and procedures

The study population consisted of healthy overweight and obese UAE nationals, aged between 18 and 75 years, who were seen at primary care and specialty outpatient clinics at Tawam hospital (obstetrics and gynecology, internal medicine, and surgery, as well as subspecialty clinics). The inclusion criteria were patients without type-2 DM, defined as having glycated hemoglobin (HbA1c) <6.5%; patients not taking anti-diabetic medications; and those with BMI $\geq$ 25 kg/m^2 at baseline. The exclusion criteria were patients with missing HbA1c data; those with a history of chronic medical conditions such as malignancy, human immunodeficiency virus infection, receiving steroids or immunosuppression medications, or stage 3–5 chronic kidney disease [estimated glomerular filtration rate (eGFR) of $\leq$59 mL/min/1.73 m^2][10]. Those who had undergone weight reduction surgery defined as either restrictive or malabsorptive bariatric surgery or pharmacotherapy for weight loss were also excluded from the study. The final study group consisted of 362 subjects with a BMI of $\geq$ 25 kg/m^2 (Fig 1).

Definitions and measurements

Initial BMI was calculated from height and weight measured at baseline using the formula weight (kg) divided by height squared (m^2). Overweight and obesity were defined according to

the World Health Organization classification[4], with a BMI between 25 and 29.99 kg/m^2 and ≥30 kg/m^2, respectively. Hypertension (HTN) was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of antihypertensive medications.[11] Dyslipidemia was defined as serum total cholesterol (TC) of ≥6.21 mmol/L or if the patient had a documented prescription of lipid-lowering medications.[12] Current or prior history of smoking tobacco was considered positive for smoking history. Patients were considered to have vascular disease if they had a documented history of either coronary heart disease, cerebrovascular disease, or peripheral vascular disease.

Outcomes

Our study endpoint was incident type-2 DM, defined as either HbA1c ≥6.5% or a diagnosis of type-2 DM established by a physician occurring at any time during the follow-up period.[13] The occurrence of incident type-2 DM was based on a review of all of the electronic medical records until April 30, 2018. All laboratory assays at baseline and follow-up were conducted at the Medical Laboratory Department at Tawam Hospital. HbA1c levels were measured using an automated analyzer Integra 400 Plus (Roche Diagnostics, Mannheim, Germany).

Statistical analyses

Differences between sexes were determined using an independent-samples t-test or the Mann-Whitney U test for normal and non-normal data, respectively, with Fisher's exact test (two-tailed) being used for categorical variables. Person-years at risk for developing type-2 DM was calculated for each subject as the time from baseline visit to the diagnosis of type-2 DM or the most-recent outpatient visit, whichever occurred first. The incidence rate of type-2 DM with 95%

confidence intervals (CI) was calculated per 1000 person-years by dividing the number of new cases of type-2 DM by the person-years at risk. Sex-specific incidence rates stratified by age and BMI categories were calculated. Kaplan-Meier time-to-event analysis was conducted with a log-rank test to compare age and BMI categories for incident type-2 DM.

Univariable and multivariable Cox proportional hazards modeling (stratified by sex) were used to examine predictors of incident type-2 DM. The following predictor variables were examined by univariable Cox modeling: age (categorized as <44 years and ≥44 years), sex (categorized as female/male), vascular disease (categorized as yes/no), HTN (categorized as yes/no), dyslipidemia (categorized as yes/no), smoking (categorized as yes/no), HbA1c (categorized as <5.7% and ≥5.7%), and BMI (categorized as overweight and obese). All covariables with P <0.1 were included in the final multivariable modeling. Results were checked by a step-wise method based on likelihood ratios, with entry and removal probabilities set at 0.05 and 0.10, respectively. The proportional hazards assumption was tested using a log-log plot and were not significant. A P-value <0.05 was considered statistically significant. SPSS version 25 (IBM Corp., Armonk, NY) was used to analyze the data.

Patient and public involvement

There was no patient or public involvement in the design and conduct of the study.

RESULTS

Characteristics of study participants

The baseline patient characteristics, including demographic, clinical, and biochemical data of the 362 subjects, are presented in Table 1. The ratio of males to females was almost 1:1. The mean

age and BMI at baseline were 44.36 ± 14.45 years and 31.69 [interquartile range (IQR) 27.64, 34.18 kg/m^2], respectively. When stratified by sex, females were older, had higher BMI and TC values, and had a higher prevalence of dyslipidemia, at baseline. Conversely, males had significantly higher baseline systolic and diastolic blood pressure values, as well as a higher prevalence of smoking history.

Table 1. Baseline characteristics of the study participants.

	Total (N=362) Mean ± SD	Males (N=170) Mean ± SD	Females (N=192) Mean ± SD	p-value*
Females (%)	53.0	-	-	-
Age (years)	44.36 ± 14.45	40.2 ± 14.7	48.09 ± 13.2	<0.001
Anthropometric values				
BMI (kg/m^2)	31.69 (27.64, 34.18)	29.56 (27.33, 32.79)	31.22 (27.91, 35.77)	0.001
SBP (mmHg)	127.93 ± 17.34	129.92 ± 17.86	126.17 ± 16.72	0.040
DBP (mmHg)	76.94 ± 11.01	79.03 ± 11.34	75.09 ± 10.40	0.001
Laboratory values				
HbA1c (%)	5.62 ± 0.48	5.59 ± 0.50	5.64 ± 0.46	0.326
eGFR (mL/min/1.73 m^2)	105.87 ± 16.81 (N=359)†	104.16 ± 18.47 (N=167)†	107.35 ± 15.13	0.073
TC (mmol/L)	5.06 ± 0.88	4.89 ± 0.95	5.21 ± 0.99	0.002
History of n (%)				
HTN	181 (50.0)	91 (53.5)	90 (46.9)	0.247
Dyslipidemia	141 (39.0)	52 (30.6)	89 (46.4)	0.002
Vascular disease	18 (5.0)	10 (5.9)	8 (4.2)	0.478
Smoking	56 (15.5)	54 (31.8)	2 (1.0)	<0.001

HTN hypertension, *BMI* body mass index, *eGFR* estimated glomerular filtration rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *SD* standard deviation, *HbA1c* glycated hemoglobin, *TC* total cholesterol.

†The difference in N is due to missing data.

*Independent-samples t-test was used to calculate p values for continuous variables and Fisher's exact test (two-tailed) for categorical variables.

Incidence

After a median follow-up time of 8.7 years (IQR, 8.2–9.0 years), 47 incident cases of type-2 DM were identified. The overall incidence rate of type-2 DM was 16.3 (95% CI: 12.1−21.4) cases per 1000 person-years and the crude incidence of type-2 DM over the same period was 13.0% (95% CI: 9.8−16.8%).

Sex-specific incidence rates, as stratified by BMI, were higher in obese females (21.1, 95% CI: 13.3−32.0 cases per 1000 person-years), when compared to overweight females (5.1, 95% CI: 1.3−14.0 cases per 1000 person-years) (P=0.013). Incidence rates for type-2 DM were higher in older females (21.3, 95% CI: 13.5–31.9 cases per 1000 person-years), when compared to younger females (3.7, 95% CI: 0.6–12.2 cases per 1000 person-years) (P=0.008), (Figs. 2 and 3, respectively). However, these differences were not significant among males.

Analyses of risk factors

We used multivariable Cox regression analyses to examine the association of age, vascular disease, dyslipidemia, smoking, HTN, BMI, and HbA1c levels with the risk of developing type-2 DM between males and females. When adjusted for all other variables, we found that in males, an HbA1c level ≥5.7% [hazard ratio (HR) = 3.02, 95% CI: 1.20−7.62] and for females age ≥44

years (HR = 4.84, 95% CI: 1.13−20.73) and obesity (HR = 3.42, 95% CI: 1.01−11.57) were significant risk factors for the development of type-2 DM (Table 2).

Table 2. Predictors of incident type-2 diabetes mellitus in the study population.

Predictor variables	Male (N=170)		Female (N=192)	
	HR (95% CI)	p-value	HR (95% CI)	p-value
Age				
<44 years	Reference		Reference	
≥44 years	0.46 (0.17–1.13)	0.135	4.84 (1.13–20.73)	0.034
History of HTN				
No	Reference		Reference	
Yes	1.89 (0.74–4.81)	0.183	1.61 (0.67–3.88)	0.292
History of dyslipidemia				
No	Reference		Reference	
Yes	2.01 (0.80–5.04)	0.135	0.80 (0.34–1.90)	0.608
History of smoking				
No	Reference		Reference	
Yes	0.36 (0.12–1.04)	0.060	4.88 (0.44–54.08)	0.196
History of vascular disease				
No	Reference		Reference	
Yes	2.46 (0.65–9.27)	0.183	0.60 (0.06–5.50)	0.647
HbA1c				
<5.7%	Reference		Reference	
≥5.7%	3.02 (1.20–7.62)	0.019	2.30 (0.83–6.39)	0.109
BMI				
Overweight	Reference		Reference	
Obese	1.17 (0.51–2.68)	0.713	3.42 (1.01–11.57)	0.048

HTN hypertension, *BMI* body mass index, *HbA1c* glycated hemoglobin, *CI* confidence intervals, *HR* hazard ratio.

DISCUSSION

The results of this study showed that the incidence of type-2 DM among overweight and obese UAE nationals was 1.49% per year during the 9-year study period. The overall incidence rate

was 16.3 per 1000 person-years. The independent risk factors for the development of type-2 DM were age (≥ 44 years) and obesity in females and HbA1c levels in males.

Incidence rates

The incidence rates of type-2 DM in the general population differ significantly worldwide. This is possibly due to variations in insulin sensitivity related to the interaction between genetic and environmental factors among different populations globally.[14] A study conducted over a 12-month period in Ajman, one of the emirates in the UAE, the incidence rate for type-2 DM in the general Emirati population was 4.8 per 1000 person-years[8], while our study had an incidence rate 3 times higher. This is not unexpected as our study focused on overweight and obese individuals and is comparable to other research in high-risk populations in the United States (15.2 per 1000 person-years)[15], while South-Asian countries e.g. India and Bangladesh reported incidence rates of 22.2 per 1000 person-years[16] and 16.4 per 1000 person-years respectively.[17]

Risk factors

This study revealed some interesting findings regarding the risk factors for developing type-2 DM in this high-risk UAE population. Sex-specific incidence rates of type-2 DM showed a female preponderance, particularly among older females. These results were not unique and were also observed among the general population of the UAE.[8] The higher incidence of type-2 DM among older females may be attributable to the high prevalence of overweight and obesity[18], sedentary lifestyle, nutritional habits[19], and early menopause witnessed in our population.[20] Local data shows that for every 1-year increase in age, the risk of obesity among females increases by 5%.[21]

Individuals with high-normal HbA1c levels have a greater risk of developing type-2 DM.[22] However, in our study, the independent predictive property of the HbA1c level was only observed in males. An explanation for this finding could be the high prevalence of male smokers seen, as smoking has been shown to increase HbA1c levels in people without diabetes.[23] Obesity in females was also an independent risk predictor for type-2 DM. Studies have shown that the risk of developing type-2 DM is significantly higher in individuals with BMI ≥30 kg/m^2 when compared to those with normal BMI.[5] Interventions that promote weight loss and decreased BMI, also reduce the risk of developing type-2 DM. An 8-week exercise intervention program in a UAE student population demonstrated a significant reduction in BMI.[24] Other controlled intervention studies in high-risk populations[6,25,26] also demonstrated a significant decrease in the risk of type-2 DM as a result of BMI reduction.

Clinical and public health implications

Results from this study demonstrate that the incidence of type-2 DM in the high-risk UAE population begins to increase by the fourth decade of life, and this trend significantly increases with higher BMI values. Thus, targeting overweight or obesity, which are modifiable risk factors for type-2 DM[27], is crucial in reducing this burden. A 2015 study of Emirati adolescents found the prevalence of pre-diabetes and type-2 DM in overweight and obese children were 5.8% and 0.87%, respectively.[28] Although alarming, the results are unsurprising when we consider the high prevalence of childhood obesity in the UAE. Furthermore, the rates of overweight and obesity in young UAE adults was 36%[29], putting them at risk for developing type-2 DM. Screening programs alone are inadequate and clinicians must strongly recommend lifestyle modifications to reduce overweight and obesity.

Strengths and limitations

The strengths of this study include the duration of follow-up for our representative sample of overweight and obese UAE nationals in the second-largest city in the Abu Dhabi Emirate of UAE. We utilized measured anthropometric and laboratory data in patient charts instead of self-reported information and diagnostic codes for the classification of risk factors and identification of incident cases. In addition, HbA1c levels or documented diagnosis by a physician were used to identify incident cases of type-2 DM instead of fasting plasma glucose, which has more variability.[30,31]

This study has some limitations. These limitations include missing baseline data regarding family history of type-2 DM, history of gestational diabetes, physical activity, and abdominal obesity, all of which are well-researched risk factors for the development of DM. A prospective study will ensure more robust data, as well as changes in lifestyle variables such as exercise, weight loss or gain.

CONCLUSIONS

The overall incidence rate of type-2 DM in overweight and obese UAE nationals was 16.3 per 1000 person-years. The HbA1c level in males and obesity in females, particularly in the older age group, were found to be independent risk factors for the development of type-2 DM. Thus, there should be a greater emphasis on reducing BMI through lifestyle modifications in these high-risk groups.

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None

Author Contributions D.R. conceived the study and its design, performed literature search and drafted the initial manuscript. S.A.S. was involved in data management, statistical analysis, interpretation of the data, and critical review of the manuscript. R.D.G. assisted in statistical analysis, contributed to the discussion, reviewed and edited the manuscript. J.A.K. performed a critical review of the manuscript was involved in data interpretation and also provided guidance in research methodology. All authors read and approved the final manuscript.

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Competing interests

The authors declare that they have no competing interests.

Patient Consent for publication

Not required

Availability of data and materials

The dataset used and analyzed during the current study is available from the corresponding author on reasonable request.

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FIGURE LEGENDS

Fig 1. Flow chart for the inclusion and exclusion of patients. *HbA1c* glycated hemoglobin, *eGFR* estimated glomerular filtration rate, *HIV* human immunodeficiency virus.

Fig 2. The sex-specific incidence rate of type-2 diabetes mellitus (cases/1000 person-years) stratified by BMI categories. *BMI* body mass index.

Fig 3. The sex-specific incidence rate of type-2 diabetes mellitus (cases/1000 person-years) stratified by age.

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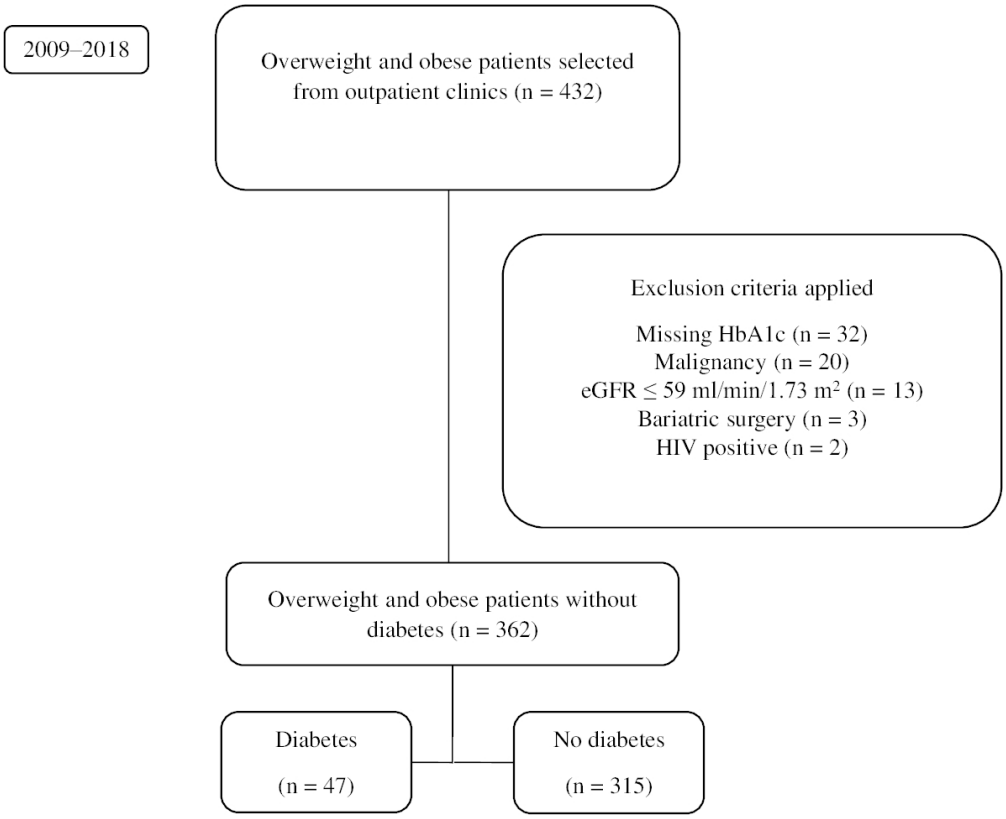
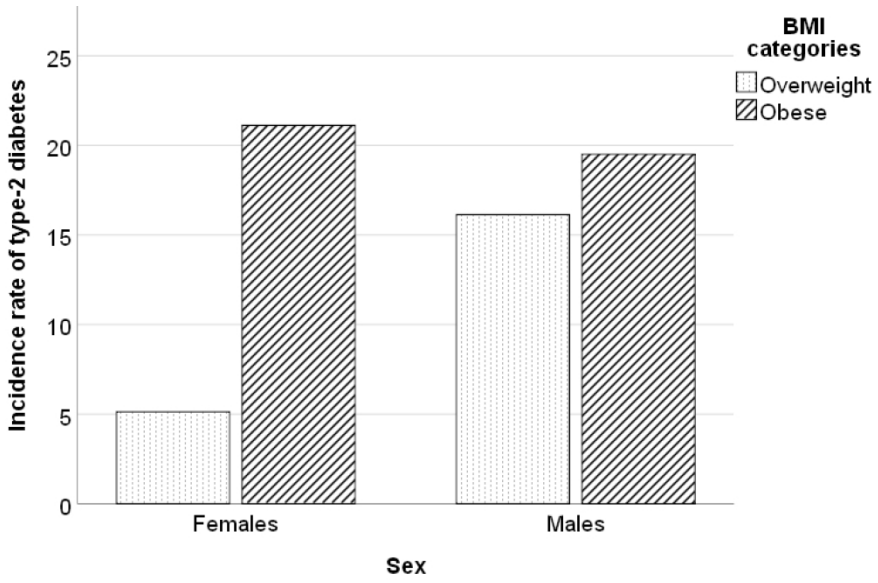


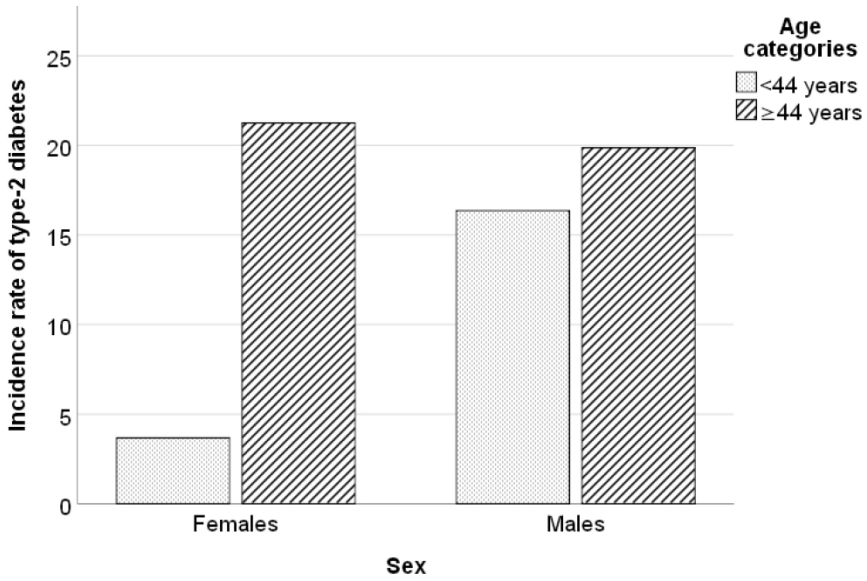
Flow chart for the inclusion and exclusion of patients.
HbA1c glycated hemoglobin, eGFR estimated glomerular filtration rate, HIV human immunodeficiency virus.

100x81mm (300 x 300 DPI)



The sex-specific incidence rate of type-2 diabetes mellitus (cases/1000 person-years) stratified by BMI categories. BMI body mass index.

144x84mm (300 x 300 DPI)



The sex-specific incidence rate of type-2 diabetes mellitus (cases/1000 person-years) stratified by age.

144x84mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	2
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	4
Objectives	3	State specific objectives, including any prespecified hypotheses	4
Methods			
Study design	4	Present key elements of study design early in the paper	4, 5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	5
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	5,6
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	
Study size	10	Explain how the study size was arrived at	5
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	6,7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	NA
		(*d*) If applicable, explain how loss to follow-up was addressed	NA
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	7,8
		(b) Indicate number of participants with missing data for each variable of interest	8
		(c) Summarise follow-up time (eg, average and total amount)	9
Outcome data	15*	Report numbers of outcome events or summary measures over time	9
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	9,10
		(*b*) Report category boundaries when continuous variables were categorized	9,10
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	9,10
Discussion			
Key results	18	Summarise key results with reference to study objectives	10
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	11,12
Generalisability	21	Discuss the generalisability (external validity) of the study results	11
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	13,14

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.

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Incidence and risk factors of type 2 diabetes mellitus in an overweight and obese population: a long-term retrospective study from a Gulf State

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Incidence and risk factors of type 2 diabetes mellitus in an overweight and obese population: a long-term retrospective study from a Gulf State

Dybesh Regmi[1], Saif Al-Shamsi[2*], Romona D. Govender[3], Juma Al Kaabi[2]

[1]Department of Family and Community Medicine, University of Toronto, Toronto, Canada

[2]Department of Internal Medicine, College of Medicine and Health Sciences, United Arab Emirates University, Al Ain, United Arab Emirates

[3]Department of Family Medicine, College of Medicine and Health Sciences, Al Ain, United Arab Emirates University, United Arab Emirates

*Corresponding author:

Saif Al-Shamsi

Department of Internal Medicine, College of Medicine & Health Sciences, United Arab Emirates University, PO Box 17666, Al Ain, United Arab Emirates

Phone: +971 3 713 7439

Fax: +971 3 767 2995

E-mail address: salshamsi@uaeu.ac.ae (SAS)

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Abstract

Objectives: A high body mass index (BMI) is associated with a risk of type 2 diabetes mellitus (DM). The United Arab Emirates (UAE) is experiencing a marked increase in obesity. Nonetheless, no data is available regarding the incidence of type 2 DM in the high-risk adult UAE population. Therefore, this study aimed to evaluate the incidence rate and risk of developing type 2 DM among individuals with above-normal BMI in the UAE.

Design: A retrospective cohort study.

Setting: Outpatient clinics at a tertiary care center in Al Ain, UAE.

Participants: Three hundred sixty-two overweight or obese adult UAE nationals who visited outpatient clinics between April 2008 and December 2008.

Primary outcome measure: Patients with type 2 DM were identified based on diagnosis established by a physician or through glycated hemoglobin (HbA1c) levels ≥6.5% during the follow-up period (until April 2018).

Results: The overall incidence rate of type 2 DM during the median follow-up time of 8.7 years was 16.3 [95% confidence interval (CI): 12.1–21.4] cases per 1000 person-years. Incidence rates in men and women were 17.7 (95% CI: 11.6–25.9) and 15.0 (95% CI: 9.8–22.2) cases per 1000 person-years, respectively. Multivariable Cox proportional hazard analysis determined older age and obesity in women, and prediabetes in men to be the independent risk factors for developing type 2 DM.

Conclusions: The incidence rate of type 2 DM in overweight and obese UAE nationals is high. In addition to screening, current strategies should strongly emphasize lifestyle modifications to decrease HbA1c and BMI levels in this high-risk population.

Article Summary

Strengths and limitations of this study

- This long-term longitudinal cohort study determines the incidence rate and risk factors of type 2 diabetes mellitus in overweight and obese United Arab Emirates nationals.
- Anthropometric and laboratory data were obtained instead of self-reported information for the classification of risk factors and identification of incident cases.
- The study's subjects were recruited from a single large public hospital's ambulatory clinics; therefore, our findings may not apply to the general UAE population.
- No data were available for review regarding additional confounders, such as family history and changes in weight and physical activity.

Keywords: incidence; obesity; risk factors; type 2 diabetes mellitus; United Arab Emirates

INTRODUCTION

A rapid worldwide increase has been observed regarding the prevalence of type 2 diabetes mellitus (DM) and obesity. The United Arab Emirates (UAE) is one of the epicenters of this epidemic. In a 2007 study, the age-standardized rates for prediabetes and type 2 DM among UAE nationals were 24.2% and 29%, respectively.[1] However, in a 2019 study of young Emirati men, the age-adjusted prevalence of prediabetes was much higher at 41.3%.[2] By contrast, the prevalence of type 2 DM in North America and Western European countries are well below 12%.[3-6] Notably, the number of people with type 2 DM in the UAE is estimated to reach over two million by 2040.[7]

Overweight, defined as body mass index (BMI) between 25 and 29.99 kg/m^2 and obesity, defined as BMI ≥30 kg/m^2,[8] are known risk factors of type 2 DM.[9] More recently, the age-adjusted prevalence of overweight and obesity among Emirati men between the ages of 18 and 30 years was noted to be 27% and 30%, respectively.[2] In contrast, the corresponding prevalence in another study was 23% and 10% among young Emirati women.[10] Both these studies determined increased BMI to be strongly associated with diabetes.

Both obesity and type 2 DM are well known cardiometabolic risk factors for vascular complications, such as coronary heart disease and peripheral vascular disease. The prevalence of these vascular diseases in the UAE is 10.5% and 11.1%, respectively.[1] These and other vascular-related complications have resulted in the UAE having one of the highest reported global death rates for cardiovascular disease—204 per 100,000 for women and 309 per 100,000 for men.[11]

The rise in the incidence of diabetes and its complications among the UAE population has been in parallel to the economic surge, resulting in growing urbanization and changing lifestyle habits in the country. Nevertheless, over the last decade, UAE has diverted its attention and endeavored to curb the burden of overweight and obesity, as well as to decrease the incidence of associated conditions like diabetes. The *Weqaya* program, a population-wide CVD screening program, was initiated in 2008[12] to enable individuals and healthcare providers to implement CVD preventative measures. For continued assessment of the effectiveness of these local interventions, ad hoc analysis of population data at pre-defined intervals over a long period is required. However, epidemiological studies on type 2 DM in the UAE have primarily focused on its prevalence in the general population.[1, 2, 13] Despite having information from the *Weqaya* program, data regarding the incidence of type 2 DM among obese and overweight UAE nationals

remains poorly researched. This lapse is primarily because of the significant resource investment required to conduct observational cohort studies with prolonged follow-up.

Therefore, in this long-term, longitudinal retrospective study, we aimed to calculate the incidence rate of type 2 DM and elucidate the effects of BMI on DM risk in adult UAE nationals who are overweight and obese.

METHODS

Study setting

A retrospective electronic medical record review was performed of adult patients who presented to outpatient clinics at Tawam Hospital in Al Ain, UAE, between April 1, 2008, and December 31, 2008. Tawam Hospital is one of the two large government hospitals in the city of Al Ain and serves an estimated 60,000 adult UAE nationals in the city who are overweight and obese.[14, 15] The Research and Ethics Board of Tawam Hospital and the UAE University granted ethical approval for this study (CRD239/13). Informed consent was waived because patient records and information were anonymized and de-identified before analysis.

Subjects and procedures

The study population consisted of UAE nationals who were overweight and obese, aged between 18 and 75 years, who were seen at the outpatient departments at Tawam Hospital. The inclusion criteria were patients without type 2 DM, defined as having glycated hemoglobin (HbA1c) <6.5%; patients not taking antidiabetic medications; and those with BMI $\geq$ 25 kg/m^2 at baseline. The exclusion criteria were patients with missing HbA1c data; those with a history of chronic medical conditions, such as malignancy, human immunodeficiency virus infection, receiving

steroids or immunosuppression medications, or stage 3–5 chronic kidney disease [estimated glomerular filtration rate (eGFR) of ≤59 mL/min/1.73 m^2].[16] Moreover, patients who had undergone weight reduction surgery, defined either as restrictive or malabsorptive bariatric surgery or pharmacotherapy for weight loss were excluded from the study. The final study group consisted of 362 subjects with a BMI of ≥ 25 kg/m^2 (Fig. 1).

Definitions and measurements

Initial BMI was calculated from baseline height and weight measurements using the formula weight (kg) divided by height squared (m^2). Overweight and obesity were defined according to the World Health Organization classification,[8] based on a BMI between 25 and 29.99 kg/m^2 and ≥30 kg/m^2, respectively. Hypertension (HTN) was defined as systolic blood pressure ≥140 mmHg, diastolic blood pressure ≥90 mmHg, or the use of blood pressure medications.[17] The definition of dyslipidemia was a serum total cholesterol (TC) of ≥6.21 mmol/L or if the patient had a documented prescription of lipid-lowering medications.[18] Prediabetes was defined as having an HbA1c level between 5.7% and 6.4%.[19] Current or prior history of smoking tobacco was considered a positive smoking history. Patients with a documented history of coronary heart disease, cerebrovascular disease, or peripheral vascular disease were identified to have a vascular disease.

Outcomes

Our study endpoint was incident type 2 DM, defined as either HbA1c ≥6.5% (based on the definition of DM by the American Diabetes Association) or a diagnosis of type 2 DM established by a physician at any time during the follow-up period.[19] The occurrence of incident type 2

DM was based on a review of all the electronic medical records until April 30, 2018. All laboratory analyses were performed at the Medical Laboratory Department of Tawam Hospital. An automated analyzer, Integra 400 Plus (Roche Diagnostics, Mannheim, Germany) was used to measure HbA1c levels. The HbA1c results were reported as a percentage using the International Federation of Clinical Chemistry-National Glycohemoglobin Standardization Program master equation.[20]

Statistical analyses

Using a formula by Rosner (2015),[21] a sample size of 353 was calculated. This was based on the anticipated incidence of diabetes of 17.3% [22] and using 80% power at a two-sided significance level of 0.05. The sample size was further increased by 20% to account for patients lost to follow-up and those with missing data.

Inter-sex differences were determined using the Mann-Whitney U test or the independent-samples *t*-test for non-normal and normal data, respectively. For categorical variables, Fisher's exact test (two-tailed) was used. Person-years at risk for incident type 2 DM was calculated for each patient as the time from the baseline visit to the diagnosis of type 2 DM or the most recent outpatient visit, whichever occurred first. The incidence rate of type 2 DM with a 95% confidence interval (CI) was calculated per 1000 person-years by dividing the number of new cases of type 2 DM by the person-years at risk. Sex-specific incidence rates were calculated stratified by age and BMI categories. Kaplan-Meier time-to-event analysis was conducted with a log-rank test to compare age and BMI categories for incident type 2 DM.

Univariable and multivariable Cox proportional hazard models were evaluated to examine predictors of incident type 2 DM in the entire cohort and stratified by sex. The following

predictor variables were examined using univariable Cox modeling: age (categorized as <44 years and ≥44 years), sex, vascular disease, HTN, dyslipidemia, smoking, HbA1c (categorized as <5.7% and ≥5.7%), and BMI (categorized as overweight and obese). All covariables with P <0.1 were included in the final multivariable model. A stepwise method based on likelihood ratios, with entry and removal probabilities set at 0.05 and 0.10, respectively, was used to check the results. The log-log plot was used to evaluate the proportional hazards assumption and was not significant. A *P* value <0.05 was considered statistically significant. SPSS version 25 (IBM Corp., Armonk, NY) was used to analyze the data.

Patient and public involvement

There was no patient or public involvement in the design and conduct of the study.

RESULTS

Characteristics of study participants

The baseline patient characteristics of the 362 subjects, are presented in Table 1. The ratio of men to women was almost 1:1. At baseline, the mean age was 44.4 ± 14.5 years and the BMI was 31.7 kg/m^2 [interquartile range (IQR) 27.6, 34.2 kg/m^2]. When stratified by sex, women were older, had higher BMI and TC values, and had a higher prevalence of dyslipidemia at baseline. Conversely, men had significantly higher baseline systolic and diastolic blood pressure values, as well as a higher prevalence of smoking history.

Table 1. Baseline characteristics of the study participants

	Total (N = 362) Mean ± SD	Men (N = 170) Mean ± SD	Women (N = 192) Mean ± SD	*P* value*
Women (%)	53.0	-	-	-
Age (years)	44.4 ± 14.5	40.2 ± 14.7	48.1 ± 13.2	<0.001
Anthropometric values				
BMI (kg/m^2)	31.7 (27.6, 34.2)	29.6 (27.3, 32.8)	31.2 (27.9, 35.8)	0.001
SBP (mmHg)	127.9 ± 17.3	129.9 ± 17.9	126.2 ± 16.7	0.040
DBP (mmHg)	76.9 ± 11.0	79.0 ± 11.3	75.1 ± 10.4	0.001
Laboratory values				
HbA1c (%)	5.6 ± 0.5	5.6 ± 0.5	5.6 ± 0.5	0.326
eGFR (mL/min/1.73 m^2)	105.9 ± 16.8 (N = 359)†	104.2 ± 18.5 (N = 167)†	107.4 ± 15.1	0.073
TC (mmol/L)	5.1 ± 0.9	4.9 ± 1.0	5.2 ± 1.0	0.002
History of n (%)				
HTN	181 (50.0)	91 (53.5)	90 (46.9)	0.247
Dyslipidemia	141 (39.0)	52 (30.6)	89 (46.4)	0.002
Vascular disease	18 (5.0)	10 (5.9)	8 (4.2)	0.478
Smoking	56 (15.5)	54 (31.8)	2 (1.0)	<0.001

HTN hypertension, *BMI* body mass index, *eGFR* estimated glomerular filtration rate, *SBP* systolic blood pressure, *DBP* diastolic blood pressure, *SD* standard deviation, *HbA1c* glycated hemoglobin, *TC* total cholesterol.

†The difference in N is because of the missing data.

*Independent-samples t-test was used to calculate *P* values for continuous variables and Fisher's exact test (two-tailed) for categorical variables.

Incidence

After a median follow-up time of 8.7 years (IQR, 8.2–9.0 years), 47 incident cases of type 2 DM were identified. The overall incidence rate of type 2 DM was 16.3 (95% CI: 12.1−21.4) cases per 1000 person-years, and the crude incidence over the same period was 13.0% (95% CI: 9.8−16.8%). The incidence rate of type 2 DM increased with patient age (Fig. 2). When stratified by sex, the incidence rates, were 17.7 (95% CI: 11.6–25.9) and 15.0 (95% CI: 9.8–22.2) cases per 1000 person-years in men and women, respectively.

Sex-specific incidence rates, as stratified by BMI, were higher in obese women (21.1, 95% CI: 13.3−32.0 cases per 1000 person-years) compared with overweight women (5.1, 95% CI: 1.3−14.0 cases per 1000 person-years) (P = 0.013). Incidence rates for type 2 DM were higher in older women (21.3, 95% CI: 13.5–31.9 cases per 1000 person-years) compared with younger women (3.7, 95% CI: 0.6–12.2 cases per 1000 person-years) (P = 0.008), (Fig. 3). However, these differences were not significant among men.

Analyses of risk factors

We used multivariable Cox regression analyses to examine the association of age, sex, vascular disease, dyslipidemia, smoking, HTN, BMI, and HbA1c levels with the risk of developing type 2 DM in the entire study cohort, as well as between men and women. When adjusted for all other variables, we observed that in men an HbA1c level ≥5.7% [hazard ratio (HR) = 3.02, 95% CI: 1.20−7.62] and in women age ≥44 years (HR = 4.84, 95% CI: 1.13−20.73) and obesity (HR = 3.42, 95% CI: 1.01−11.57) were significant risk factors for the development of type 2 DM (Table 2).

Table 2. Predictors of incident type 2 diabetes mellitus in the study population

Predictor	Total (N = 362)	Men (N = 170)	Women (N = 192)

variables	HR (95% CI)	*P* value	HR (95% CI)	*P* value	HR (95% CI)	*P* value
Age						
<44 years	Reference		Reference		Reference	
≥44 years	1.20 (0.59–2.44)	0.619	0.46 (0.17–1.13)	0.135	4.84 (1.13–20.73)	0.034
Sex						
Women	Reference					
Men	1.60 (0.83–3.05)	0.160				
History of HTN						
No	Reference		Reference		Reference	
Yes	1.78 (0.94–3.37)	0.075	1.89 (0.74–4.81)	0.183	1.61 (0.67–3.88)	0.292
History of dyslipidemia						
No	Reference		Reference		Reference	
Yes	1.32 (0.70–2.51)	0.393	2.01 (0.80–5.04)	0.135	0.80 (0.34–1.90)	0.608
History of smoking						
No	Reference		Reference		Reference	
Yes	0.58 (0.23–1.49)	0.259	0.36 (0.12–1.04)	0.060	4.88 (0.44–54.08)	0.196
History of vascular disease						
No	Reference		Reference		Reference	
Yes	1.57 (0.54–4.54)	0.408	2.46 (0.65–9.27)	0.183	0.60 (0.06–5.50)	0.647
HbA1c						
<5.7%	Reference		Reference		Reference	
≥5.7%	2.29 (1.16–4.52)	0.016	3.02 (1.20–7.62)	0.019	2.30 (0.83–6.39)	0.109
BMI						
Overweight	Reference		Reference		Reference	
Obese	1.86 (0.99–3.50)	0.053	1.17 (0.51–2.68)	0.713	3.42 (1.01–11.57)	0.048

HTN hypertension, *BMI* body mass index, *HbA1c* glycated hemoglobin, *CI* confidence intervals, *HR* hazard ratio.

DISCUSSION

The results of this study revealed that the crude incidence of type 2 DM among the UAE nationals who are overweight and obese was 1.49% per year during the 9-year study period. The overall incidence rate was 16.3 per 1000 person-years. The independent predictors for the development of type 2 DM were age (≥44 years) and obesity in women and prediabetes in men.

Incidence rates

The incidence rates of type 2 DM in high-risk populations differ worldwide. This difference is probably because of variations in insulin sensitivity related to the interaction between genetic and environmental factors among different ethnic and population groups globally.[23] In a United States study of predominantly overweight and obese African-American women, reported the incidence rate of type 2 DM was 15.2 per 1000 person-years[24] and is comparable to our study. There has been only one other study that has assessed the incidence rate of type 2 DM in the UAE.[13] The study was conducted over 12 months in Ajman, one of the emirates in the UAE and revealed that the incidence rate for type 2 DM was 4.8 per 1000 person-years. However, this study cannot be directly compared with our study because it was conducted on the general population, and our study cohort comprised only overweight and obese UAE nationals.

Risk factors

This study revealed some interesting findings regarding the risk factors for developing type 2 DM in the high-risk UAE population. Sex-specific incidence rates of type 2 DM exhibited a female preponderance, particularly older women. Nevertheless, these results were not unique and were also observed among the general population of the UAE.[13] The higher incidence of type 2 DM among older women may be attributable to the high prevalence of overweight and obesity, sedentary lifestyle, nutritional habits, and early menopause witnessed in our population.[25-28]

Furthermore, individuals with high-normal HbA1c levels have a greater risk of developing type 2 DM.[29] However, when we stratified our cohort by sex, the independent predictive property of the HbA1c level was only observed in men. An explanation for this finding could be the high prevalence of smoking history in men, as smoking has been shown to increase HbA1c levels in individuals without diabetes.[30] Moreover, obesity in women was noted to be an independent risk predictor for type 2 DM. Studies have demonstrated that the risk of developing type 2 DM is significantly higher in individuals with BMI ≥30 kg/m^2 compared with those with normal BMI.[9] Therefore, interventions that promote weight loss and reduce BMI can reduce the risk of developing type 2 DM. Notably, an eight-week exercise intervention program in a UAE student population demonstrated a significant reduction in BMI.[31] In addition, other controlled intervention studies in high-risk populations[32,33] demonstrated a significant decrease in the risk of type 2 DM consequent to BMI reduction.

Clinical and public health implications

In the UAE, much of the increase in type 2 DM has occurred because of social and economic changes—from traditional, semi-nomadic lifestyle to sedentary, urban, and high-income lifestyle. Consequently, the progression toward type 2 DM and cardiovascular disease starts early in the UAE because of the high prevalence of childhood obesity.[1, 34] A 2015 study of Emirati children and adolescents with a BMI ≥25 kg/m^2 determined the prevalence of prediabetes and type 2 DM to be 5.4% and 0.87%, respectively.[35] Therefore, reducing the burden of type 2 DM in the UAE will require intensive population-wide interventions to promote regular physical activity and a healthy diet,[33, 36] particularly among the Emirati youth.

Furthermore, the results of this study highlight the need to focus on Emirati women as a specific target group for obesity prevention programs. These programs should begin in childhood

because 21% are obese by the time they are 30 years of age.[26] In addition, it is imperative to have a multidisciplinary approach to address the high incidence of type 2 DM, wherein pediatricians, primary care providers, dieticians, and specialists work collaboratively toward promoting weight reduction and maintaining a healthy BMI in our population.

Strengths and limitations

The strengths of this study include the long duration of follow-up for our representative sample of overweight and obese individuals in the second-largest city in the Abu Dhabi Emirate of UAE. We used the anthropometric and laboratory data documented in patient charts instead of self-reported information and diagnostic codes for the classification of risk factors and identification of incident cases. In addition, HbA1c levels or physician diagnosis formed the basis to identify incident cases of type 2 DM instead of fasting plasma glucose that has more variability.[37,38]

Nonetheless, this study had some limitations. Baseline data regarding family history of type 2 DM, history of gestational diabetes, physical activity, and abdominal obesity were unavailable—all of which are well-researched risk factors for the development of DM. Nevertheless, a prospective study can provide more robust results. Furthermore, data on additional confounders, such as family history, changes in weight and physical activity, were unavailable for review. Finally, subjects for this study were recruited from a single largest tertiary care hospital's ambulatory clinics; thus, our findings may not apply to the general UAE population.

CONCLUSIONS

The overall incidence rate of type 2 DM in UAE nationals who are overweight and obese was 16.3 per 1000 person-years. Notably, prediabetes in men and obesity in women, particularly older women, were determined to be independent predictors for the development of incident type

2 DM. Hence, it is imperative to emphasize BMI reduction through lifestyle modifications in these high-risk groups.

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AUTHOR CONTRIBUTIONS

D.R. conceived the study and its design, performed literature search and drafted the initial manuscript. S.A.S. was involved in data management, statistical analysis, interpretation of the data, and critical review of the manuscript. R.D.G. assisted in statistical analysis, contributed to the discussion, reviewed and edited the manuscript. J.A.K. performed a critical review of the manuscript was involved in data interpretation and also guided the research methodology. All authors read and approved the final manuscript.

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COMPETING INTERESTS

The authors declare that they have no competing interests.

PATIENT CONSENT FOR PUBLICATION

Not required

AVAILABILITY OF DATA AND MATERIALS

The dataset used and analyzed during the current study is available from the corresponding author on reasonable request.

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FIGURE LEGENDS

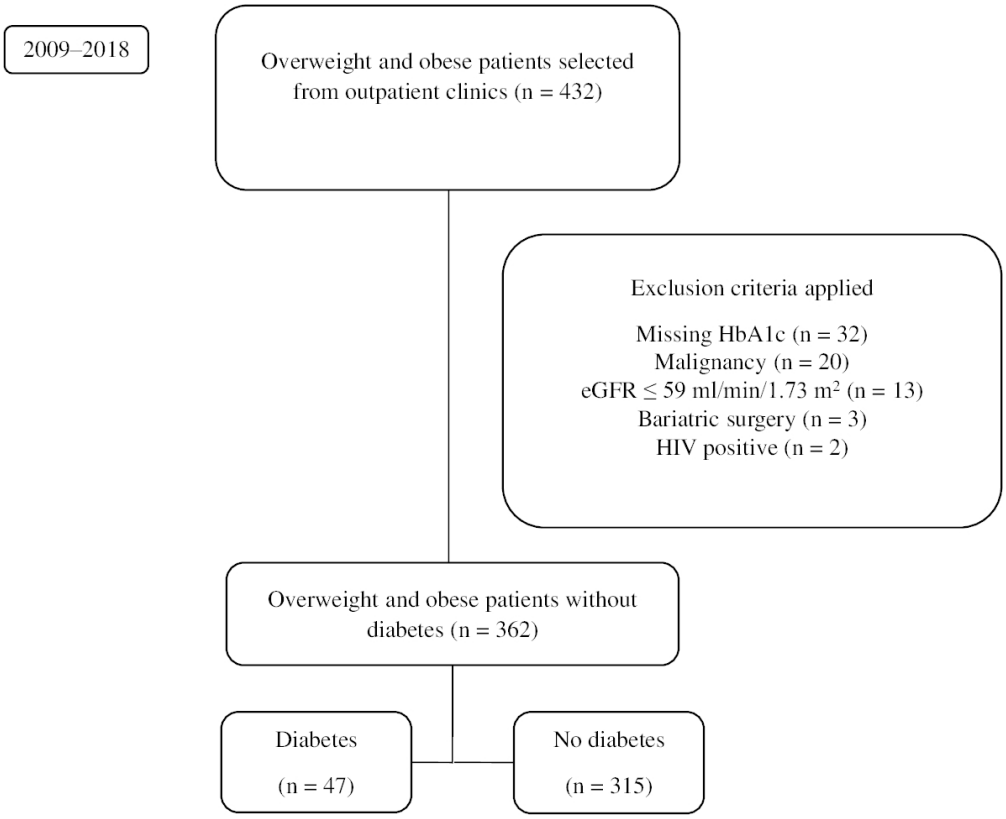
Figure 1. Flow chart for the inclusion and exclusion of patients

HbA1c glycated hemoglobin, *eGFR* estimated glomerular filtration rate, *HIV* human immunodeficiency virus.

Figure 2. Overall incidence rate of type 2 diabetes mellitus (cases/1000 person-years) by increasing age

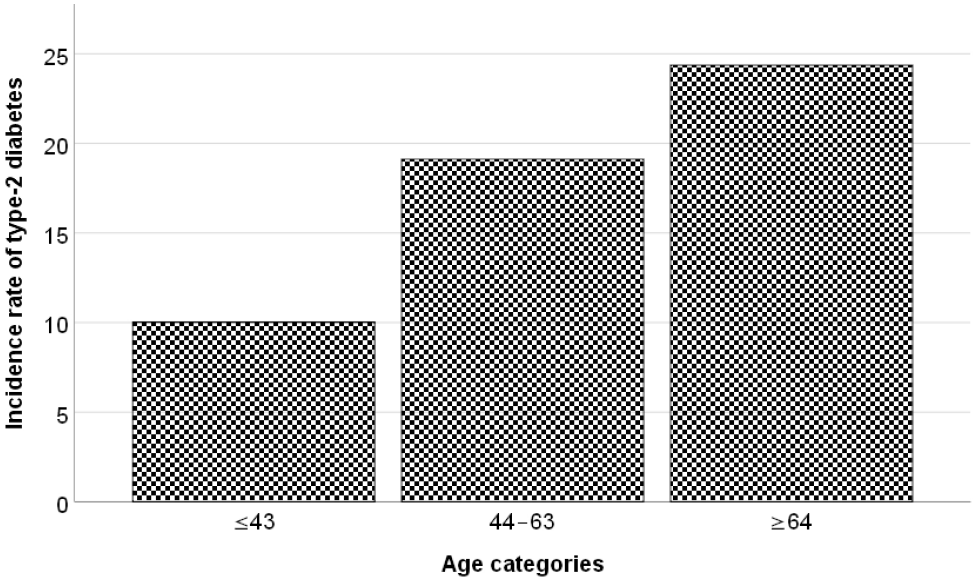
Figure 3. Sex-specific incidence rate of type 2 diabetes mellitus (cases/1000 person-years) stratified by BMI categories (A) and by age (B)

BMI body mass index.



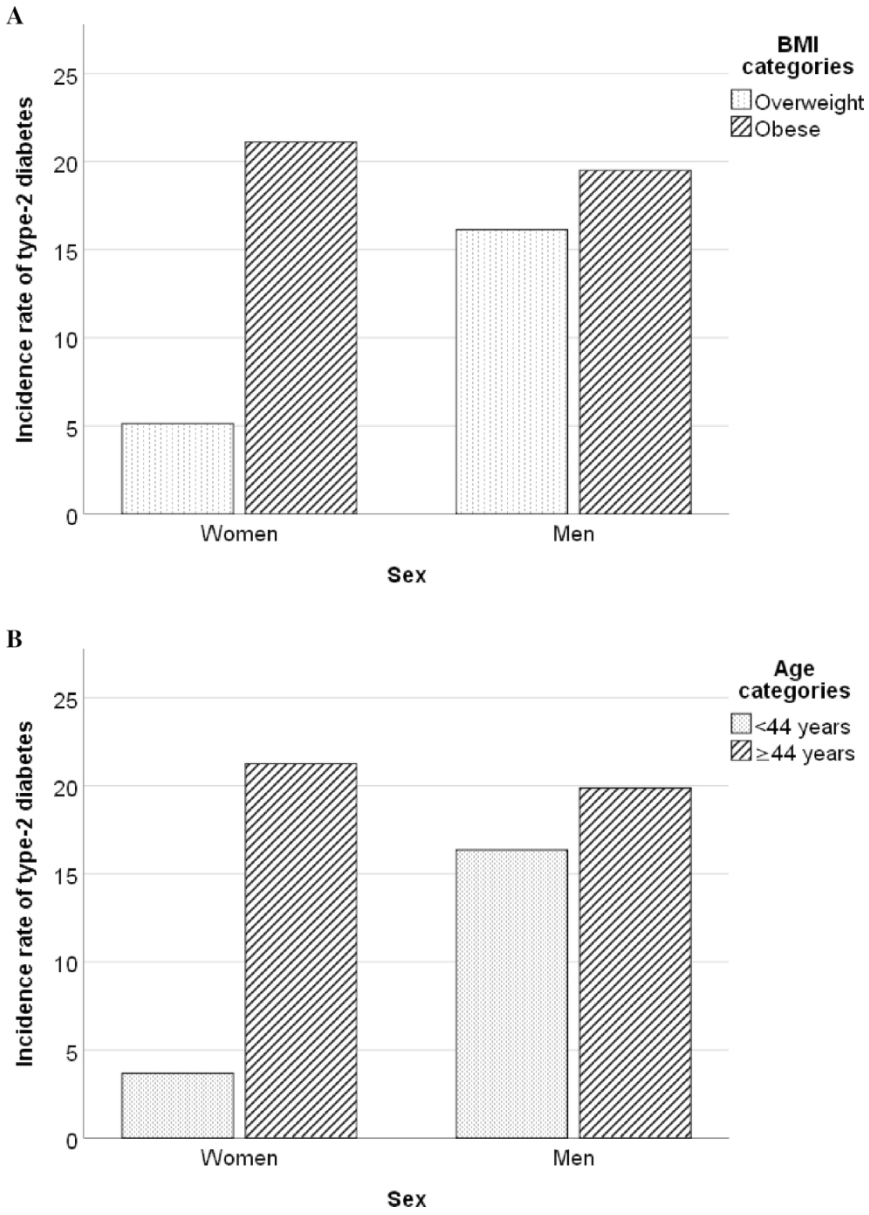
Flow chart for the inclusion and exclusion of patients.
HbA1c glycated hemoglobin, eGFR estimated glomerular filtration rate, HIV human immunodeficiency virus.

100x81mm (300 x 300 DPI)



Overall incidence rate of type 2 diabetes mellitus (cases/1000 person-years) by increasing age

144x84mm (300 x 300 DPI)



Sex-specific incidence rate of type 2 diabetes mellitus (cases/1000 person-years) stratified by BMI categories (A) and by age (B)

158x222mm (300 x 300 DPI)

STROBE 2007 (v4) Statement—Checklist of items that should be included in reports of *cohort studies*

Section/Topic	Item #	Recommendation	Reported on page #
Title and abstract	1	(*a*) Indicate the study's design with a commonly used term in the title or the abstract	1
		(*b*) Provide in the abstract an informative and balanced summary of what was done and what was found	2
Introduction			
Background/rationale	2	Explain the scientific background and rationale for the investigation being reported	3, 4
Objectives	3	State specific objectives, including any prespecified hypotheses	4, 5
Methods			
Study design	4	Present key elements of study design early in the paper	5
Setting	5	Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection	5, 6
Participants	6	(*a*) Give the eligibility criteria, and the sources and methods of selection of participants. Describe methods of follow-up	6, 7
		(*b*) For matched studies, give matching criteria and number of exposed and unexposed	NA
Variables	7	Clearly define all outcomes, exposures, predictors, potential confounders, and effect modifiers. Give diagnostic criteria, if applicable	6, 7
Data sources/ measurement	8*	For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group	6,7
Bias	9	Describe any efforts to address potential sources of bias	NA
Study size	10	Explain how the study size was arrived at	7
Quantitative variables	11	Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why	7
Statistical methods	12	(*a*) Describe all statistical methods, including those used to control for confounding	7
		(*b*) Describe any methods used to examine subgroups and interactions	7
		(*c*) Explain how missing data were addressed	5
		(*d*) If applicable, explain how loss to follow-up was addressed	5
		(*e*) Describe any sensitivity analyses	NA
Results			

Participants	13*	(a) Report numbers of individuals at each stage of study—eg numbers potentially eligible, examined for eligibility, confirmed eligible, included in the study, completing follow-up, and analysed	5, 6
		(b) Give reasons for non-participation at each stage	5
		(c) Consider use of a flow diagram	Figure 1
Descriptive data	14*	(a) Give characteristics of study participants (eg demographic, clinical, social) and information on exposures and potential confounders	Table 1
		(b) Indicate number of participants with missing data for each variable of interest	Table 1
		(c) Summarise follow-up time (eg, average and total amount)	10
Outcome data	15*	Report numbers of outcome events or summary measures over time	10
Main results	16	(*a*) Give unadjusted estimates and, if applicable, confounder-adjusted estimates and their precision (eg, 95% confidence interval). Make clear which confounders were adjusted for and why they were included	Table 2
		(*b*) Report category boundaries when continuous variables were categorized	Table 2
		(*c*) If relevant, consider translating estimates of relative risk into absolute risk for a meaningful time period	NA
Other analyses	17	Report other analyses done—eg analyses of subgroups and interactions, and sensitivity analyses	10
Discussion			
Key results	18	Summarise key results with reference to study objectives	12
Limitations			
Interpretation	20	Give a cautious overall interpretation of results considering objectives, limitations, multiplicity of analyses, results from similar studies, and other relevant evidence	12–14
Generalisability	21	Discuss the generalisability (external validity) of the study results	14
Other information			
Funding	22	Give the source of funding and the role of the funders for the present study and, if applicable, for the original study on which the present article is based	15

*Give information separately for cases and controls in case-control studies and, if applicable, for exposed and unexposed groups in cohort and cross-sectional studies.

Note: An Explanation and Elaboration article discusses each checklist item and gives methodological background and published examples of transparent reporting. The STROBE checklist is best used in conjunction with this article (freely available on the Web sites of PLoS Medicine at http://www.plosmedicine.org/, Annals of Internal Medicine at http://www.annals.org/, and Epidemiology at http://www.epidem.com/). Information on the STROBE Initiative is available at www.strobe-statement.org.