

BMJ Open Association between body mass index and onset of hypertension in men and women with and without diabetes: a cross-sectional study using national health data from the State of Kuwait in the Arabian Peninsula

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ABSTRACT

Objective: Obesity contributes directly to the risk of diabetes and hypertension. Effective management of diabetes is essential to prevent or delay the onset of comorbid hypertension. In this study, we delineate the association body mass index (BMI) has with risk and age at onset of hypertension and explore how this association is modulated by sex and the pre-existing condition of diabetes.

Design: Cross-sectional study using retrospective data.

Setting: Kuwait Health Network that integrates primary health and hospital laboratory data into a single system.

Participants: We considered 3904 native Kuwaiti comorbid individuals who had the onset of type 2 diabetes prior to that of hypertension, and 1403 native Kuwaiti hypertensive individuals with no incidence of diabetes. These participants have been regularly monitored for BMI, glycated haemoglobin and blood pressure measurements. Mean variance in BMI per individual over the period from registration is seen to be low.

Main outcome measures: Association between age at onset of hypertension and BMI (as measured at hypertension diagnosis); HRS for developing hypertension.

Results: Risk of hypertension increases with obesity levels, and is higher in patients with diabetes than in patients without diabetes but of similar obesity levels. Age at onset of hypertension is inversely related to BMI; this relationship is seen to be stronger in men compared to women (slope estimate in men, -0.62 years per unit increase in BMI; in women -0.18) and in individuals (particularly women) with diabetes compared to those without (slope estimate in women, -0.39 vs -0.18 , $p < 0.001$; in men -0.66 vs -0.62 ; $p = 0.66$).

Conclusions: The observation that the presence of diabetes doubles the slope of inverse relationship between hypertension onset age and BMI in women (while the slope is high in men irrespective of diabetes

Strengths and limitations of this study

- This is the first report to examine associations between body mass index and age at onset (and risk) of hypertension in individuals with diabetes versus those without diabetes.
- For the first time, sex specific differences in the impact of the preexisting condition of diabetes on the above-mentioned associations are demonstrated.
- Absence of assessment of residual confounding by family history, lifestyle factors and dietary patterns may be considered as potential limitations of the study. Other limitations include absence of other indices of obesity, such as waist circumference.

status) leads to a possible proposition that pre-existing diabetes narrows down sex-specific differences in the impact of obesity on blood pressure.

INTRODUCTION

Arterial hypertension is a chronic medical condition in which blood pressure in the arteries is elevated. Blood pressure is generated when the heart contracts against the resistance of blood vessels. The relationship between increasing age and hypertension prevalence has been illustrated.^{1 2} The increase in blood pressure with age is associated mostly with structural changes (such as stiffness) in the arteries. Pathophysiological factors influencing the onset of hypertension include impaired kidney sodium excretion, altered renal and sodium metabolism, reset baroreflexes, reset local autoregulation responses, altered renin-aldosterone relationship and increased responsiveness to sympathetic nervous system

stimuli.^{3 4} Obesity-induced hypertension, the subject of this study, most often involves the aforementioned factors (that mediate ageing-related hypertension). Obese individuals have increased fatty tissue which elevates vascular resistance and subsequently increases the workload on the heart to pump blood. Obesity provides an impetus for sympathetic nervous system activation as well as for changes in renal structure and function. The arterial-pressure control mechanism of diuresis and natriuresis seems to shift to higher blood pressure levels in obese individuals. Leptin⁵ and other neuropeptides are possible links between obesity and hypertension. Other mechanisms involved in obesity-induced hypertension are hyperinsulinaemia and insulin-induced sodium retention.

Obesity acts as the foremost risk factor for hypertension^{6 7} in adults⁸ and children.⁹ Body mass index (BMI) exhibits a direct linear relationship with the risk of hypertension;^{10–14} the association seems to hold in multiethnic populations, though the extent can vary.¹⁵ Increase in risk per unit increase in BMI is high in men compared to women. Age at onset of hypertension is related to a lifetime risk of cardiovascular disease.¹⁶ Despite the above reports on BMI and risk of hypertension, a clear illustration of associations between BMI and age at onset of hypertension is not available.

Hypertension is an extremely common comorbid condition in diabetes. Depending on obesity levels and ethnicity, approximately 20–60% of patients with diabetes are affected with hypertension.¹⁷ Obesity acts as a common factor in the aetiology of hypertension and diabetes.¹⁸ Diabetes and hypertension share common biological pathways^{6 19} and influence the development of one another in the same individual. It is seen that in as many as 70% of instances of Kuwaiti native comorbid individuals, onset of diabetes either precedes or occurs simultaneously with onset of hypertension.²⁰ Despite these observations, the impact of a pre-existing condition of diabetes on relationships between BMI and hypertension onset has not been quantified.

In this study, we aim to evaluate the association between BMI and age at onset of hypertension, and to assess the sex-specific differences that exist in such an association. We further examine whether the pre-existing condition of type 2 diabetes impacts the extent of the association.

MATERIALS AND METHODS

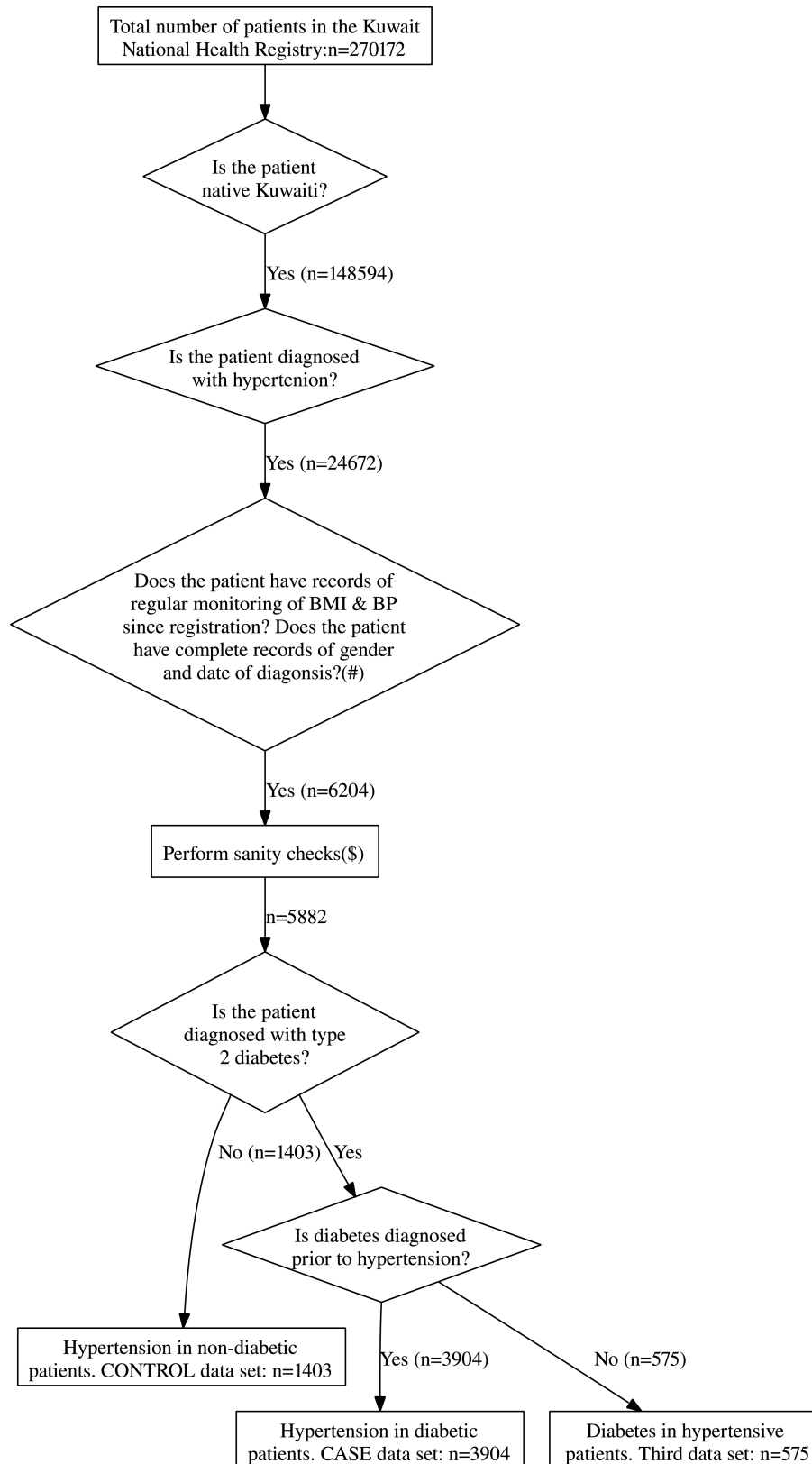
The study was approved by the Ethics Committee at Dasman Diabetes Institute. It uses epidemiology data on human participants from Kuwait.

The data for this study were taken from Kuwait Health Network,^{20 21} which is an initiative of Dasman Diabetes Institute in collaboration with the Ministry of Health (MOH) and the Public Authority of Civil Information (PACI) of the State of Kuwait. The network integrates health data from MOH primary health centres, with

laboratory data from the MOH hospitals across Kuwait. The data registry contains information on 270 172 unique participants that includes both natives and expatriates (see online supplementary appendix 1 for ethnicity distribution). The data records are retrospective over the past 12 years. Of the 270 172 participants, 74 134 and 58 745 were diagnosed with type 2 diabetes and hypertension, respectively. A total of 30 522 participants were diagnosed with comorbidity of hypertension and diabetes. For each of these patients, the data registry holds as many records as the number of times the patient has visited the hospitals. Measurements such as BMI, glycated hemoglobin (HbA1c) levels, and blood pressure readings were made as per international guidelines (see online supplementary appendix 2). Clinical guidelines were followed to ascertain the diagnosis for diabetes and hypertension (see online supplementary appendix 3). Since the participating clinics and hospital laboratories are part of MOH, the protocols and diagnosis criteria used by the participating clinics are uniform and standardised. The names and civil identification numbers of the patients were anonymised before the data were exported to us.

We carved out the following two data sets: (1) native comorbid patients with diagnosis for diabetes preceding hypertension (n=3904); and (2) native hypertensive patients with no incidence of diabetes (n=1403). The methods adopted to carve out the data sets are as outlined in figure 1 and as detailed in online supplementary appendix 4.

The study considers only those patients who have been regularly monitored for BMI (at least every 6 months) over the period from the date of registration to the date of hypertension diagnosis. The average variance in BMI per individual is seen to be low at 1.60 (data set of hypertension in patients with diabetes) and 1.81 (data set of hypertension in patients with non-diabetes). These observed average variances translate to variances of 4.36 and 4.92 kg in weight at an average height of 1.65 m (average heights of Kuwaiti native men and women are 1.72 and 1.58 m, respectively). This does not necessarily imply a gain in weight in all the individuals; it just represents the dynamics in weight over the period from registration to onset of hypertension. Though the variance in terms of weight seems to be large, the variance in BMI does not necessarily mean a transition into a higher or lower obesity class. The difference in these average variances in BMI between the two data sets is statistically insignificant (p=0.066). To reduce complexities arising due to the BMI dynamics while building the models, we considered the BMI measurements made at the time of hypertension diagnosis in our analysis. While it is essential to consider the BMI taken at the time of registration in studies relating to prognosis models, consideration of BMI at the time of onset in our study is in agreement with the practice as exemplified in.²²



(#) See supplementary information for details on other filtering procedures adopted.

(\$) Sanity checks to ascertain that the date of diagnosis of hypertension refers to actual date of onset: Exclude patients who, during the period preceding diagnosis of hypertension, had abnormal blood pressure readings or had antihypertensive medications

Figure 1 Flow chart for the methodologies used to carve out data sets used in this study.

Table 1 Descriptive statistics of the data sets used in the study

	Hypertension in patients with T2DM (n=3904)	Hypertension in patients without diabetes (n=1403)	p Value*
Mean age at the time of registration	47.48±10.92	43.24±10.74	<0.001
Mean blood pressure values in mm Hg at registration	SP=122.05±9.07 DP=79.09±6.77	SP=120.98±10.12 DP=79.39±8.32	<0.001 0.225
Mean BMI in kg/m ²	32.58±6.16	33.11±6.66	0.11
Mean blood pressure values in mm Hg at onset of hypertension	SP=141.11±21.48 DP=84.0±10.75	SP=145.89±19.76 DP=91.69±11.71	<0.001 <0.001
Mean HbA1C values in %	8.68±1.90	5.9±0.47	<0.001
Mean duration of T2DM before onset of Hypertension in years	2.85±1.94	NA	
Mean duration of registration before the onset of hypertension in years	8.81±6.19	4.52±2.58	
Sex distribution			
Men	41.0% (n=1599)	42.6% (n=597)	0.51
Women	59.0% (n=2305)	57.4% (n=806)	0.59
BMI distribution			
Normal weight	7.9% (n=307)	8.3% (n=117)	0.56
Overweight	29.6% (n=1157)	28.2% (n=396)	0.55
Class I obesity	30.5% (n=1191)	28.4% (n=398)	0.21
Class II obesity	18.9% (n=738)	20.2% (n=284)	0.35
Class III obesity	13.1% (n=511)	14.8% (n=208)	0.19

*The mean values presented in the previous two columns are compared using t test. BMI, body mass index; HbA1C, glycated haemoglobin; T2DM, type 2 diabetes.

BMI classifications approved by the WHO were used to categorise patients: normal weight (BMI=18.5–24.9 kg/m²), overweight (25.0–29.9), class I obesity (30.0–34.9), class II obesity (35.0–39.9) and class III obesity (≥40). HRs, using Cox Proportional Hazards Regression models, were calculated to evaluate the risk of developing hypertension by BMI categories for those with and without diabetes; the HRs were calculated against the baseline characteristics of patients with non-diabetes from the normal weight category and were adjusted for age and sex. Sex differences in HRs were evaluated by introducing an interaction term between BMI category and sex in the Cox regression model.

We evaluated associations between BMI and age at onset of hypertension by performing multiple linear regression analysis with age at onset of hypertension as the dependent variable, and sex and BMI measurements (as measured at the time of hypertension diagnosis) as independent variables. Effect modifications due to diabetes (or sex) were evaluated by performing test of interaction between the terms of presence/absence of diabetes (or sex) and BMI in the regression models. Differences in mean onset ages in various BMI categories were evaluated by considering BMI as a categorical variable and performing ANOVA (ANalysis Of VAriance) tests.

Data analyses were performed using the R Project for Statistical Computing (<http://www.r-project.org/>). Differences among groups were assessed using t tests. Results are considered statistically significant at p values <0.05. Normality assumptions are assessed by examining normal probability plots. Quantitative data are expressed

as mean and SD, while categorical data are expressed as absolute subject numbers and percentages.

RESULTS

Descriptive statistics on the data sets carved out for the study

Descriptive statistics on the two data sets are summarised in [table 1](#). The mean BMI and percentage distributions of participants as per BMI classifications or as per sex do not differ significantly between the two data sets. The mean HbA1c values at the time of diagnosis for hypertension are significantly different between patients with and without diabetes. The mean blood pressure values measured at onset of hypertension point to stage 1 hypertension in both the data sets while those measured at the time of registration are normal.

The mean age of the participants at the time of registration is around 45±10 years. The mean time period between registration and onset of hypertension is 8.81±6.19 years in the case of hypertension in patients with diabetes, and 4.52±2.58 years in the case of hypertension in patients without diabetes. The mean duration of type 2 diabetes before onset of hypertension is seen at 2.85±1.94 years.

Associations between obesity levels and risk of hypertension in patients with diabetes versus those without diabetes—HRs for developing hypertension in patients with and without diabetes from increasingly obese categories

We evaluated Cox proportional HRs (adjusted for age and sex) for developing hypertension in patients with and without diabetes against the baseline characteristics

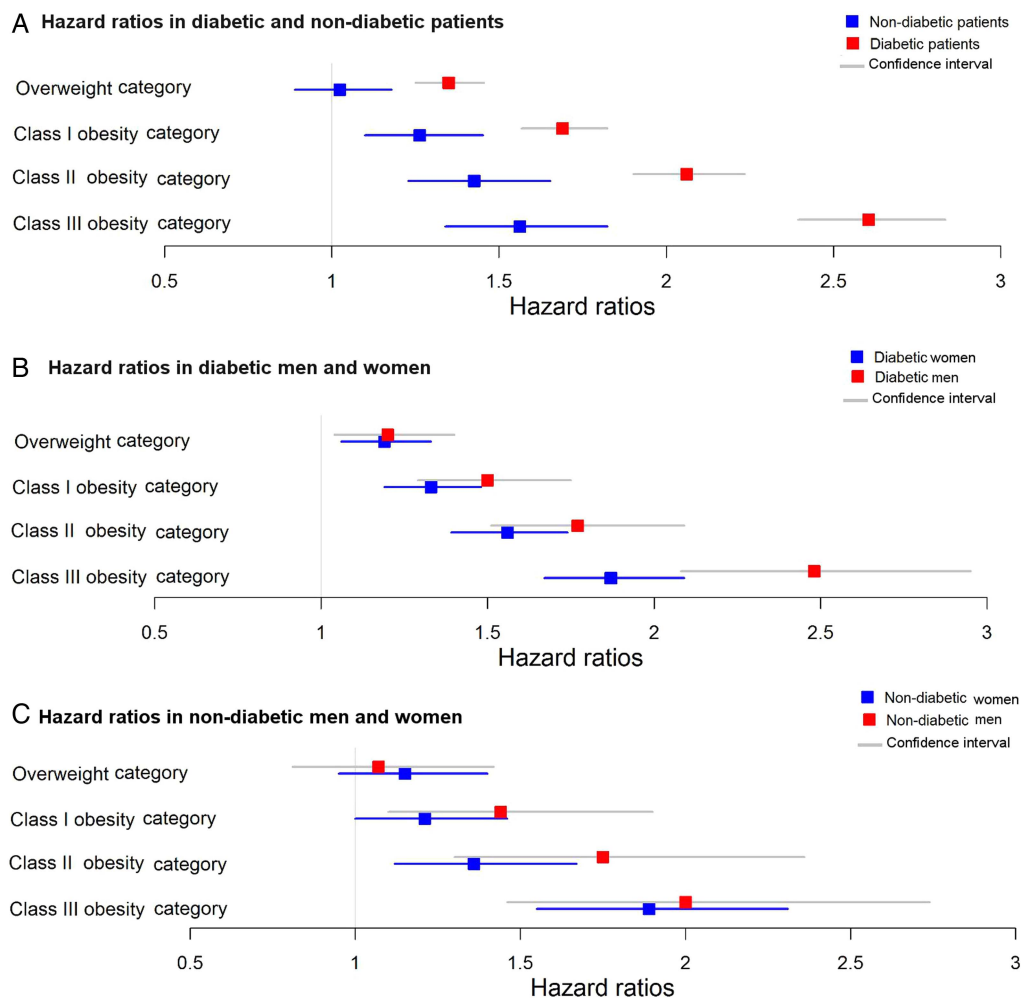


Figure 2 Forest plots to illustrate (A) differences in HRs for developing hypertension in individuals with diabetes versus those without diabetes, (B) sex differences in HRs for developing hypertension in individuals with diabetes, and (C) sex differences of HRs for developing hypertension in individuals without diabetes. HRs are calculated against the baseline characteristics of individuals without diabetes from the normal weight category.

of patients without diabetes from the normal weight category. The variability in HRs in different BMI categories is presented in figure 2A and online supplementary table S1. The results point to the following observations: (A) the risk of developing hypertension increases with BMI levels in both patients with and without diabetes (the fold increase in hazard in obese categories is in the range of 1.69–2.61 in individuals with diabetes, and 1.26–1.56 in individuals without diabetes); and (B) the risk is higher in patients diabetes with than in patients without diabetes in every BMI category (eg, the hazard of developing hypertension in individuals with diabetes from class III obese category increases 2.61-fold, while the increase is only 1.56-fold in individuals without diabetes from the same BMI category). Thus, there is a contribution to risk of hypertension from both the obesity level and pre-existing condition of diabetes. Sex differences in HRs in different BMI categories are presented in figure 2B (patients with diabetes) and figure 2C (patients without diabetes) (also see online supplementary table S2). It is seen that HRs are higher

in men than in women in every obese category—the difference is prominent in the case of class III obesity category for which the fold increase in hazard for men with diabetes is 2.48 as opposed to 1.87 for women with diabetes.

Propositions on associations between BMI and age at onset of hypertension, on impact of diabetes and on sex-specific differences

In order to first demonstrate that high BMI is associated with younger onset age for hypertension in Kuwaiti population, we examined the mean age at onset of hypertension at various BMI measurements. This was achieved by using the data set of hypertensive patients with no incidence of diabetes. We observed that age at onset of hypertension was higher at lower BMI values, and the drop in onset age per unit increase in BMI was very sharp (at -0.40 years per unit increase in BMI; $p < 0.001$) (see online supplementary figure S1).

We explicitly test the hypothesis that association between BMI and age at onset of hypertension can be

Table 2 Regression models, derived in this study, for hypertension onset age

To examine	Data set	Regression model
Interaction term between diabetes status and BMI	Pooled data—both the data sets are pooled together (N=5307)	$\hat{Y}=60.49-0.36(\times \text{BMI})-2.94(\times \text{sex}=\text{male})-0.12(\text{BMI}\times \text{diabetes status}=\text{yes})+12.73(\times \text{diabetes status}=\text{yes})$ p Value for the term (BMI×diabetes status=yes)=0.02
Interaction term between sex and BMI	Pooled data—both the data sets are pooled together (N=5307)	$\hat{Y}=65.70-0.33(\times \text{BMI})-9.0(\times \text{sex}=\text{male})-0.37(\text{BMI}\times \text{sex}=\text{male})$ p Value for the term (BMI×sex=male) <0.001
Association of BMI with age at onset of hypertension in patients with diabetes	Data set of hypertension in patients with diabetes (N=3904)	$\hat{Y}=70.13-[(0.39\times(\text{BMI}))]-[(0.27\times \text{sex}=\text{male})\times(\text{BMI})]+[5.6\times(\text{sex}=\text{male})]$ Translates onto Onset age (in men)=75.73–0.66×(BMI): Onset age (in women)=70.13–0.39×(BMI) Slope of onset age on BMI (men)=–0.66 Slope of onset age on BMI (women)=–0.39
Association of BMI with age at onset of hypertension in patients without diabetes	Data set of hypertension in patients without diabetes (N=1403)	$\hat{Y}=54.34-[0.18\times(\text{BMI})]-[(0.44\times \text{sex}=\text{male})\times(\text{BMI})]+[11.72\times(\text{sex}=\text{male})]$ Translates onto Onset age (in men)=66.06–0.62×(BMI): Onset age (in women)=54.34–0.18×(BMI): Slope of onset age on BMI (men)=–0.62 Slope of onset age on BMI (women)=–0.18
Confounding due to antidiabetic medication	Data set of hypertension in patients with diabetes (N=3904)	$\hat{Y}=70.28-[0.39\times(\text{BMI})]-[(0.27\times \text{sex}=\text{male})\times(\text{BMI})]+[5.6\times(\text{Sex}=\text{male})]-[0.39(\times \text{medication status}=\text{yes})]$ p Value for the term (medication status=yes)=0.4
Association of BMI with age at onset of hypertension in participants destined to develop diabetes	Data set of diabetes onset after that of hypertension (N=575)	$\hat{Y}=61.64-[-0.32\times(\text{BMI})]-[(0.36\times \text{Sex}=\text{male})\times(\text{BMI})]+[9.13\times(\text{sex}=\text{male})]$

BMI, body mass index.

different in patients with diabetes versus those without diabetes. We achieve this by pooling together the two data sets and performing a test of interaction between diabetes status and BMI in a regression analysis (with sex as a covariate and age at onset of hypertension as a dependent parameter). The resultant regression model (table 2) points to a significant interaction (p=0.02) between BMI and diabetes status in the determination of age at onset of hypertension.

We further tested the hypothesis that the association between BMI and age at onset of hypertension can be different in men versus women. We carried this out by performing a test of interaction between sex and BMI in a regression analysis. The resultant model (see table 2) points to a significant interaction (p value <0.001) between sex and BMI on age at onset of hypertension.

Quantifying the association of BMI with age at onset of hypertension in men and women with diabetes versus those without diabetes

Having tested the different propositions on the impact of diabetes and sex-specificity on the association between BMI and age at onset of hypertension, we set out to quantify the associations. We performed linear regression analysis with an interaction term between the

predictor variables of BMI and sex. The slopes for the association of BMI with age at onset of hypertension, as observed with the resultant models (see table 2), were: –0.66 (95% CI (–0.83 to –0.48)) in men with diabetes and –0.39 (95% CI (–0.45 to –0.32)) in women with diabetes; and –0.62 (95% CI (–0.90 to –0.33)) in men without diabetes and –0.18 (95% CI (–0.29 to –0.07)) in women without diabetes. While the slopes are similar in men with diabetes versus those without diabetes, they are significantly different in women (p value <0.001). The difference in onset age for hypertension in men versus women (both in patients with diabetes and non-diabetes) becomes increasingly prominent with increasing levels of BMI (see online supplementary figure S2). Confounders, such as the use of antidiabetic medication by patients in the year preceding the onset of hypertension, seem to have no influence on the associations mentioned above (see table 2, and online supplementary appendix 5).

As hypertension and diabetes are comorbid conditions, it is desirable to examine whether the observed association of BMI with age at onset of hypertension also holds in individuals who are destined to become diabetic. For this purpose, we considered a third set of patients with onset of hypertension succeeding that of

Table 3 Change in the observed mean age at onset of hypertension (in years) for patients with overweight and obese diabetes as compared with that of patients with normal weight diabetes

BMI categories of patients	Overweight	Class I obesity	Class II obesity	Class III obesity
(A) Both men and women (corrected for sex)				
Normal weight	–3.29 years (95% CI –5.11 to –1.47) p<0.001	–6.2 years (95% CI –7.98 to –4.4) p=0.00	–7.7 years (95% CI –9.59 to –5.75) p=0.00	–10.1 years (95% CI –12.16 to –8.07) p=0.00
(B) Men				
Normal weight	–3.5 years (95% CI –6.0 to –1.07) p<0.001	–7.6 years (95% CI –10.18 to –5.07) p=0.00	–10.8 years (95% CI –13.8 to –7.7) p=0.00	–13.2 years (95% CI –16.61 to –9.86) p=0.00
(C) Women				
Normal weight	–3.2 years (95% CI –5.9 to –0.41) p<0.05	–5.7 years (95% CI –8.33 to –2.98) p<0.001	–7.19 years (95% CI –9.93 to –4.45) p=0.00	–9.7 years (95% CI –12.53 to –6.84) p=0.00

diabetes (see figure 1 and online supplementary figure S3). The slope of the association of BMI with age at onset of hypertension in patients destined to become diabetic is seen at –0.32 (see table 2) and it is of the same order as that observed with patients who are already diabetic.

BMI as a categorical variable: reduction in age at onset of hypertension in patients of increasing BMI categories—Impact of diabetes and sex-specific differences

We consider BMI as a categorical variable (as opposed to considering it as a quantitative variable in the analysis presented so far) and examine the changes in age at onset of hypertension across different BMI categories of patients with and without diabetes (tables 3 and 4). Considering the increase in body weight measurements from normal to obese categories, the mean onset age for hypertension is seen to decrease considerably. The decrease in the case of patients with diabetes is in the range of 3.3 years (overweight category) to 10.1 years (class III obesity category) (table 3A), and the decrease

in the case of patients without diabetes is in the range of 3.0 (class I obesity category) to 7.8 years (class III obesity category) (table 4A). The decrease in age at onset of hypertension (against the increases in body weight) is seen to be sex-specific: in the case of men, statistically significant decreases are seen with both patients with and without diabetes (tables 3B and 4B); however, in women, statistically significant differences are seen only with patients with diabetes (table 3C) but not in patients without diabetes (table 4C).

DISCUSSION

Prevalence of diabetes and of the accompanying hypertension is an increasing problem, particularly in the Arab States of the Gulf (GCC).^{20 23} The chronic nature and long-term economic burden make diabetes and hypertension prototypical public health problems.^{24 25} Obesity is a major cause for metabolic syndromes which leads to the development of hypertension and diabetes. Hypertension has a tendency to develop more often in

Table 4 Changes in the observed mean age at onset of hypertension (in years) for overweight and obese patients with diabetes as compared with that of normal weight patients without diabetes

BMI categories of patients	Overweight	Class I obesity	Class II obesity	Class III obesity
(A) Both men and women (corrected for sex)				
Normal weight	–3.0 years* (95% CI –6.04 to 0.12) p=0.07	–3.3 years (95% CI –6.36 to 0.20) p=0.03	–4.1 years (95% CI –7.31 to 0.87) p<0.005	–7.8 years (95% CI –11.17 to 4.41) p=0.00
(B) Men				
Normal weight	–5.8 years (95% CI –10.05 to –1.54) p<0.005	–6.9 years (95% CI –11.22 to –2.6) p<0.001	–10.1 years (95% CI –14.85 to –5.4) p=0	–15.2 years (95% CI –20.51 to –9.95) p=0
(C) Women				
Normal weight	–0.3 years* (95% CI –4.76 to 4.1) p=1	–0.6 years* (95% CI –4.9 to 3.8) p=1	–0.7 years* (95% CI –5.2 to 3.8) p=1	–2.9 years* (95% CI –7.5 to 1.7) p=0.4

*These values are not significant. p Value >0.05.

patients with diabetes^{17 20 26} and can lead to severe complications including diabetic retinopathy, cardiovascular disorders and kidney disease.^{26–28} This study examines the associations that BMI has with risk and age at onset of hypertension, and illustrates how these associations are differentially modified by sex and pre-existing condition of diabetes. It considers BMI both as a quantitative variable (continuous risk) and as a categorical variable (threshold risk).

Enumeration of Cox proportional HRs illustrates that the risk of developing hypertension increases with BMI levels in both patients with and without diabetes, and that the risk is higher in patients with diabetes than in patients without diabetes in every BMI category. HRs were higher in men than in women in every obese category—the difference was prominent in the case of class III obesity category for which the fold increase in hazard for men with diabetes was 2.48 as compared to 1.87 for women with diabetes.

A negative correlation between BMI and age at onset of hypertension is observed. The slope of the association is larger in men than in women. An alteration in the slope due to the presence of diabetes was seen prominently in women (−0.39 vs −0.18; *p* value <0.001) than in men (−0.66 vs −0.62; *p*=0.66). Age at onset of hypertension in men is significantly decreased in overweight and increasingly obese categories of patients with and without diabetes; however, in women, a significant decrease is seen only in patients with diabetes.

The participants considered in this study are natives from each of the six governorates of Kuwait (namely Hawally, Farwaniya, Jahara, Ahmadi, Mubarak Al-Kabeer and Al Asimah); thus, the study generalises the population. In general, Kuwaiti natives are observed to be more obese than people from other ethnicities—the mean BMI, as calculated using data from Kuwait Health Network, of Kuwaiti natives (from the age group of 30–60 years) is 33.0±6.6 (class I obesity) while that of Asian expatriates is less at 27.0±4.00 (overweight). As a future work, it would be interesting to evaluate whether the observations made with the Kuwaiti population will hold true for lean populations such as Asians. In general, associations between BMI and risk of hypertension seem to hold in multiethnic populations, though the extent can vary.¹⁴

Earlier literature reports have pointed out that men develop diabetes at lower body mass indices than women.^{29 30} In this study, we point out that at a given BMI men develop hypertension earlier than women, and that being diabetic can accelerate the onset of hypertension in women.

A pre-existing condition of diabetes makes high blood pressure and cardiovascular problems more likely because diabetes complications damage arteries and make them targets for hardening (atherosclerosis). Gorya *et al*³¹ indicate that the prevalence of coronary atherosclerosis among younger women in the absence of diabetes is lower than among men; and among those

younger women with diabetes, the prevalence of atherosclerosis increases to the level seen in men. Sex-specific differences are seen in clinical characteristics of hypertension onset³² and in the regulation of blood pressure.^{33 34} In general, blood pressure is higher in men than in women of similar ages; however, after menopause, blood pressure in women increases to levels even higher than in men. The mechanisms responsible for the increase in blood pressure are multifactorial and include loss of oestrogen, oxidative stress, endothelial dysfunction, modification in renin-angiotensin system spillover and sympathetic activation.

Delaying the onset of hypertension reduces the lifetime risk of heart disease and stroke. Individuals who experience increases in blood pressure during middle age have been associated with a higher lifetime risk of cardiovascular disorders.¹⁶ Clinical practice guidelines that help in the prevention of hypertension present recommendations on dealing with the associated risk factors. The risk factors are at least of three types: (1) Modifiable risk factors such as obesity, diabetes, unhealthy diet and low physical activity; (2) Non-modifiable risk factors such as sex, family history and ethnicity; and (3) environmental risk factors such as low socioeconomic status and religious practices. Impact due to risk factors on onset of hypertension is exerted through a combinatorial interplay of factors of the above three types. Delineation of this interplay, such as that reported in this study (namely the impact of interplay among BMI, sex and pre-existence of diabetes on the age at onset of hypertension), will help in developing further the current guidelines on hypertension prevention and management.

CONCLUSIONS

The study clearly demonstrates the added risk due to the presence of diabetes for developing hypertension in obese individuals. Hazard for developing hypertension increases with obesity levels, and is higher in patients with diabetes compared to patients without diabetes of similar obesity levels. HRs are higher in men than in women in every obese category. We further demonstrate that age at onset of hypertension is inversely related to BMI; this relationship is seen to be stronger in men compared to women and in persons with diabetes compared to those without. A pre-existing condition of diabetes doubles the impact of obesity on age at onset of hypertension in women. The results of our cross-sectional study present a case for initiating future prospective follow-up studies that consider various confounding factors.

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Contributors TAT undertook the study design, directed the reported work and directed the development of the manuscript. KB participated in the study design and discussions. AMC handled data extraction and performed all the reported data analysis; he contributed significantly to the writing of the manuscript. BF participated in discussions.

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Data sharing statement No additional data are available.

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