

## RESEARCH ARTICLE

# The association between hypertension and other cardiovascular risk factors among non-diabetic Saudis adults—A cross sectional study

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## Abstract

Population specific associations between cardiovascular disease with various risk factors including pre-hypertension and hypertension were reported. We aimed to investigate the association of higher than optimal blood pressure with measures of dysglycemia, dyslipidemia, and markers of inflammation in non-diabetic Saudi adults hoping to improve current Saudi guidelines to prevent cardiovascular disease. Volunteers were recruited randomly from public healthcare centers in Jeddah. Demographic information, blood pressure (BP), and anthropometric measurements were taken. Fasting blood samples were drawn, then again following 1-hour oral glucose tolerance test. Glycated hemoglobin, fasting plasma glucose (FPG), lipid profile, highly sensitive C- reactive protein, gamma glutamyl transferase, and 1-hour plasma glucose were measured. Complete data was found for 742 men and 592 women. Pre-hypertension was found in 47.2% of men, and 24.7% of women, while 15.1% of men, and 14.6% of women were hypertensive. Means of measured variables differed significantly between normotensive, pre-hypertensive, and hypertensive groups of men and women in gender specific manner. Association between measured variables and elevated BP, and hypertension were assessed using logistic regression models. After adjustment for age, body mass index and waist circumference, elevated blood pressure was associated with elevated triglycerides in men, while hypertension was significantly associated with elevated fasting plasma glucose, total cholesterol, triglycerides, low density lipoprotein- cholesterol, and low high density lipoprotein- cholesterol in men, and elevated triglycerides, and total cholesterol in women. Therefore, it is strongly recommended to measure lipid profile, specifically TG, for all diagnosed pre-hypertensive and hypertensive patients in addition to FPG for men.

**Competing interests:** The authors have declared that no competing interests exist.

## Background

Type 2 diabetes (T2D) is a risk factor for cardiovascular diseases (CVD) [1]. Dyslipidemia, smoking, chronic inflammation, and abdominal obesity are also known risk factors for CVD [2–6]. Moreover, various epidemiological studies have indicated that blood pressure (both diastolic and systolic) is a most important risk factor, which has an independent, continuous, and direct association with CVD outcomes [7–10]. Furthermore, the increased risk of CVD was found to be associated with high-normal blood pressure (BP) values [11]. Obesity, hypertension, dyslipidemia and impaired glucose tolerance (IGT) had been found to cluster together [12–17], thus suggesting the possibility of a common aetiological mechanism, with the association between elevated BP and those other cardiovascular risk factors having long been acknowledged [18]. It has also been reported that obesity, and abdominal obesity are risk factors for the other CVD risk factors: hypertension, dyslipidemia, and diabetes mellitus [19]. Evidence for the relationship between increased weight and increased BP was reported much earlier based on findings in the nationwide "Community Hypertension Evaluation Clinic Screening" of more than 1 million men and women in the USA [20], and the "Framingham Study", where it was demonstrated that BP increased in both men and women with increased overweight [21]. These findings were verified later in a Canadian study especially in young adults 18 to 34 years of age [22], and in female nurses in USA [23].

Moreover, the presence of other cardiovascular risk factors, which cause endothelial dysfunction, has been suggested to contribute to the pathophysiology of hypertension [24], and studies of the association between hypertension and other CVD risk factors are numerous. A Japanese study showed that high normal BP, and hypertension increased the risk of T2D [25]. In addition, elevated BP was found to be increased in people with impaired glucose tolerance (IGT) in young, American, black adults [26]. Furthermore, a large meta-analysis of 4.1 million people showed that high BP was associated with elevated incidence of T2D [3]. Moreover, a more recent study reported that people with high BP are nearly 60% more likely to develop T2D [27], and a longitudinal Chinese study reported that time-cumulated exposure to elevated BP was significantly associated with an elevated incidence of IGT and diabetes [28]. Association between dyslipidemia and elevated BP has also been investigated, and is well discussed by Ruben et al (2006) [29]. Dyslipidemia leads to endothelial damage resulting in loss of vasomotor activity, which could cause hypertension (Nickenig et al, 2002) [30]. Similarly, elevated BP had been reported to be associated with inflammation in the general population [31, 32], and even at the typically observed low levels of inflammation in the general population, there is an association between the level of C-reactive protein (CRP), as a marker of inflammation, and systolic BP (SBP) [33].

Studies on mentioned associations did not include people from the Arab world. Genetic factors, and hence ethnicity play an important role in susceptibility to disease [34, 35]. In an earlier study, conducted in Jeddah, Saudi Arabia, [36], we reported an association between above than normal weight with dysglycemia, and hypertension, which was gender specific. Moreover, in another survey, conducted in the same city at a later date, high LDL-C was found to be associated with an increased probability of pre-diabetes (Al amri et al 2019), which points to the clustering of the three CVD risk factors, excess weight increased blood pressure and dysglycemia in the Saudi population, as noted in studies from other countries [12–17]. Up to date, there are no official guidelines for laboratory investigations in non-diabetic people with hypertension in Saudi Arabia. Therefore, we aimed at investigating the association between higher than optimal blood pressure and other known laboratory measured risk factors for CVD, including measures of dysglycemia, lipid profile, C-reactive protein (CRP) [37, 38], and

gamma glutamyl transferase (GGT) [39–41], in a non-diabetic Saudi population in the hope of providing evidence for improved management to prevent the progression to CVD.

## Materials and methods

### Study design and sample collection

Data included in this study were obtained from a survey conducted in the city of Jeddah between July 2016 and February 2017. Approval was given by the Committee on the Ethics of Human Research at the Faculty of Medicine-King Abdulaziz University, Jeddah (Reference No. 338–10). A full explanation of sampling methodology has been outlined earlier [42], and is summarized here as follows: non-diabetic adults (age  $\geq 18$  years) were recruited from attendees of Primary Health Care (PHC) centers in Jeddah, Saudi Arabia. Following signing an informed consent form, demographic, dietary, and lifestyle variables, as well as medical history and family history of chronic diseases were collected from recruits using a predesigned questionnaire. Fasting blood sample was taken, for determination of fasting plasma glucose (FPG), glycated hemoglobin (HbA1c), lipid profile, high-sensitivity CRP (hs-CRP) and GGT, followed by 1-hour oral glucose tolerance test (OGTT) [43, 44] to screen for diabetes and pre-diabetes. Anthropometric measurements [weight, height, waist circumference (WC)], and blood pressure (BP) were measured using standardized equipment and techniques. Weight and height were used to calculate the body mass index (BMI).

### Biochemical assays

Whole blood, serum and plasma samples were sent regularly to an accredited laboratory by the College of American Pathologist at the National Guard Hospital in Jeddah. Plasma glucose and serum hs-CRP, GGT, total cholesterol (TC), high density lipoprotein-cholesterol (HDL-C) and triglycerides (TG) levels were measured by spectrophotometric methods using Architect c8000 auto-analyzer (ABBOTT- USA). Low-density lipoprotein-cholesterol (LDL-C) was calculated using the Friedewald equation [45]. HbA1c was measured with high pressure liquid chromatography (HPLC) using automated HbA1c analyzer G8 (TOSOH Corporation-Japan).

**a) Diagnosis of pre-hypertension and hypertension.** Pre-hypertension was defined according to recommendations by the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure (JNC) VII report [46] as systolic blood pressure: 120 to 139 mm Hg, and diastolic blood pressure 85 to 89 mm Hg, while hypertension was defined as SBP  $\geq 140$  and/or DBP  $\geq 90$  mm Hg or taking antihypertensive drug treatment.

### Statistical analysis

IBM SPSS statistics version 20.0 for Windows was used to enter and analyze collected data. The baseline characteristics of study population were calculated statistically and described as mean, standard deviations (SD), and frequencies.

Demographic, lifestyle and clinical factors of elevated blood pressure were analyzed by comparing participants who were identified to have pre-hypertension or hypertension and those with normal blood pressure. Factors with continuous variables were analyzed using ANOVA to compare the three groups, and independent t-test to compare two groups, while those with categorical variables were analyzed using Chi-square test or Fisher's exact test, as appropriate. Fisher's exact test was applied when the number of people per cell was 5 or less.

Unadjusted and adjusted logistic regression models were used for assessing association between laboratory measured risk factors for CVD and outcome variables: elevated BP, and hypertension.

## Results

A total of 1733 adults were approached, but only 1477 adults accepted to participate and were originally recruited. Individuals were excluded when laboratory samples were missing for various reasons (hemolysis, missing labels, or broken tubes). After laboratory analysis of collected blood samples, and excluding those discovered to have previously undiagnosed diabetes, as well as excluding cases with missing data, complete data for the present analysis were available for 1334 individuals, 742 men and 592 women. Due to the exclusion criteria, very few of the included people (11 men and 7 women) were >64 years of age. Details of the different stages of sample collection are outlined in (Fig 1).

Demographic, clinical, and biochemical characteristics of study population are presented in Table 1 for men, and Table 2 for women:

Hypertensive men and women were significantly older than their pre-hypertensive and normotensive counterparts. Moreover, means of BMI, and WC, of both pre-hypertensive, and hypertensive groups of men or women were significantly higher than those of their respective normotensive groups.

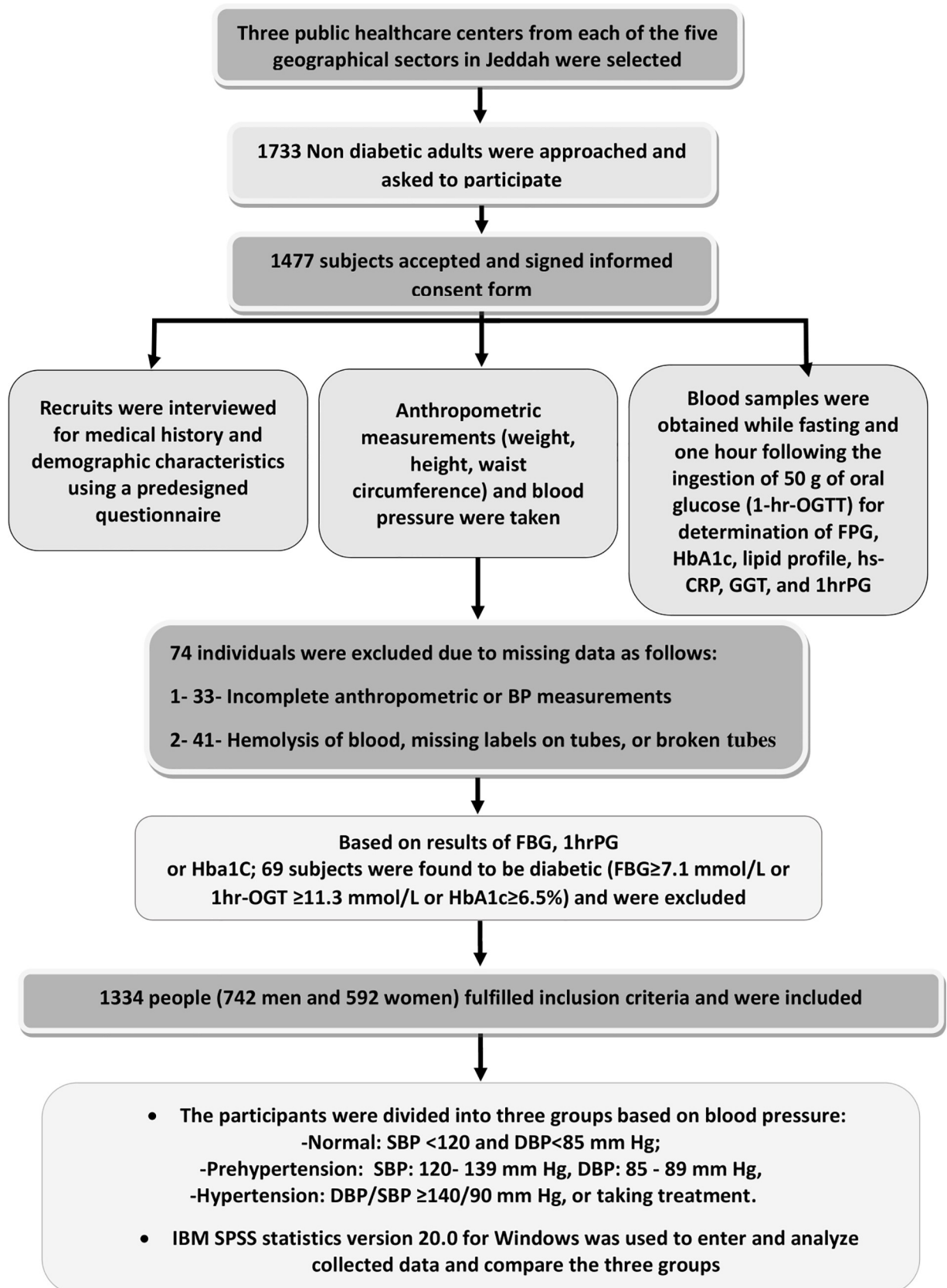
The means of all measures of glycemia (FPG, 1-h PG, and HbA1c) were all significantly higher in hypertensive compared with normotensive groups of men. However, only the means of FPG and 1-h PG in hypertensive group of women were significantly higher than those of the normotensive group. The percentages of men or women with IGT were significantly higher in the hypertensive groups compared with their respective normotensive groups.

The means of TC, hs-CRP, and GGT of pre-hypertensive and hypertensive groups of men were significantly higher than the means of normotensive group. Moreover, a higher percentage of elevated GGT (Saudi upper limit for men is 86 UL) [47] was also noted in both the pre-hypertensive (6.2%) and hypertensive (4.5%) compared with normotensive (1.8%) group of men. However, the means of TG, and LDL-C were found to be significantly higher, and that of HDL-C lower only in the group of hypertensive men compare to the corresponding means in the normotensive group.

Different results were obtained for women. Only the means of TC, TG, LDL-C, and hs-CRP in the hypertensive group of women were significantly higher than those corresponding means in the normotensive group. In addition, the mean TG was significantly higher in the pre-hypertensive group compared with that of the normotensive group. Elevated GGT (Saudi upper limit for women > 30 UL) [47] was noted in the normotensive group (8.4%), as well as the pre-hypertensive (7.7%) and hypertensive (10.7%) groups of women.

Following multiple logistic regression, the unadjusted odds ratio (OR) and confidence interval (CI) and those adjusted for age alone, and again for age, BMI and WC for the association between the combined groups of people with higher than acceptable BP (pre-hypertension and hypertension), as well as the hypertensive groups alone with CVD risk covariates in men and women is presented in Tables 3 and 4, respectively:

After adjusting for age, elevated TG, hs-CRP, and GGT remained significantly associated with higher than optimal blood pressure in men, but no association was noted in women. After adjusting for age, BMI, and WC, only elevated TG remained significantly associated with higher than optimal blood pressure in men, while no significant associations remained in women with any of the measured variables (Table 3).



**Fig 1. Outline of the different stages of sample collection.** A total 37.7% of men and 61% of women had normal blood pressure. Elevated BP was mainly due to increased SBP in both sexes.

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After adjusting for age only, elevated FPG, TC, TG, LDL-C, and low HDL-C remained significantly associated with hypertension in men, but only elevated TC, TG and LDL-C maintained association in women. After adjusting for age, BMI, and WC, elevated FPG, TC, TG and LDL-C, as well as low HDL-C remained significantly associated with hypertension in men, while in women an association was found only for elevated TG and TC (Table 4)

## Discussion

Increased risks of CVD and mortality are associated with higher than optimal blood pressure [7–10]. The risk has been reported to be further increased when combined with diabetes or pre-diabetes in Chinese population [48]. The presence of other risk factors for CVD, such as chronic inflammation, and dyslipidemia, in addition to increased blood pressure might raise the risk of the disease further [49]. However, there are differences in relative weight of CVD risk factors between ethnic groups [50], and there are no such studies conducted on Saudi

**Table 1. Demographic, clinical and biochemical characteristics of men by the study groups presented as mean  $\pm$  standard deviation (SD).**

Variable	Non-hypertensive (Mean $\pm$ SD) (N = 280)	Prehypertensive (Mean $\pm$ SD) (N = 350)	Hypertensive (Mean $\pm$ SD) (N = 112)	P-Value
Age (years)	29.2 $\pm$ 9.0	29.9 $\pm$ 8.8	37.2 $\pm$ 14.3 <sup>b</sup>	<0.001
BMI (kg/m <sup>2</sup> )	25.6 $\pm$ 0.3	28.0 $\pm$ 5.7 <sup>a</sup>	30.4 $\pm$ .67 <sup>b</sup>	<0.001
Waist Circumference (cm) Individuals with high values (WC >94 cm), (n,%)	91.5 $\pm$ 13.8 (124), 44.4%	97.7 $\pm$ 14.9 <sup>a</sup> (204), 59.0%	104.4 $\pm$ 16.6 <sup>b</sup> (80), 74.1%	<0.001 <0.001
SBP(mean $\pm$ SD) Individuals with high values (SBP $\geq$ 120 mmHg), (n,%)	110 $\pm$ 6.4	125 $\pm$ 5.6 <sup>a</sup> (343), 98.0%	137 $\pm$ 15.3 <sup>b</sup> (104), 92.9%	<0.001 <0.001
DBP Individuals with high values (DBP $\geq$ 85 mmHg), (n,%)	68 $\pm$ 9.10	76 $\pm$ 8.0 <sup>a</sup> (50), 14.3%	88 $\pm$ 11.7 <sup>b</sup> (77), 68.5%	<0.001 <0.001
FPG, mmol/l Individuals with high values (FPG $\geq$ 6.1mmol/l), (n,%)	4.2 $\pm$ 0.74 (1), 0.4%	4.0 $\pm$ 1.21 <sup>a</sup> (2), 0.8%	4.6 $\pm$ 0.94 <sup>b</sup> (9), 6.9%	<0.001 <0.001
1-h, PG mmol/l Individuals with high values (1-h, PG $\geq$ 8.6mmol/l), (n,%)	6.3 $\pm$ 1.83 (29),11.2%	5.9 $\pm$ 2.34 <sup>a</sup> (36),11.4%	7.0 $\pm$ 1.91 <sup>b</sup> (22), 22.7%	<0.001 0.010
HbA1c, % Individuals with high values (HbA1c $\geq$ 5.7%), (n,%)	5.2 $\pm$ 0.42 (22), 8.2%	5.2 $\pm$ 0.38 (34), 10.2%	5.3 $\pm$ 0.43 <sup>b</sup> (18), 17.8% 34.2 $\pm$ 4.75 <sup>b</sup> (16), 15.7%	0.036 0.030
mmol/mol Individuals with high values (HbA1c $\geq$ 39 mmol/mol), (n,%)	33.1 $\pm$ 0.453 (21),7.9%	33.7 $\pm$ 4.14 (28), 8.4%		0.039 0.014
Individuals with IGT with any definition (FBG $\geq$ 6.1mmol/l or 1-h, PG $\geq$ 8.6mmol/l or HbA1c $\geq$ 5.7%) (n,%)	(46), 16.4%	(63), 18.0%	(37), 33.3%	0.001
TC (mmol/L)	4.65 $\pm$ 0.99	4.86 $\pm$ 0.92 <sup>a</sup>	4.93 $\pm$ 0.90 <sup>b</sup>	0.006
TG (mmol/L)	1.28 $\pm$ 0.96	1.41 $\pm$ 1.00	1.74 $\pm$ 1.03 <sup>b</sup>	0.000
HDL- C (mmol/L)	1.26 $\pm$ 0.23	1.28 $\pm$ 0.26	1.18 $\pm$ 0.24 <sup>b</sup>	0.001
LDL- C (mmol/l)	3.15 $\pm$ 0.94	3.29 $\pm$ 0.82	3.41 $\pm$ 0.86 <sup>b</sup>	0.021
hs-CRP (mg/L)	2.41 $\pm$ 3.04	3.22 $\pm$ 3.58 <sup>a</sup>	3.54 $\pm$ 3.95 <sup>b</sup>	0.003
GGT (IU/L)	28.63 $\pm$ 18.04	37.53 $\pm$ 32.64 <sup>a</sup>	38.83 $\pm$ 24.68 <sup>b</sup>	<0.001

n, number of subjects in subgroup; FPG, fasting plasma glucose; 1-hPG, 1-hour plasma glucose; TC, serum total cholesterol; HDL- C, serum high density lipoprotein cholesterol; LDL, serum low density lipoprotein cholesterol; TG, serum triglycerides; hs-CRP, serum highly sensitive C-reactive protein; GGT, gamma glutamyl transferase; P value of ANOVA test for differences between the three groups

a: P<0.05 between normal and pre-hypertensive groups

b: P<0.05 between normal and hypertensive groups

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**Table 2. Demographic and biochemical characteristics of women by studied groups presented as mean  $\pm$  standard deviation (SD).**

Variable	Non-hypertensive (Mean $\pm$ SD) (N = 361)	Prehypertensive (Mean $\pm$ SD) (N = 146)	Hypertensive (Mean $\pm$ SD) (N = 85)	P-Value
Age (years)	31.4 $\pm$ 10.5	33.5 $\pm$ 12.3 <sup>a</sup>	40.9 $\pm$ 14.3 <sup>b</sup>	<0.001
BMI (kg/m <sup>2</sup> )	26.0 $\pm$ 5.6	28.7 $\pm$ 6.4 <sup>a</sup>	31.1 $\pm$ 7.5 <sup>b</sup>	<0.001
Waist Circumference (cm)	84.3 $\pm$ 14.3 (202), 57.7%	91.4 $\pm$ 16.3 <sup>a</sup> (109), 77.3%	98.0 $\pm$ 0.162 <sup>b</sup> (75), 88.2%	<0.001
Individuals with high values (WC>80 cm), (n,%)				<0.001
SBP(mean $\pm$ SD)	104 $\pm$ 8.2	122 $\pm$ 4.9 <sup>a</sup>	133 $\pm$ 18.7 <sup>b</sup> (72), 84.7%	<0.001
Individuals with high values (SBP $\geq$ 120 mmHg), (n,%)		(135), 92.5%		<0.001
DBP	65 $\pm$ 7.9	75 $\pm$ 8.8 <sup>a</sup>	87 $\pm$ 11.7 <sup>b</sup> (57), 67.1%	<0.001
Individuals with high values (DBP $\geq$ 85 mmHg), (n,%)		(22), 15.1%		<0.001
FPG, mmol/l	4.2 $\pm$ 0.66	4.3 $\pm$ 0.77	4.4 $\pm$ 0.77 <sup>b</sup> (5), 5.9%	0.117
Individuals with high values (FBG $\geq$ 6.1mmol/l), (n,%)	(6), 1.7%	(1), 0.7%		0.019
1-h PG mmol/l	6.2 $\pm$ 1.62	6.5 $\pm$ 1.69	6.9 $\pm$ 1.82 <sup>b</sup>	0.007
Individuals with high values (1-h, PG $\geq$ 8.6mmol/l), (n,%)	(29), 8.7%	(12), 9.0%	(16), 21.6%	0.004
HbA1c, %	5.2 $\pm$ 0.37	5.3 $\pm$ 0.37	5.3 $\pm$ 0.45	0.389
Individuals with high values (HbA1c $\geq$ 5.7%), (n,%)	(34), 9.7%	(15), 10.9%	(14), 17.5%	0.135
Mmol/mol	33.6 $\pm$ 4.00	34.0 $\pm$ 3.95	34.3 $\pm$ 4.96	0.364
Individuals with high values (HbA1c $\geq$ 39 Mmol/mol), (n,%)	(31), 8.9%	(13), 9.4%	(13), 16.3%	0.556
Individuals with IGT with any definition (FBG $\geq$ 6.1mmol/l or 1-h, PG $\geq$ 8.6mmol/l or HbA1c $\geq$ 5.7%) (n,%)	(62), 17.2%	(23), 15.8%	(28), 32.9% <sup>b</sup>	0.002
TC (mmol/L)	4.76 $\pm$ 0.93	4.80 $\pm$ 0.88	5.13 $\pm$ 0.98 <sup>b</sup>	0.004
TG (mmol/L)	0.96 $\pm$ 0.48	1.08 $\pm$ 0.63 <sup>a</sup>	1.30 $\pm$ 0.70 <sup>b</sup>	<0.001
HDL- C (mmol/L)	1.48 $\pm$ 0.28	1.48 $\pm$ 0.32	1.45 $\pm$ 0.25	0.542
LDL- C (mmol/L)	3.09 $\pm$ 0.81	3.12 $\pm$ 0.83	3.43 $\pm$ 0.84 <sup>b</sup>	0.003
hs-CRP (mg/L)	3.42 $\pm$ 3.84	4.02 $\pm$ 4.40	5.13 $\pm$ 5.07 <sup>b</sup>	0.004
GGT (IU/L)	17.82 $\pm$ 18.19	19.08 $\pm$ 13.09	21.85 $\pm$ 26.42	0.195

n, number of subjects in subgroup; FPG, fasting plasma glucose; 1-hPG, 1-hour plasma glucose; TC, serum total cholesterol; HDL- C, serum high density lipoprotein cholesterol; LDL, serum low density lipoprotein cholesterol; TG, serum triglycerides; hs-CRP, serum highly sensitive C-reactive protein; GGT, gamma glutamyl transferase; P value of ANOVA test for differences between the three groups

a: P<0.05 between normal and pre-hypertensive studied groups

b: P<0.05 between normal and hypertensive studied groups

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population in spite of the high prevalence of pre-hypertension and hypertension as reported earlier [51–53], and as noted also in this study, as well as the high prevalence of diabetes and pre-diabetes among the Saudis [54]. Therefore, this study was conducted to investigate an important aspect related to improvement in healthcare, namely the association between higher than optimal blood pressure and other known laboratory measured risk factors of CVD in our population, in the hope of formulating guideline for necessary basic laboratory tests that should be requested by practitioners treating non diabetic patients with higher than optimal blood pressure.

A high percentage of our study population had elevated blood pressure, with only 37.7% of men, and 61% of women having normal values, and with pre-hypertension being present in 47.2% of men, and 24.7% women, while 15.1% of men and 14.6% of women and were hypertensive. In the latest Saudi national survey conducted in 2013 [52], 15.2% and 40.6% of Saudis aged 15 years or older were hypertensive or borderline hypertensive, which is close to our findings. Furthermore, similar to our findings, the same survey reported higher risk of hypertension among men compared to women [52]. In addition, a lower prevalence of hypertension and pre-hypertension among women compared to men was also reported in a more recent Saudi study [51]. This is in agreement with reports from studies in other countries in the region [55], as well as older studies on populations from different parts of the globe [56].

**Table 3. Unadjusted, age adjusted, and age, BMI and WC adjusted odds ratio (OR) and confidence interval (CI) for CVD risk covariates associated with pre-hypertension and hypertension combined in men and women.**

Covariate	Men			Women		
	Unadjusted OR, CI 95%, P-Value	Age adjusted OR, CI 95%, P-Value	Age, BMI and WC adjusted OR, CI 95%, P-Value	Unadjusted OR, CI 95%, P-Value	Age adjusted OR, CI 95%, P-Value	Age, BMI and WC adjusted OR, CI 95%, P-Value
Elevated FPG, mmol/l (FBG $\geq$ 6.1mmol/l),	6.81(0.87–52.99),0.067	5.41(0.69–42.6),0.106	4.25(0.54–33.8),0.171	1.58(0.50–4.95),0.435	0.96(0.29–3.17),0.950	0.91(0.28–3.04),0.883
Elevated 1-h PG mmol/l (1-h, PG $\geq$ 8.6mmol/l),	1.27(0.79–2.06),0.313	1.09(0.66–1.78),0.746	0.96(0.58–1.60),0.879	1.63(0.94–2.84),0.081	1.22(0.69–2.18),0.493	1.16(0.64–2.13),0.626
Elevated HbA1c, % (HbA1c $\geq$ 5.7%), (HbA1c $\geq$ 39 Mmol/mol),	1.51(0.89–2.55),0.124 1.32(0.77–2.27),0.319	1.28(0.74–2.20),0.380 1.09(0.62–1.92),0.766	1.07(0.61–1.88),0.816 0.89(0.49–1.60),0.686	1.43(0.84–2.42),0.187 1.39(0.80–2.42),0.238	1.04(0.60–1.82),0.886 1.00(0.56–1.79),0.994	0.94(0.52–1.68),0.823 0.89(0.48–1.65),0.713
Elevated TC, mmol/l TC $\geq$ 5.18mmol/l	1.45(1.05–1.99), <b>0.024</b>	1.33(0.96–1.84),0.089	1.23(0.88–1.72),0.230	1.35(0.95–1.92),0.096	1.01(0.69–1.47),0.978	0.89(0.60–1.33),0.576
Elevated TG, mmol/l TG $\geq$ 1.70mmol/l	1.95(1.36–2.81), <b>0.000</b>	1.74(1.20–2.53), <b>0.004</b>	1.52(1.03–2.24), <b>0.035</b>	1.97(1.21–3.21), <b>0.006</b>	1.45(0.87–2.42),0.159	1.21(0.71–2.08),0.490
Low HDL- C level, mmol/l HDL-C $<$ 1.04 M mmol/l, $<$ 1.3F mmol/l	1.45(0.99–2.12),0.055	1.24(0.84–1.84),0.279	1.14(0.75–1.71),0.542	1.32(0.92–1.92) 0.136	1.22(0.83–1.77),0.312	1.04(0.70–1.55),0.851
Elevated LDL- C, mmol/l LDL-C $\geq$ 3.37 mmol/l	1.31(0.97–1.78),0.081	1.23(0.90–1.67),0.198	1.12(0.81–1.54),0.503	1.56(1.11–2.21), <b>0.011</b>	1.30(0.91–1.87),0.198	1.11(0.76–1.62),0.590
Elevated hs-CRP, mg/l hs-CRP $>$ 3mg/l	1.81(1.29–2.55), <b>0.001</b>	1.81(1.28–2.55), <b>0.001</b>	1.30(0.90–1.87),0.168	1.45(1.03–2.06), <b>0.035</b>	1.16(0.81–1.68),0.423	0.70(0.45–1.07),0.100
Elevated GGT, U/l GGT $>$ 86 U/l M, $>$ 30U/l F	3.28(1.24–8.64), <b>0.016</b>	3.25(1.23–8.58), <b>0.018</b>	2.60(0.96–6.98),0.059	1.06(0.59–1.91),0.851	0.80(0.43–1.49),0.486	0.68(0.35–1.29),0.238

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Aging is well-known to be associated with increased risk of hypertension in various populations [57–59], and also noted in previous Saudi studies [51–53]. In concordance with this, the mean age of people with hypertension in our study was significantly higher than the mean age of normotensive people. In addition, the means of BMI and WC in the hypertensive and pre-hypertensive people were significantly higher than the corresponding means of those with normal BP. Overweight and obesity, especially when accompanied with abdominal obesity, are major causes of hypertension [60–62]. In previous Saudi studies, higher than normal weight was reported to be associated with increased prevalence [53] and increased risk of hypertension [51, 52]. However, these studies had not investigated sex differences in risk assessment, nor did they adjust for age when reporting association. In an earlier survey conducted in Jeddah by our group, obesity and overweight were found to be associated with an increased risk of hypertension in men but not in women after adjusting for age [36]. Therefore, in this study while investigating the association between increased blood pressure and laboratory measured CVD risk factors, age alone, as well as age, BMI and WC were adjusted for to account for their possible influence on results.

After adjustment for age, elevated TG, hs-cRP, and GGT remained significantly associated with higher than optimal blood pressure (pre-hypertension and hypertension combined) in men, but no association was noted in women. However, following similar adjustment, elevated FPG, TC, TG, LDL-C, and low HDL-C remained significantly associated with hypertension in men, but only elevated TC, TG and LDL-C maintained association in women.



**Table 4. Unadjusted, age adjusted, and age, BMI and WC adjusted odds ratio (OR), and confidence interval (CI) for CVD risk covariates associated with hypertension in men and women.**

Covariate	Men			Women		
	Unadjusted OR, CI 95%, P-Value	Age adjusted OR, CI 95%, P-Value	Age, BMI and WC adjusted OR, CI 95%, P-Value	Unadjusted OR, CI 95%, P-Value	Age adjusted OR, CI 95%, P-Value	Age, BMI and WC adjusted OR, CI 95%, P-Value
Elevated FPG, mmol/l (FBG $\geq$ 6.1mmol/l),	18.26(4.86–68.58), <b>0.000</b>	12.81(3.26–50.32), <b>0.000</b>	10.98(2.75–43.79), <b>0.001</b>	4.46(1.38–14.41), <b>0.012</b>	2.22(0.63–7.79),0.212	2.19(0.62–7.71),0.224
Elevated 1-h PG mmol/l (1-h, PG $\geq$ 8.6mmol/l),	2.27(1.32–3.89), <b>0.003</b>	1.47(0.82–2.64),0.197	1.34(0.73–2.44),0.346	2.85(1.51–5.41), <b>0.001</b>	1.79(0.90–3.57),0.096	1.69(0.85–3.39),0.137
Elevated HbA1c, % (HbA1c $\geq$ 5.7%), (HbA1c $\geq$ 39 Mmol/mol),	2.09(1.17–3.72), <b>0.013</b> 2.09(1.14–3.84), <b>0.017</b>	1.28(0.68–2.41),0.453 1.23(0.63–2.41),0.543	1.09(0.57–2.08),0.799 1.02(0.513–2.02),0.965	1.96(1.00–3.82), <b>0.049</b>	1.12(0.56–2.26),0.747 1.14(0.55–2.35),0.720	1.08(0.53–2.19),0.835 1.09(0.52–2.27),0.817
Elevated TC, mmol/l TC $\geq$ 5.18mmol/l	1.90(1.27–2.86), <b>0.002</b>	1.60(1.05–2.45), <b>0.030</b>	1.60(1.03–2.49), <b>0.036</b>	2.77(1.73–4.42), <b>0.000</b>	1.87(1.13–3.08), <b>0.015</b>	1.78(1.07–2.97), <b>0.027</b>
Elevated TG, mmol/l TG $\geq$ 1.70mmol/l	2.51(1.65–3.81), <b>0.000</b>	1.94(1.25–3.01), <b>0.003</b>	1.72(1.09–2.71), <b>0.021</b>	3.48(2.00–6.05), <b>0.000</b>	2.23(1.24–4.03), <b>0.008</b>	2.03(1.12–3.70), <b>0.020</b>
Low HDL- C level, mmol/l HDL-C $<$ 1.04 M mmol/l, $<$ 1.3F mmol/l	2.70(1.75–4.18), <b>0.000</b>	1.89(1.18–3.02), <b>0.008</b>	1.77(1.09–2.88), <b>0.021</b>	1.66(1.02–2.70) <b>0.041</b>	1.46(0.88–2.43),0.139	1.27(0.76–2.14),0.366
Elevated LDL- C, mmol/l LDL-C $\geq$ 3.37 mmol/l	1.85(1.23–2.77), <b>0.003</b>	1.62(1.06–2.47) <b>0.025</b>	1.59(1.02–2.47), <b>0.039</b>	2.21(1.39–3.53), <b>0.001</b>	1.67(1.02–2.73), <b>0.040</b>	1.50(0.91–2.48),0.112
Elevated hs-CRP, mg/l hs-CRP $>$ 3mg/l	1.32(0.86–2.02),0.207	1.29(0.82–2.02),0.272	0.89(0.54–1.46),0.648	1.52(0.94–2.46),0.091	1.00(0.60–1.69),0.992	0.64(0.35–1.17),0.148
Elevated GGT, U/l GGT $>$ 86 U/l M, $>$ 30U/l F	1.06(0.40–2.82),0.909	1.09(0.40–2.94),0.872	0.83(0.29–2.36),0.723	1.34(0.63–2.87),0.451	0.90(0.39–1.97),0.754	0.76(0.34–1.72),0.509

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After adjustment for age, BMI and WC, above than optimal blood pressure (pre-hypertension and hypertension combined) was associated only with increased level of serum TG in men but not women. However, following similar adjustments, hypertension was significantly associated with elevated FPG, TC, TG, and LDL-C, as well as low HDL-C in men, while significant association was found only for elevated TG, and TC in women. These results emphasize gender differences in our population, and should be taken into account when considering management.

However, no significant association was found between high blood pressure and hs-CRP or GTT, even though both are considered as markers of inflammation and are associated with increased risk of CVD. Indeed, serum CRP level is reported to be a powerful predictor of ischemic CVD events in apparently healthy subjects, as well as in patients with stable or unstable angina [37, 38]. Furthermore, CRP and blood pressure are considered to be independent determinants of CVD risk, increasing the risk when combined [63, 64]. In addition, the same group of researchers, as well as others reported that CRP level was positively associated with systolic blood pressure, and hypertension [63, 64]. However, another study contradicted this and found that elevated CRP levels were not associated with, and did not appear to lead to elevated blood pressure, after adjustment for various confounders [65], which substantiates our results when adjustment was made for age, BMI and WC.

GGT has been reported to be involved in the pathogenesis of hypertension in a Chinese three-year follow-up study on normotensive and hypertensive subjects [66], while another Chinese study reported that GGT showed strong positive correlations with systolic blood

pressure and diastolic blood pressure [67]. In addition, a Korean study reported that high serum GGT levels, and even high normal level, were associated with a higher risk of incident hypertension, particularly in alcohol drinkers and non-overweight individuals [68]. Moreover, young patients with pre-hypertension were reported to have higher serum GGT levels compared with healthy subjects in a small case-control study in Turkey [69]. In our study, elevated levels of GGT was noted also among normotensive women, in addition to women with high blood pressure, while pre-hypertensive and hypertensive men had a significantly higher mean level of GGT compared with normotensive men. Additionally, in this study an association with higher than optimal blood pressure was found after adjustment for age only in men, but not women. Yet, after adjusting for age, BMI and WC no significant association was found between GGT and higher than optimal blood pressure. A recent meta-analysis evaluating association between development of hypertension and GGT level found that the reported direct association between GGT level and risk of hypertension was more significant in Asians and male subgroups compared to non-Asians and female subgroups, explaining this by the fact that Asians have more prevalence of hepatic diseases, which was not accounted for in these studies, and that men drink more alcoholic beverages than women in the studied populations [70]. In addition, when they performed subgroup analysis in non-drinkers, only a non-statistically significant increased trend was found, which is comparable to our results since our study participants were non-drinkers.

The Saudi Hypertension Guidelines 2018 [71] recommended the measurement of complete lipid profile, and fasting blood glucose in all diagnosed hypertensive patients as basic investigations to improve management and decrease risk of CVD. This is in keeping with the European [72] and American [46] guidelines. However, these guidelines were not endorsed by the "Saudi Ministry of Health", and hence, have not been adhered to strictly, leaving the matter to the interest and judgment of the treating physician. Furthermore, there are no specific Saudi guidelines for basic investigations in the case of pre-hypertension, which means that no specific laboratory investigations are usually requested. As mentioned earlier, the risk of CVD is very much increased when combined with diabetes or pre-diabetes [48], especially with elevated post-challenge glucose. Indeed, the co-existence of multiple CVD risk factors in any person results in an effect that is greater than the sum of the effects of its individual components [72], leading to a shift towards higher risk stratification and necessitating different management strategy to prevent, or at least delay, the development of CVD, which contributes to 31% of all deaths globally [73], and to 45% of all deaths in Saudi Arabia (Al Habib, 2020) [74] mainly due to poor preventive management strategies. Therefore, this study provides important, evidence based information, much needed in our region to improve measures for the prevention of CVD by guiding treating physicians to the most likely required set of tests for risk stratification, and hence improved management.

Our study has a few limitations. The first one is common to all cross-sectional studies where only an association between studied variables, but not causation, can be inferred. Another limitation is that only few people were included in the older age group (>64 years) due to being already diagnosed with diabetes one of the conditions in the exclusion criteria. Strengths of our study include the involvement of well-trained data collectors and the use of well-standardized methods for data collection. Secondly, to avoid bias, PHCCs and participants were selected randomly. Moreover, accuracy of laboratory results was assured by conducting all measurements in one accredited laboratory.

In conclusion, based on our results, hypertensive men and women, and pre-hypertensive men are more likely to have dyslipidemia, increasing their risk for CVDs. Furthermore, hypertensive men are more likely to have impaired fasting glucose with a further increase in risk. Therefore, it is highly recommended that all physicians include the estimation of lipid profile

and fasting plasma glucose in their routinely requested tests for all diagnosed hypertensive patients. In addition, the estimation of fasting serum TG at least, if not lipid profile, should be requested for all pre-hypertensive men. Failure to do so is expected to lead to less than optimal management of elevated blood pressure needed for the prevention of CVD.

## Supporting information

### S1 Data.

(XLSX)

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## References

1. Haffner SM, Lehto S, Ronnema T, Pyorala K, Laakso M. Mortality from coronary heart disease in subjects with type 2 diabetes and in nondiabetic subjects with and without prior myocardial infarction. *N Engl J Med.* 1998; 339(4):229–34. <https://doi.org/10.1056/NEJM199807233390404> PMID: 9673301
2. Barter P, Gotto AM, LaRosa JC, Maroni J, Szarek M, Grundy SM, et al. HDL cholesterol, very low levels of LDL cholesterol, and cardiovascular events. *N Engl J Med.* 2007; 357(13):1301–10. <https://doi.org/10.1056/NEJMoa064278> PMID: 17898099
3. Emdin CA, Anderson SG, Woodward M, Rahimi K. Usual Blood Pressure and Risk of New-Onset Diabetes: Evidence From 4.1 Million Adults and a Meta-Analysis of Prospective Studies. *J Am Coll Cardiol.* 2015; 66(14):1552–62. <https://doi.org/10.1016/j.jacc.2015.07.059> PMID: 26429079
4. Lopez-Candales A, Hernandez Burgos PM, Hernandez-Suarez DF, Harris D. Linking Chronic Inflammation with Cardiovascular Disease: From Normal Aging to the Metabolic Syndrome. *J Nat Sci.* 2017; 3(4). PMID: 28670620
5. Miller M, Stone NJ, Ballantyne C, Bittner V, Criqui MH, Ginsberg HN, et al. Triglycerides and cardiovascular disease: a scientific statement from the American Heart Association. *Circulation.* 2011; 123(20):2292–333. <https://doi.org/10.1161/CIR.0b013e3182160726> PMID: 21502576

6. Wormser D, Kaptoge S, Di Angelantonio E, Wood AM, Pennells L, Thompson A, et al. Separate and combined associations of body-mass index and abdominal adiposity with cardiovascular disease: collaborative analysis of 58 prospective studies. *Lancet*. 2011; 377(9771):1085–95. [https://doi.org/10.1016/S0140-6736\(11\)60105-0](https://doi.org/10.1016/S0140-6736(11)60105-0) PMID: 21397319
7. Kannel WB. Blood pressure as a cardiovascular risk factor: prevention and treatment. *JAMA*. 1996; 275(20):1571–6. PMID: 8622248
8. O'Donnell CJ, Ridker PM, Glynn RJ, Berger K, Ajani U, Manson JE, et al. Hypertension and borderline isolated systolic hypertension increase risks of cardiovascular disease and mortality in male physicians. *Circulation*. 1997; 95(5):1132–7. <https://doi.org/10.1161/01.cir.95.5.1132> PMID: 9054841
9. Stamler J, Stamler R, Neaton JD. Blood pressure, systolic and diastolic, and cardiovascular risks. US population data. *Arch Intern Med*. 1993; 153(5):598–615. <https://doi.org/10.1001/archinte.153.5.598> PMID: 8439223
10. van den Hoogen PC, Feskens EJ, Nagelkerke NJ, Menotti A, Nissinen A, Kromhout D. The relation between blood pressure and mortality due to coronary heart disease among men in different parts of the world. Seven Countries Study Research Group. *N Engl J Med*. 2000; 342(1):1–8. <https://doi.org/10.1056/NEJM200001063420101> PMID: 10620642
11. Vasan RS, Larson MG, Leip EP, Evans JC, O'Donnell CJ, Kannel WB, et al. Impact of high-normal blood pressure on the risk of cardiovascular disease. *N Engl J Med*. 2001; 345(18):1291–7. <https://doi.org/10.1056/NEJMoa003417> PMID: 11794147
12. Barret-Connor E, Criqui MH, Klauber MR, Holdbrook M. Diabetes and hypertension in a community of older adults. *Am J Epidemiol*. 1981; 113(3):276–84. <https://doi.org/10.1093/oxfordjournals.aje.a113097> PMID: 7468582
13. Butler WJ, Ostrander LD Jr., Carman WJ, Lamphiear DE. Diabetes mellitus in Tecumseh, Michigan. Prevalence, incidence, and associated conditions. *Am J Epidemiol*. 1982; 116(6):971–80. <https://doi.org/10.1093/oxfordjournals.aje.a113499> PMID: 7148821
14. Chiang BN, Perlman LV, Epstein FH. Overweight and hypertension. A review. *Circulation*. 1969; 39(3):403–21. <https://doi.org/10.1161/01.cir.39.3.403> PMID: 4885946
15. Jarrett RJ, Keen H, McCartney M, Fuller JH, Hamilton PJ, Reid DD, et al. Glucose tolerance and blood pressure in two population samples: their relation to diabetes mellitus and hypertension. *Int J Epidemiol*. 1978; 7(1):15–24. <https://doi.org/10.1093/ije/7.1.15> PMID: 659046
16. Medalie JH, Papier CM, Goldbourt U, Herman JB. Major factors in the development of diabetes mellitus in 10,000 men. *Arch Intern Med*. 1975; 135(6):811–7. PMID: 1130926
17. Sims EA. Mechanisms of hypertension in the overweight. *Hypertension*. 1982; 4(5 Pt 2):III43–9. [https://doi.org/10.1161/01.hyp.4.5\\_pt\\_2.iii43](https://doi.org/10.1161/01.hyp.4.5_pt_2.iii43) PMID: 6286482
18. Reaven GM, Lithell H, Landsberg L. Hypertension and associated metabolic abnormalities—the role of insulin resistance and the sympathoadrenal system. *New England Journal of Medicine*. 1996; 334(6):374–82.
19. Aronow WS, Fleg JL, Pepine CJ, Artinian NT, Bakris G, Brown AS, et al. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus Documents. *Circulation*. 2011; 123(21):2434–506. <https://doi.org/10.1161/CIR.0b013e31821daaf6> PMID: 21518977
20. Stamler R, Stamler J, Riedlinger WF, Algera G, Roberts RH. Weight and blood pressure: findings in hypertension screening of 1 million Americans. *Jama*. 1978; 240(15):1607–10. <https://doi.org/10.1001/jama.240.15.1607> PMID: 691146
21. Higgins M, Kannel W, Garrison R, Pinsky J, Stokes J 3rd. Hazards of obesity—the Framingham experience. *Acta medica Scandinavica Supplementum*. 1988; 723:23–36. <https://doi.org/10.1111/j.0954-6820.1987.tb05925.x> PMID: 3164971
22. Rabkin SW, Leiter L, Reeder BA, Chen Y, Liu L. Risk factor correlates of body mass index. *Canadian Medical Association Journal*. 1997; 157(1):S26. PMID: 9220951
23. Huang Z, Willett WC, Manson JE, Rosner B, Stampfer MJ, Speizer FE, et al. Body weight, weight change, and risk for hypertension in women. *Annals of internal medicine*. 1998; 128(2):81–8. <https://doi.org/10.7326/0003-4819-128-2-199801150-00001> PMID: 9441586
24. Oparil S, Zaman MA, Calhoun DA. Pathogenesis of hypertension *Ann Intern Med*. 2003; 139:761–76. <https://doi.org/10.7326/0003-4819-139-9-200311040-00011> PMID: 14597461
25. Hayashi T, Tsumura K, Suematsu C, Endo G, Fujii S, Okada K. High normal blood pressure, hypertension, and the risk of type 2 diabetes in Japanese men. The Osaka Health Survey. *Diabetes Care*. 1999; 22(10):1683–7. <https://doi.org/10.2337/diacare.22.10.1683> PMID: 10526735

26. Falkner B, Sherif K, Sumner AE, Kushner H. Blood pressure increase with impaired glucose tolerance in young adult american blacks. *Hypertension*. 1999; 34(5):1086–90. <https://doi.org/10.1161/01.hyp.34.5.1086> PMID: 10567186
27. Lastra G, Syed S, Kurukulasuriya LR, Manrique C, Sowers JR. Type 2 diabetes mellitus and hypertension: an update. *Endocrinol Metab Clin North Am*. 2014; 43(1):103–22. <https://doi.org/10.1016/j.ecl.2013.09.005> PMID: 24582094
28. Wu YT, Song L, Liu XX, Gao JS, Zheng XM, Ruan CY, et al. Time-cumulated blood pressure exposure and incident impairment of glucose tolerance and diabetes mellitus. *BMC Cardiovasc Disord*. 2017; 17(1):106. <https://doi.org/10.1186/s12872-017-0537-y> PMID: 28464794
29. Halperin RO, Sesso HD, Ma J, Buring JE, Stampfer MJ, Michael Gaziano J. Dyslipidemia and the risk of incident hypertension in men. *Hypertension*. 2006; 47(1):45–50. <https://doi.org/10.1161/01.HYP.0000196306.42418.0e> PMID: 16344375
30. Nickenig G, Harrison DG. The AT1-type angiotensin receptor in oxidative stress and atherogenesis: part I: oxidative stress and atherogenesis. *Circulation*. 2002; 105(3):393–6. <https://doi.org/10.1161/hc0302.102618> PMID: 11804998
31. Bautista L, Vera L, Arenas I, Gamarra G. Independent association between inflammatory markers (C-reactive protein, interleukin-6, and TNF- $\alpha$ ) and essential hypertension. *Journal of human hypertension*. 2005; 19(2):149–54. <https://doi.org/10.1038/sj.jhh.1001785> PMID: 15361891
32. Sesso HD, Buring JE, Rifai N, Blake GJ, Gaziano JM, Ridker PM. C-reactive protein and the risk of developing hypertension. *Jama*. 2003; 290(22):2945–51. <https://doi.org/10.1001/jama.290.22.2945> PMID: 14665655
33. Yu Z, Kim SC, Vanni K, Huang J, Desai R, Murphy SN, et al. Association between inflammation and systolic blood pressure in RA compared to patients without RA. *Arthritis research & therapy*. 2018; 20(1):1–8. <https://doi.org/10.1186/s13075-018-1597-9> PMID: 29855349
34. Christensen KD, Roberts JS, Royal CD, Fasaye G-A, Obisesan T, Cupples LA, et al. Incorporating ethnicity into genetic risk assessment for Alzheimer disease: the REVEAL study experience. *Genetics in medicine*. 2008; 10(3):207–14. <https://doi.org/10.1097/GIM.0b013e318164e4cf> PMID: 18344711
35. Golden SH, Yajnik C, Phatak S, Hanson RL, Knowler WC. Racial/ethnic differences in the burden of type 2 diabetes over the life course: a focus on the USA and India. *Diabetologia*. 2019; 62(10):1751–60. <https://doi.org/10.1007/s00125-019-4968-0> PMID: 31451876
36. Al-Raddadi R, Bahijri SM, Jambi HA, Ferns G, Tuomilehto J. The prevalence of obesity and overweight, associated demographic and lifestyle factors, and health status in the adult population of Jeddah, Saudi Arabia. *Ther Adv Chronic Dis*. 2019; 10:2040622319878997. <https://doi.org/10.1177/2040622319878997> PMID: 31632623
37. Arad Y, Goodman KJ, Roth M, Newstein D, Guerci AD. Coronary calcification, coronary disease risk factors, C-reactive protein, and atherosclerotic cardiovascular disease events: the St. Francis Heart Study. *J Am Coll Cardiol*. 2005; 46(1):158–65. <https://doi.org/10.1016/j.jacc.2005.02.088> PMID: 15992651
38. Ridker PM. Clinical application of C-reactive protein for cardiovascular disease detection and prevention. *Circulation*. 2003; 107(3):363–9. <https://doi.org/10.1161/01.cir.0000053730.47739.3c> PMID: 12551853
39. Lee DH, Jacobs DR Jr., Gross M, Kiefe CI, Roseman J, Lewis CE, et al. Gamma-glutamyltransferase is a predictor of incident diabetes and hypertension: the Coronary Artery Risk Development in Young Adults (CARDIA) Study. *Clin Chem*. 2003; 49(8):1358–66. <https://doi.org/10.1373/49.8.1358> PMID: 12881453
40. Mason JE, Starke RD, Van Kirk JE. Gamma-glutamyl transferase: a novel cardiovascular risk biomarker. *Prev Cardiol*. 2010; 13(1):36–41. <https://doi.org/10.1111/j.1751-7141.2009.00054.x> PMID: 20021625
41. Lee DH, Silventoinen K, Hu G, Jacobs DR Jr., Jousilahti P, Sundvall J, et al. Serum gamma-glutamyltransferase predicts non-fatal myocardial infarction and fatal coronary heart disease among 28,838 middle-aged men and women. *Eur Heart J*. 2006; 27(18):2170–6. <https://doi.org/10.1093/eurheartj/ehl086> PMID: 16772340
42. Bahijri S, Al-Raddadi R, Ajabnoor G, Jambi H, Al Ahmadi B, Borai A, et al. Dysglycemia risk score in Saudi Arabia: A tool to identify people at high future risk of developing type 2 diabetes. *J Diabetes Investig*. 2020. <https://doi.org/10.1111/jdi.13213> PMID: 31957345
43. Phillips L, Ziemer D, Kolm P, Weintraub W, Vaccarino V, Rhee M, et al. Glucose challenge test screening for prediabetes and undiagnosed diabetes. *Diabetologia*. 2009; 52(9):1798–807. <https://doi.org/10.1007/s00125-009-1407-7> PMID: 19557386

44. Pareek M, Bhatt DL, Nielsen ML, Jagannathan R, Eriksson K-F, Nilsson PM, et al. Enhanced predictive capability of a 1-hour oral glucose tolerance test: a prospective population-based cohort study. *Diabetes care*. 2018; 41(1):171–7. <https://doi.org/10.2337/dc17-1351> PMID: 29138275
45. Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem*. 1972; 18(6):499–502. PMID: 4337382
46. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr., et al. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension*. 2003; 42(6):1206–52. <https://doi.org/10.1161/01.HYP.0000107251.49515.c2> PMID: 14656957
47. Borai A, Ichihara K, Al Masaud A, Tamimi W, Bahijri S, Armbuster D, et al. Establishment of reference intervals of clinical chemistry analytes for the adult population in Saudi Arabia: a study conducted as a part of the IFCC global study on reference values. *Clin Chem Lab Med*. 2016; 54(5):843–55. <https://doi.org/10.1515/cclm-2015-0490> PMID: 26527074
48. Qiu M, Shen W, Song X, Ju L, Tong W, Wang H, et al. Effects of prediabetes mellitus alone or plus hypertension on subsequent occurrence of cardiovascular disease and diabetes mellitus: longitudinal study. *Hypertension*. 2015; 65(3):525–30. <https://doi.org/10.1161/HYPERTENSIONAHA.114.04632> PMID: 25624343
49. Ormazabal V, Nair S, Elfeky O, Aguayo C, Salomon C, Zuñiga FA. Association between insulin resistance and the development of cardiovascular disease. *Cardiovascular diabetology*. 2018; 17(1):122. <https://doi.org/10.1186/s12933-018-0762-4> PMID: 30170598
50. Forouhi NG, Sattar N. CVD risk factors and ethnicity—a homogeneous relationship? *Atheroscler Suppl*. 2006; 7(1):11–9. <https://doi.org/10.1016/j.atherosclerosissup.2006.01.003> PMID: 16500156
51. Aldiab A, Shubair MM, Al-Zahrani JM, Aldossari KK, Al-Ghamdi S, Househ M, et al. Prevalence of hypertension and prehypertension and its associated cardioembolic risk factors; a population based cross-sectional study in Alkharj, Saudi Arabia. *BMC Public Health*. 2018; 18(1):1327. <https://doi.org/10.1186/s12889-018-6216-9> PMID: 30497425
52. El Bcheraoui C, Memish ZA, Tuffaha M, Daoud F, Robinson M, Jaber S, et al. Hypertension and its associated risk factors in the kingdom of Saudi Arabia, 2013: a national survey. *Int J Hypertens*. 2014; 2014:564679. <https://doi.org/10.1155/2014/564679> PMID: 25170423
53. AlNozha MM, Abdullah M, Arafah M, Khalil MZ, Khan NB, Almazrou Y, et al. Hypertension in Saudi Arabia. *Saudi Med J*. 2007; 28(1):77–84. PMID: 17206295
54. Bahijri SM, Jambi HA, Al Raddadi RM, Ferns G, Tuomilehto J. The Prevalence of Diabetes and Prediabetes in the Adult Population of Jeddah, Saudi Arabia—A Community-Based Survey. *PLoS One*. 2016; 11(4):e0152559. <https://doi.org/10.1371/journal.pone.0152559> PMID: 27035920
55. Alsheikh-Ali AA, Omar MI, Raal FJ, Rashed W, Hamoui O, Kane A, et al. Cardiovascular risk factor burden in Africa and the Middle East: the Africa Middle East Cardiovascular Epidemiological (ACE) study. *PLoS One*. 2014; 9(8):e102830. <https://doi.org/10.1371/journal.pone.0102830> PMID: 25090638
56. Wolf HK, Tuomilehto J, Kuulasmaa K, Domarkiene S, Cepaitis Z, Molarius A, et al. Blood pressure levels in the 41 populations of the WHO MONICA Project. *J Hum Hypertens*. 1997; 11(11):733–42. <https://doi.org/10.1038/sj.jhh.1000531> PMID: 9416984
57. Adeloje D, Basquill C. Estimating the prevalence and awareness rates of hypertension in Africa: a systematic analysis. *PLoS One*. 2014; 9(8):e104300. <https://doi.org/10.1371/journal.pone.0104300> PMID: 25090232
58. Mozaffarian D, Benjamin EJ, Go AS, Arnett DK, Blaha MJ, Cushman M, et al. Heart disease and stroke statistics—2015 update: a report from the American Heart Association. *Circulation*. 2015; 131(4):e29–322. <https://doi.org/10.1161/CIR.0000000000000152> PMID: 25520374
59. Vasan RS, Beiser A, Seshadri S, Larson MG, Kannel WB, D'Agostino RB, et al. Residual lifetime risk for developing hypertension in middle-aged women and men: The Framingham Heart Study. *JAMA*. 2002; 287(8):1003–10. <https://doi.org/10.1001/jama.287.8.1003> PMID: 11866648
60. Garrison RJ, Kannel WB, Stokes J, 3rd, Castelli WP. Incidence and precursors of hypertension in young adults: the Framingham Offspring Study. *Prev Med*. 1987; 16(2):235–51. [https://doi.org/10.1016/0091-7435\(87\)90087-9](https://doi.org/10.1016/0091-7435(87)90087-9) PMID: 3588564
61. Hall JE. The kidney, hypertension, and obesity. *Hypertension*. 2003; 41(3 Pt 2):625–33.
62. Jones DW, Kim JS, Andrew ME, Kim SJ, Hong YP. Body mass index and blood pressure in Korean men and women: the Korean National Blood Pressure Survey. *J Hypertens*. 1994; 12(12):1433–7. <https://doi.org/10.1097/00004872-199412000-00018> PMID: 7706705
63. Chae CU, Lee RT, Rifai N, Ridker PM. Blood pressure and inflammation in apparently healthy men. *Hypertension*. 2001; 38(3):399–403. <https://doi.org/10.1161/01.hyp.38.3.399> PMID: 11566912

64. Engstrom G, Janzon L, Berglund G, Lind P, Stavenow L, Hedblad B, et al. Blood pressure increase and incidence of hypertension in relation to inflammation-sensitive plasma proteins. *Arterioscler Thromb Vasc Biol.* 2002; 22(12):2054–8. <https://doi.org/10.1161/01.atv.0000041842.43905.f3> PMID: 12482834
65. Davey Smith G, Lawlor DA, Harbord R, Timpson N, Rumley A, Lowe GD, et al. Association of C-reactive protein with blood pressure and hypertension: life course confounding and mendelian randomization tests of causality. *Arterioscler Thromb Vasc Biol.* 2005; 25(5):1051–6. <https://doi.org/10.1161/01.ATV.0000160351.95181.d0> PMID: 15731495
66. Cheung BM, Ong KL, Tso AW, Cherny SS, Sham PC, Lam TH, et al. Gamma-glutamyl transferase level predicts the development of hypertension in Hong Kong Chinese. *Clin Chim Acta.* 2011; 412(15–16):1326–31. <https://doi.org/10.1016/j.cca.2011.03.030> PMID: 21466796
67. Jung CH, Yu JH, Bae SJ, Koh EH, Kim MS, Park JY, et al. Serum gamma-glutamyltransferase is associated with arterial stiffness in healthy individuals. *Clin Endocrinol (Oxf).* 2011; 75(3):328–34. <https://doi.org/10.1111/j.1365-2265.2011.04060.x> PMID: 21521327
68. Kim NH, Huh JK, Kim BJ, Kim MW, Kim BS, Kang JH. Serum gamma-glutamyl transferase level is an independent predictor of incident hypertension in Korean adults. *Clin Exp Hypertens.* 2012; 34(6):402–9. <https://doi.org/10.3109/10641963.2012.665539> PMID: 22471622
69. Celik T, Yuksel UC, Kilic S, Yaman H, Iyisoy A, Karaeren H. The relationship of gamma-glutamyltransferase to aortic elastic properties in young patients with prehypertension. *Clin Exp Hypertens.* 2010; 32(6):377–84. <https://doi.org/10.3109/10641961003628528> PMID: 21029002
70. Liu CF, Gu YT, Wang HY, Fang NY. Gamma-glutamyltransferase level and risk of hypertension: a systematic review and meta-analysis. *PLoS One.* 2012; 7(11):e48878. <https://doi.org/10.1371/journal.pone.0048878> PMID: 23145005
71. Saudi Hypertension Guidelines 2018. Saudi Commission for Health Specialities. 2018.
72. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Bohm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: the Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). *J Hypertens.* 2013; 31(7):1281–357. <https://doi.org/10.1097/01.hjh.0000431740.32696.cc> PMID: 23817082
73. WHO. Cardiovascular diseases (CVDs) 2017 [Available from: [https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-\(cvds\)](https://www.who.int/news-room/fact-sheets/detail/cardiovascular-diseases-(cvds))].
74. Alhabib KF, Batais MA, Almigbal TH, Alshamiri MQ, Altaradi H, Rangarajan S, et al. Demographic, behavioral, and cardiovascular disease risk factors in the Saudi population: results from the Prospective Urban Rural Epidemiology study (PURE-Saudi). *BMC public health.* 2020; 20(1):1–14. <https://doi.org/10.1186/s12889-019-7969-5> PMID: 31898494