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Research Article

Obesity Accompanied by an Odd Lipid Profile is a Major Risk Factor for Hypertension Among Women

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Abstract

Background and Objective: Hypertension (HTN) is a common health issue in most countries, including Saudi Arabia. It is a strong risk factor for other Cardiovascular Diseases (CVDs) as well as renal and neurological disorders. The present study aimed to evaluate the risk factors modulating hypertension among Saudi women. **Materials and Methods:** A cross-sectional study was conducted on 160 Saudi women, who were randomly selected from different districts in Riyadh, Saudi Arabia. The study design included an interview questionnaire survey, anthropometric measurements, body composition analysis and blood biochemical tests. The selected participants were not previously diagnosed with any chronic diseases. They were categorized into four groups based on Body Mass Index (BMI). **Results:** The data showed that weight significantly affected the lipid profile. Total cholesterol (TC), triglyceride (TG) and Low-Density Lipoprotein (LDL-C) levels gradually increased with weight and showed maximum levels in group 4 (i.e., obesity II+III). Systolic (SBP) and diastolic (DBP) blood pressures also significantly ($p \leq 0.05$) increased with weight. The SBP was significantly ($p \leq 0.01$) and positively correlated with DBP, age, BMI, waist circumference (WC), TG, weight and blood glucose (G) level. Similarly, DBP was also significantly ($p \leq 0.01$) correlated with SBP, weight, BMI, WC and LDL-C levels. **Conclusion:** The findings of this study showed that Saudi women with a higher age, BMI, TG and G levels are at a greater risk for high blood pressure. In addition, Saudi women with a high BMI and LDL-C level are at high risk for increased DBP.

Key words: Hypertension, body mass index, obesity, anthropometric measurements, lipid profile, mineral contents

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Data Availability: All relevant data are within the paper and its supporting information files.

INTRODUCTION

Hypertension (HTN) and other related complications are recognized as emerging clinical and public health problems¹. It is considered a strong risk factor for other Cardiovascular Diseases (CVDs), renal disorders and neurological disorders². The prevalence of risk factors for CVDs is increasing in Saudi Arabia. This increase has turned into higher mortality and could be attributed to several reasons, such as lifestyle changes toward urbanization and the adoption of dietary habits that resulted in HTN and the increasing prevalence of obesity in the Kingdom of Saudi Arabia (KSA)³. In the cross-sectional survey conducted by Althumiri *et al.*⁴ among 3120 Saudi women, they showed that a higher BMI (>30) was considered a risk factor associated with diabetes mellitus (DM), HTN, hypercholesterolemia, rheumatoid arthritis and other diseases. The data obtained from the Saudi General Authority for Statistics (2017) revealed that Saudi women are more susceptible to HTN, which is more prevalent among the elderly, with remarkable variation between different regions in Saudi Arabia⁵.

The Seventh Report of the Joint National Committee (JNC) on Prevention, Detection, Evaluation and Treatment of High Blood Pressure defines HTN as a blood pressure (BP) of $\geq 140/90$ mmHg⁶. Furthermore, in the eighth report of the JNC, individuals with DM and a high systolic (SBP) of more than 140 mmHg or diastolic (DBP) of more than 90 mmHg should be considered hypertensive and require health-promoting lifestyle modifications to prevent CVD, in addition to regular HTN treatments, such as thiazide diuretics, CCB and an ACEi/ARB⁷.

According to the Global Burden of Disease 2013 research, HTN was the greatest cause of death in KSA⁸. According to a Report from the American Heart Association, HTN accounted for about 65.3% of all CVD and circulatory disease mortality between 2009 and 2019⁹. From 1990 to 2010, the prevalence of HTN in KSA remained relatively high⁸. A recent statistical review of the studies between 2010 and 2021 revealed that 47.3% of dyslipidemia patients didn't recognize they were hypertensive and only 22.5% of them adhered to antihypertensive treatment¹⁰. Lipids have gained great interest from the medical community as they play an important role in human physiology, but excess lipids are a risk factor for many diseases such as coronary artery disease, as well as cerebrovascular and peripheral vascular diseases^{11,12}. Hyperlipidemia could be primarily caused by genetically determined disorders or could occur secondarily due to acquired causes. In KSA, the prevalence of coronary artery disease caused by hyperlipidemia is increasing¹³.

The current study was designed and conducted to correlate weight (overweight or obese) and the effect of lipid profile as a risk factor for HTN in Saudi female subjects. The outcome of this study will enhance the perception of overweight and hyperlipidemia as current and actively progressing medical risk factors for HTN.

MATERIALS AND METHODS

Subjects: A cross-sectional study was conducted on 160 Saudi women, who didn't suffer from any previously diagnosed chronic diseases. They were randomly selected from different districts in Riyadh City, Saudi Arabia. The inclusion criteria included all Saudi women in Riyadh City aged 15-68 years. Males, non-Saudis, those not living in Riyadh and those underweight ($<18.5 \text{ kg m}^{-2}$), were excluded from the study.

Study area: The study was conducted in Riyadh City, Saudi Arabia. Data collection and analysis take place in the period between January 2023 and May 2023.

Study design: The study tools included an interview questionnaire survey, anthropometric measurements, recoding of the blood pressure, body composition analysis and blood biochemical tests.

Anthropometric measurements: The variables selected for anthropometric evaluation were weight (kg) and height (cm) for calculating the BMI and waist circumference (WC). The BMI calculation is a simple and widely used method for estimating body fat mass¹⁴. The BMI is calculated by dividing weight by the square of height:

$$\text{BMI} = \frac{\text{Body weight (kg)}}{\text{Body height (m}^2\text{)}}$$

The most commonly used definitions for BMI are as follows: Underweight ($\text{BMI} < 18.5 \text{ kg m}^{-2}$), normal weight ($\text{BMI} = 18.5\text{-}24.9 \text{ kg m}^{-2}$), overweight ($\text{BMI} = 25.0\text{-}29.9 \text{ kg m}^{-2}$), class I obesity ($\text{BMI} = 30.0\text{-}34.9 \text{ kg m}^{-2}$), class II obesity ($\text{BMI} = 35.0\text{-}39.9 \text{ kg m}^{-2}$) and class III obesity ($\text{BMI} \geq 40.0 \text{ kg m}^{-2}$)¹⁵. In the current study, the participants were divided equally into four groups ($n = 40$) based on Body Mass Index (BMI):

- **Group 1:** Control ($\text{BMI} = 18.5\text{-}24.9 \text{ kg m}^{-2}$)
- **Group 2:** Overweight ($\text{BMI} = 25.0\text{-}29.9 \text{ kg m}^{-2}$)
- **Group 3:** Class I obesity ($\text{BMI} \geq 35 \text{ kg m}^{-2}$)
- **Group 4:** Class II+III obesity ($\text{BMI} \geq 35 \text{ kg m}^{-2}$)

Blood pressure assessment: Several sources define HTN levels as DBP more than 85 mmHg and SBP greater than 140 mmHg^{6,16}. Blood pressure values were obtained and recorded at the time of administration in the current investigation.

Biochemical assessment: Blood samples (4 mL) were drawn from all subjects by a qualified nurse after overnight fasting (>12 hrs) and transferred immediately into two non-heparinized tubes. Serum samples were stored at -80°C until required for analysis. Kits from the United Diagnostic Industry (UDI, Dammam, KSA) were used to assess fasting serum levels of blood glucose (G), lipid parameters (triglyceride (TG), High Density Lipoprotein Cholesterol (HDL-C), total cholesterol (TC)) and minerals (calcium (Ca) and phosphorus (P)) using a UDICHEM-300 chemistry analyzer. Potassium was measured using a UDI electrolyte analyzer. The Low-Density Lipoprotein Cholesterol (LDL-C) levels were calculated using the Friedewald equation¹⁷:

$$\text{LDL (mg dL}^{-1}\text{)} = \text{Total cholesterol} - \text{HDL} - \frac{\text{Triglycerides}}{5}$$

Statistical analysis: Quantitative data are statistically presented as minimum, maximum, mean and standard deviation. The differences among the dietary treatment groups were analyzed using a One-way Analysis of Variance (ANOVA) with multiple comparisons (Dunnett's test) to compare each group with the control group (parametric data).

Qualitative data is statistically presented as numbers and percentages. Correlation analysis between various variables was performed using the Pearson correlation coefficient (R) for parametric variables and the Spearman rank correlation coefficient (R) for nonparametric variables, with graphic representations using linear regression. A probability (P) value of less than 0.05 was considered significant. All statistical analyses were performed using the statistical software Statistical Package for the Social Sciences (SPSS) version 16.0.

RESULTS

Subjects were categorized into four groups according to BMI. The weight of subjects in group 1, designated as the normal (control) group, ranged from 50-71.3 kg, with an average BMI of $22.83 \pm 1.53 \text{ kg m}^{-2}$. The weight of subjects in group 2, designated as the overweight group, ranged from 52.2 to 87.3 kg, with an average BMI of $28.27 \pm 1.76 \text{ kg m}^{-2}$. The weight of subjects in group 3, designated as obesity group I, ranged from 67.1-95.5 kg, with an average BMI of $32.6 \pm 1.15 \text{ kg m}^{-2}$. Finally, the weight of subjects in group 4, designated as the obesity class II+III, ranged from 82.2-121.6 kg, with an average BMI of $39 \pm 3.6 \text{ kg m}^{-2}$ (Table 1). The age ranged from 15-68 years, whereas the height ranged from 145-176 cm. A highly significant ($p \leq 0.05$) difference was observed when the age, weight, BMI and waist circumference of group 1 were compared with those of the obese groups and even when the comparison was made among all groups.

Table 1: Anthropometric characteristics and risk factors for HTN in Saudi women

Parameters	G	Category	Minimum	Maximum	Mean \pm SD	Change (%)	p-value ^a	p-value ^b
Age (years)	1	Control	15	50	29.78 \pm 9.36	0		0.019*
	2	Overweight	15	68	35.5 \pm 11.15	+5.73	0.041*	
	3	Obesity I	16	54	36.83 \pm 9.51	+7.05	0.08**	
	4	Obesity II+III	15	62	33.9 \pm 11.6	+4.12	0.192	
Height (cm)	1	Control	150	176	160.78 \pm 5.88	0		0.463
	2	Overweight	145	172	159.3 \pm 5.56	-1.48	0.471	
	3	Obesity I	148	169	158.96 \pm 5.05	-1.94	0.306	
	4	Obesity II+III	149	166.5	159.81 \pm 4.99	-0.96	0.763	
Weight (kg)	1	Control	50	71.3	59.52 \pm 5.07	0		<0.001***
	2	Overweight	52.2	87.3	71.55 \pm 6.81	+12.03	<0.001***	
	3	Obesity I	67.1	95.5	82.25 \pm 6.37	+22.63	<0.001***	
	4	Obesity II+III	82.2	121.6	99.56 \pm 9.88	+40.04	<0.001***	
BMI (kg m ⁻²)	1	Control	20	25	22.83 \pm 1.53	0		<0.001***
	2	Overweight	25.2	30.5	28.27 \pm 1.76	+5.44	<0.001***	
	3	Obesity I	30.6	34.7	32.60 \pm 1.15	+9.79	<0.001***	
	4	Obesity II+III	35.04	49.4	39 \pm 3.6	+16.17	<0.001***	
WC (cm)	1	Control	63	84	73.51 \pm 8.36	0		<0.001***
	2	Overweight	74	93	81.56 \pm 11.18	+8.05	<0.001***	
	3	Obesity I	75	99	89.03 \pm 6	+15.56	<0.001***	
	4	Obesity II+III	85	121	100.35 \pm 8.6	+26.84	<0.001***	
SBP (mmHg)	1	Control	96	132	116.1 \pm 9.07	0		0.004**
	2	Overweight	105	160	122.58 \pm 12.67	6.48	0.042*	

Table 1: Continue

Parameters	G	Category	Minimum	Maximum	Mean±SD	Change (%)	p-value ^a	p-value ^b
DBP (mmHg)	3	Obesity I	94	149	123.02±13.62	+6.49	0.027*	<0.001***
	4	Obesity II+III	100	159	125.58±11.69	+9.48	01**	
	1	Control	51	85	72.18±7.86	0		
	2	Overweight	58	86	73.7±7.05	+1.53	0.767	
TC (mg dL ⁻¹)	3	Obesity I	64	100	79.28±9.25	+6.49	01**	0.02*
	4	Obesity II+III	56	98	76.95±9.96	+9.48	0.038*	
	1	Control	131	265	181.32±31.5	0		
	2	Overweight	127	258	184.32±30.65	+3	0.956	
TG (mg dL ⁻¹)	3	Obesity I	137	287	207.28±33.88	+25.91	0.002**	<0.001***
	4	Obesity II+III	107	266	187.9±34.88	+6.58	0.697	
	1	Control	40	350	81.67±53.87	0		
	2	Overweight	47	212	93.23±39.96	+11.57	0.033*	
HDL (mg dL ⁻¹)	3	Obesity I	40	406	121.66±69.25	+39.08	0.001**	0.28
	4	Obesity II+III	35	339	104.5±58.16	+22.83	0.011*	
	1	Control	45.8	88.4	61.15±10.92	0		
	2	Overweight	42.5	83	59.21±9.21	-2.16	0.802	
LDL (mg dL ⁻¹)	3	Obesity I	38.5	88	57.55±12.43	-3.87	0.375	0.02*
	4	Obesity II+III	24.6	83.4	56.31±13.38	-5.06	0.161	
	1	Control	54.5	168.1	103.32±28.69	0		
	2	Overweight	58.8	175.5	105.69±31.56	+2.7	0.972	
K (mmol L ⁻¹)	3	Obesity I	66.9	188.1	123.28±29.74	+20.42	0.012*	0.078
	4	Obesity II+III	52.4	199.5	110.44±31.24	+7.45	0.595	
	1	Control	3.6	5.1	4.2±0.36	0		
	2	Overweight	3.69	5.1	4.32±0.32	+0.12	0.263	
Ca (mg dL ⁻¹)	3	Obesity I	3.51	5.1	4.35±0.34	+0.14	0.132	0.497
	4	Obesity II+III	3.7	5.3	4.39±0.35	+0.19	0.036*	
	1	Control	8.2	9.9	8.98±0.39	0		
	2	Overweight	8.1	9.9	8.90±0.4	-0.08	0.804	
P (mg dL ⁻¹)	3	Obesity I	8.1	10.5	9.06±0.62	+0.11	0.759	0.357
	4	Obesity II+III	8.3	10.2	8.97±0.44	-0.01	0.999	
	1	Control	2.6	5	3.76±0.59	0		
	2	Overweight	2.6	4.9	3.61±0.51	-0.16	0.353	
G (mg dL ⁻¹)	3	Obesity I	2.9	4.5	3.61±0.48	-0.14	0.366	0.03*
	4	Obesity II+III	3	4.4	3.59±0.34	-0.17	0.27	
	1	Control	60	113	85.36±10.29	0		
	2	Overweight	68	115	88.50±10.07	+3.28	0.478	
	3	Obesity I	72	112	91.08±11.64	+6.26	0.074	
	4	Obesity II+III	65	133	92.74±13.69	+7.7	0.014*	

^ap-value between each group and the control group, ^bp-value between all groups, *p<0.05, **p-value<0.01, ***p-value<0.001, BMI: Body Mass Index, WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TC: Total cholesterol, TG: Triglycerides, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, K: Potassium, Ca: Calcium, P: Phosphorous, G: Glucose and SD: Standard deviation

The data revealed that weight significantly affected the lipid profile. Obese women were more likely to have hyperlipidemia than overweight or normal women (Table 1). The TC, TG and LDL levels gradually increased with weight and the highest levels were observed in group 4. The levels of TC, TG and LDL in group 4 were 187.9±34.88, 104.5±58.16 and 110.44±31.24 mg dL⁻¹, respectively, whereas the respective values in the control group were 181.32±31.5, 81.67±53.87 and 103.32±28.69 mg dL⁻¹.

The serum electrolyte and blood G levels showed values within the reference range in all groups. The SBP and DBP also significantly ($p \leq 0.05$) increased with weight.

The SBP was significantly and positively correlated with DBP, age, BMI, waist circumference, TG level, weight and G level at $p = 0.01$ (Table 2, Fig. 1 and 2). These results verified that elderly Saudi women with high BMI, TG and G levels were at a high risk of increased SBP. In contrast, a negative correlation was found between SBP and height, HDL-C, K and P levels.

Similarly, DBP was significantly correlated with SBP, weight, BMI, waist circumference and LDL-C level at $p < 0.01$ (Table 2 and Fig. 2). This shows that Saudi women with high BMI and LDL-C levels are at a high risk of increased DBP. In contrast, there was a negative correlation between DBP and height, HDL level and phosphorus level.

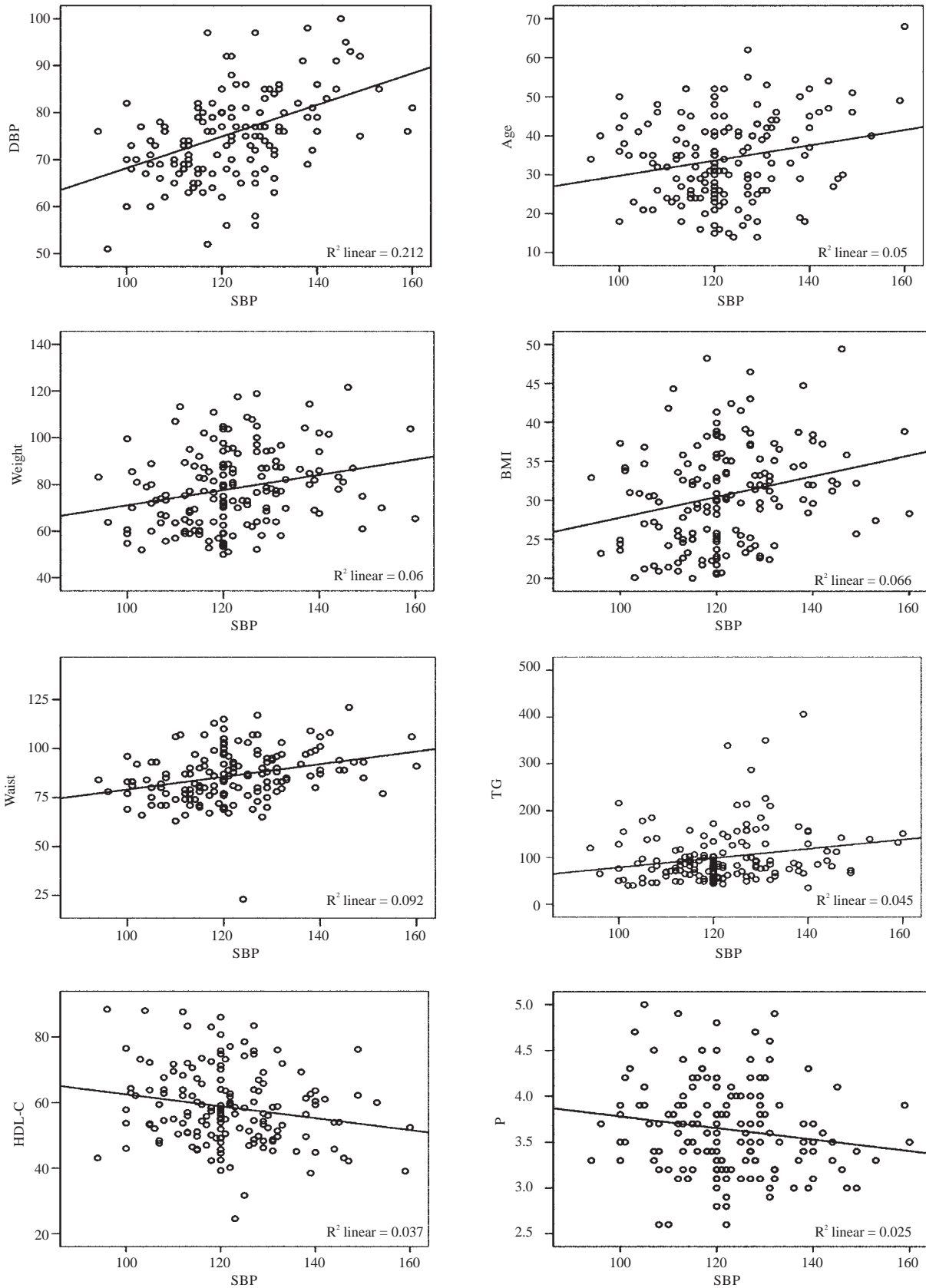


Fig. 1: Correlation between SBP and other parameters with best-fit line curves

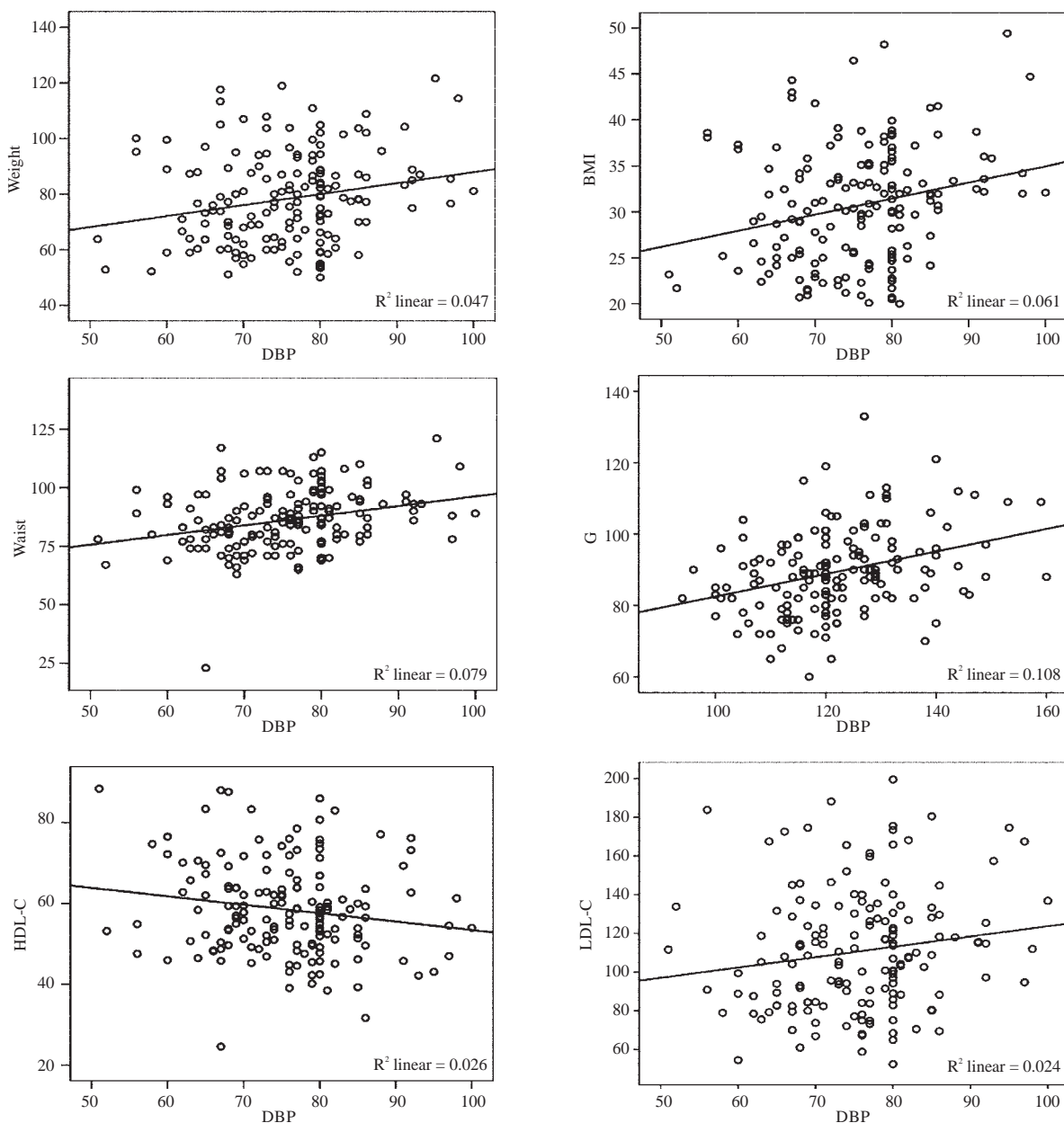


Fig. 2: Correlation between DBP and other parameters with best-fit line curves

DISCUSSION

The HTN is a widespread health issue in most nations, including Saudi Arabia⁸. It is a major risk factor for morbidity and death^{18,19}. Untreated high blood pressure causes a variety of major health problems, including stroke, aneurysms, hypertensive heart disease, coronary artery disease and renal disease. The HTN CVD risk factors are directly connected to SBP and DBP²⁰.

The current study revealed significant effect of woman age, weight, BMI and waist circumference on the lipid profile.

Obese women often were at the risk of hyperlipidemia with abnormal measurements of TC, TG and LDL levels. Researchers have investigated isolated and combined elevations in SBP and DBP. The resulting HTN subtypes, such as systolic-diastolic HTN (SDH), seem to reflect unique biological processes, perhaps with distinct clinical implications^{21,22}. Guidelines from several authorities, including those in KSA, recommend controlling HTN to BP levels <140/85 mmHg^{6,16}. Subjects with isolated diastolic HTN were shown to be particularly prone (23.1 times) to acquire SDH at follow-up in the Framingham Heart Study²³. Furthermore, patients with normal

Table 2: Correlations of different parameters with blood pressure

SBP			DBP		
Parameter	R	p-value	Parameter	R	p-value
DBP	+0.46	0.001**	SBP	+0.46	0.001**
Age	+0.224	0.004**	Age	+0.04	0.612
Height	-0.056	0.482	Height	-0.102	0.199
Weight	+0.244	0.002**	Weight	+0.216	0.006**
BMI	+0.257	0.001**	BMI	+0.248	0.002**
WC	+0.303	0.001**	WC	+0.282	0.001**
TC	+0.084	0.288	TC	+0.053	0.507
TG ^a	+0.238	0.002**	TG ^a	+0.031	0.696
HDL-C	-0.192	0.016*	HDL-C	-0.16	0.044*
LDL-C	+0.115	0.149	LDL-C	+0.154	0.050*
K	-0.007	0.931	Ka	+0.036	0.653
Ca	+0.137	0.084	Ca	+0.007	0.934
P	-0.157	0.047*	P	-0.122	0.125
G	+0.329	0.001**	G	+0.141	0.077

*Correlation is significant at the 0.05 level, **Correlation is significant at the 0.01 level, ^aSpearman correlation, R: Pearson correlation, BMI: Body Mass Index, WC: Waist circumference, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, TC: Total cholesterol, TG: Triglycerides, HDL: High Density Lipoprotein, LDL: Low Density Lipoprotein, K: Potassium, Ca: Calcium, P: Phosphorous, G: Glucose and SD: Standard deviation

or high-normal BP at baseline were 3.32 and 7.96 times more likely to develop SDH at follow-up, respectively, than those with optimum BP²³. Furthermore, in Saudi Arabia, the prevalence of SDH was 12.5% in the 1995-2000 survey, 7-18% in other communities and 25-65% among hypertensive patients. In contrast, almost 9.0% (n = 413) of 4,588 subjects developed SDH in a study conducted in 2017. It was also observed that SDH was significantly associated with some sociodemographic characteristics, including age, sex, employment, education, geographic location, smoking, physical activity, diabetes mellitus, obesity and hypercholesterolemia²⁴. The current study was in agreement with the previous studies in that age group, where DM, obesity and hypercholesterolemia were found to be risk factors and significant predictors of SDH.

A global analysis showed that the frequency of uncontrolled HTN (>140/90 mmHg) increased from 600 million in 1980 to nearly 1 billion in 2008 and this number is expected to increase to 1.56 billion by 2025, which means 29% of the worldwide adult population will have HTN²⁵. Preventing HTN has a significant role in controlling the disease, which can be achieved by either controlling the risk factors or increasing awareness in the community, in addition to changing attitudes and practices toward the condition. A study in Saudi Arabia showed that the awareness level concerning HTN was high in the majority of the subjects (72.6%), whereas the knowledge level was average at 54.7%. On the other hand, the self-care practice level was below average in 74.4% of the subjects. Awareness, knowledge and self-management practices were found to be significantly poor among those with old age (>50 years), male subjects and

less educated patients²⁶. In that study, some of the subjects experienced asymptomatic HTN because they had some risk factors that significantly affected both SBP and DBP, such as high age, BMI, TG and G level²⁶. Another study from Jazan, Saudi Arabia, demonstrated that poor knowledge about HTN and its risks and treatment was common among almost 60% of patients with higher blood pressure²⁷. Increasing awareness and knowledge of risk factors in Saudi Arabia has been positively affected by reducing the incidence and mortality rates of the disease²⁸.

In a similar study from Palestine, the authors recruited 1337 hypertensive patients and showed that the anthropometric measurements were strongly correlated to SBP and DBP in both males and females²⁹. Another study on the risk factors of isolated systolic HTN (ISH) in Saudi patients showed that out of 4,551 patients, 358 (7.9%) had ISH, which was significantly related to sociodemographic, geographic, anthropometric and morbidity characteristics. Almost 47% of patients with ISH were using some form of treatment: 84.5% were taking prescribed drugs, 69.1% had diet modifications and 25% engaged in exercise-related activities. The significant predictors of ISH were education, retirement, obesity, diabetes mellitus and dyslipidemia²⁹. Given the risk of CVD associated with ISH, current study findings were consistent with the previous study's findings that SBP is substantially connected with age, weight, BMI, TG and G levels.

According to the findings of an analysis done in Dammam, Saudi Arabia, to investigate the incidence of pre-HTN and associated risk factors among young adult women, 13.5% of the 370 female students were prehypertensive and 16.3% of prehypertensive students had three or more risk

factors. Overweight/obesity was the most accurate indicator of pre-HTN in a logistic regression study³⁰. Current study findings showed that overweight/obesity was the primary risk factor for HTN in Saudi women, with a strong connection between SBP and DBP with weight, BMI, WC, TC and TG levels.

Height, hip circumference (HC), WC, BMI and total body fat (TBF) were all measured. Body weight, fat mass and fat-free mass were all measured using a body composition analyzer. The Dinamap vital signs monitor was used to measure SBP and DBP. Males and females both had substantial strong positive relationships with mean SBP and mean DBP. The SBP had the strongest correlation with waist circumference in all individuals ($r = 0.444$ in females, $r = 0.422$ in males), whereas DBP had the most correlation with WC in men ($r = 0.386$), but with TBF in females ($r = 0.256$). Blood pressure levels may be managed by reducing fat percentage, WC, HC and BMI, all of which are impacted by excess weight and a lack of activity.

Because electrolyte levels have a direct influence on blood pressure, it was critical to measure certain electrolytes (K, Ca and P) in this investigation. Electrolyte imbalances may be much more than an annoyance; if ignored, they might have serious consequences. It is critical to recognize electrolyte imbalances to treat them appropriately and immediately. However, many electrolyte imbalances self-correct without causing harm, while others might be addressed by just consuming more fluids^{31,32}.

CONCLUSION

The study found that the primary risk factors for HTN among women were old age, a higher BMI, raised serum TG and blood G levels. Accordingly, maintaining a normal body weight and commitment to a healthy diet and routine physical activity might decrease the risk of HTN and other cardiovascular diseases at young ages. The risk increases with age, where controlling HTN requires specific medication for older ages. So, the study findings might suggest early awareness campaigns to warn Saudi females about the risk of obesity and unhealthy diet that might decrease the probability of higher blood pressure and further critical cardiac disorders. The study was limited to the community of Saudi females in Riyadh City, so further studies might be required to investigate these findings in other areas of the Kingdom of Saudi Arabia.

SIGNIFICANCE STATEMENT

The current multicenter study highlighted the effect of abnormal anthropometric measurements on the rise of female hypertension. The main objective of the study is to investigate the direct correlation between body weight, lipid profile and minerals levels with hypertension among Saudi females. As shown in the results, the disturbance in the lipid profile contributed to high diastolic pressure. That might increase our awareness of the most related risk factors associated with obesity and further complicated medical issues, such as hypertension and cardiovascular diseases.

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