

## Association between Ischemic Heart Disease and Dyslipidemia Among Adult Hypertensive Patients- A Case-Control Study in Kingdom of Saudi Arabia

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### ABSTRACT

**Background:** Hypertension is a major health problem, affecting a large population across the world. Approximately 7.5 million people die of hypertension every year worldwide.

**Objective:** To determine the association between Ischemic Disease Heart (IHD) and dyslipidemia among hypertensive patients.

**Methods:** A case-control study was conducted at the cardiology outpatient departments of Prince Sattam-Bin-Abdul-Aziz University hospital between September 2015 and February 2017. The association of ischemic heart disease (dependent variable) was assessed against dyslipidemia (independent variable). Ischemic heart disease (IHD), body mass index (BMI) and dyslipidemia were defined. The data from the patients were collected into the medical notes that were later transferred into an excel spreadsheet. The data was analyzed using SPSS version 23. Pearson's chi-square test was applied and a P-value of  $\leq 0.05$  was considered significant.

**Results:** A total of 160 respondents were included in the study and 39.4% (n=63) had a positive history of ischemic heart disease. The average age in our study population was  $49.16 \pm 11.7$  and average BMI was  $29.11 \pm 5.04$ . A significant correlation was noted between dyslipidemia and IHD ( $p=0.000$ ; OR 3.39). It was noted that the chances of IHD with dyslipidemia were higher among individuals in the 31-50 years age group ( $p=0.001$ ; OR 6.75). In addition, a statistically significant correlation was noted between the risk of IHD and dyslipidemia in overweight and obese patients.

**Conclusion:** The combination of hypertension and dyslipidemia is a significant risk of IHD for male gender, 31-50 years old, overweight, obese, diabetics or smokers.

**Key words:** Dyslipidemias, Myocardial ischemia, Coronary artery disease, Saudi Arabia

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## INTRODUCTION

Hypertension (HTN) or elevated blood pressure is an important non-communicable disease (NCD) which considered as one of the strongest risk factors for cardiovascular diseases (CVDs) including ischemic heart disease (IHD), left ventricular hypertrophy (LVH) and heart failure, cerebrovascular attack, peripheral arterial disease (PAD) and renal failure [1]. Globally, 1.13 billion adults suffer from HTN and 7.5 million people die of it every year [2,3]. Coronary artery disease (CAD) or IHD is one of the major CVDs, contributing to nearly 7.4 million annual deaths worldwide [4]. There are several risk factors involved in the pathogenesis of IHD including modifiable and non-modifiable risk factors. Modifiable risk factors of IHD include unhealthy lifestyle (i.e., poor diet or bad fats, stress, obesity, physical inactivity, sleep deprivation, smoking, alcohol and substance abuse), diabetes, hyperlipidemia, high blood pressure and poor socio-economic status while non-modifiable risk factors include family history of IHD, old age, gender, ethnicity and menopause [5,6].

Dyslipidemia is a highly prevalent but modifiable risk factor for IHD and other cardiovascular events [7]. The global prevalence of raised total cholesterol is 39%, accounting for 2.6 million annual deaths worldwide [8]. More than 50% of patients with IHD have coexistent dyslipidemia while alone hypercholesterolemia accounts for one-third of IHD worldwide [9,10]. Both HTN and dyslipidemia are major and established risk factors for CVDs or IHD. There has been a significant relationship found between dyslipidemia and incidence of IHD among hypertensive patients. It has been reported that hypertensive patients with dyslipidemia develop IHD 18 times greater than those without dyslipidemia [9]. Therefore, coexistence of HTN and hyperlipidemia accelerates atherosclerosis, leading to increased incidence of CAD or IHD [9]. Atherosclerosis plays a main role in the pathogenesis of IHD through the formation of atherosclerotic plaques.

In Saudi Arabia, hypertension is one of the leading

causes of death with overall prevalence of 4.9% in the country [11]. Similarly, the prevalence of HTN among the population suffering from CVDs is 31.4% [11]. As far as dyslipidemia is concerned, its prevalence has been reported to be 33% in Saudi population [12]. These statistics reflect that there is substantial risk of IHD existing in Saudi population in the form of hypertension and dyslipidemia. If other risk factors of IHD such as old age, gender, obesity, diabetes and smoking are considered, it will further add to the risk of incidence of IHD or CAD in Saudi population. In other words, the risk of CAD development rises as the number of risk factors increases. In addition, modifiable risk factors are highly prevalent in Saudi Arabia, adding to the risk of IHD. Moreover, studies on the determination of the number of risk factors for IHD and their cumulative effect on the incidence of other CVDs among Saudi individuals is lacking. Unfortunately, lack of awareness about substantial risk factors of CAD or IHD among Saudi individuals is upsetting and requires mass awareness campaigns [13].

The literature on association between dyslipidemia and IHD is scarce from Saudi Arabia. Therefore, this case control study was carried out to determine the association between IHD and dyslipidemia among hypertensive patients.

## METHODOLOGY

This case-control study was conducted at the cardiology outpatient departments of Prince Sattam Bin Abdul-Aziz University hospital between September 2015 and February 2017. Written consent was obtained from the patient and the study was approved by the ethics approval committee of the concerned hospital. The association of ischemic heart disease (dependent variable) was assessed against dyslipidemia (independent variable). Other confounding variables assessed were history of hypertension, sex, age, weight status, diabetes (based on the history of diagnosed diabetes or taking anti-diabetes medication), and history of smoking.

The inclusion criteria included patients with a history of primary hypertension; adults of both genders and aged 18 years or more, patients with varying BMIs (from underweight to obese); both diabetics and non-diabetics; smokers and non-smoker; and patients presenting in the outpatients who consented to participate

in the study. Patients without the history of established hypertension or who had secondary hypertension; children and adolescents; inpatients, and outpatients who did not consent to participate were excluded from the study.

The variables included in the study were defined as follows.

**Ischemic heart disease:** The patients were labeled to have ischemic heart disease if they had a positive history of either myocardial infarction, coronary angioplasty or coronary artery bypass surgery, positive stress electrocardiogram, or angiographic evidence of luminal narrowing of coronary arteries or ischemic changes evident on an electrocardiogram with a positive history of chest pain and raised cardiac enzymes (including troponin) levels.

**BMI:** It was calculated after assessing patients' height and weight and patients were classified into underweight, normal, obese, and overweight categories (obesity stages as defined by the Center for Disease Control and Prevention).

**Blood pressure:** It was assessed on two separate instances during the clinic appointment using a mercury sphygmomanometer. The blood pressure was divided into three stages: (a) Stage 1- Clinic blood pressure 140/90 mmHg to 159/99 mmHg; (b) Stage 2- Clinic blood pressure 160/100 mmHg or higher less than 180/120 mmHg, and (c) Stage 3- Clinic systolic blood pressure greater than 180 mmHg.

**Dyslipidemia:** It was established following a complete lipid profile from the patients. The levels of LDL, HDL, triglycerides and cholesterol were interpreted based on the American College of Cardiology guidelines.

The sample size was calculated using an Open-epi sample calculator where confidence level was set at 95%, power was 80%, frequency of dyslipidemia in cases of IHD was set as 17.3% and in controls it was set as 50%. The computed results gave us a sample size of 160 with 63 cases and 97 controls. The data from the patients was collected into the medical notes that were later transferred retrospectively into an excel spreadsheet. The data was analyzed using SPSS version 23 and descriptive statistics were computed for study variables. Pearson's chi-square test was applied and a P-value of  $\leq 0.05$  was considered significant. Odds ratios

with (95% CI) were calculated to check the association between dyslipidemia and IHD and  $OR > 1$  was considered as significant. The results were represented as tables and figures.

**RESULTS**

Out of the 160 respondents, 39.4% (n=63) had a positive history of ischemic heart disease. The average age in our study population was  $49.16 \pm 11.7$  and average BMI was  $29.11 \pm 5.04$  (Figure 1). Majority of our population were males (n=90; 56.2%), were above 50 years (n=77; 48.1%), were obese (n= 93; 58.1%), had stage one hypertension (n=102; 63.7%), were non-diabetics (n=90; 56.2%), and non-smokers (n= 131; 81.9%). Table 1 describes the demographics and distribution of confounding variables among the study population in detail.

We noted a significant correlation between dyslipidemia and IHD ( $p = 0.000$ ;  $OR 3.39$  (95% CI: 1.72-6.62)) (Figure 2). When the association between IHD and dyslipidemia was assessed based on the patient's characteristics, we noted several trends (Table 2 summarizes these trends). We noted that the chances of IHD with dyslipidemia were higher among individuals in the 31-50 years age group ( $p = 0.001$ ;  $OR 6.75$  (95% CI 2.23-20.44)). There was no statistically significant correlation between these variables in the remaining age groups. Although both genders had an increased risk of IHD with dyslipidemia, this risk was higher among males than females ( $p = 0.003$ ;  $OR 3.63$  (95% CI 1.51-8.67) in males vs.  $p = 0.051$ ;  $OR 3.051$  (95% CI 0.97-9.62) in females).

We also noted a statistically significant correlation between the risk of IHD and

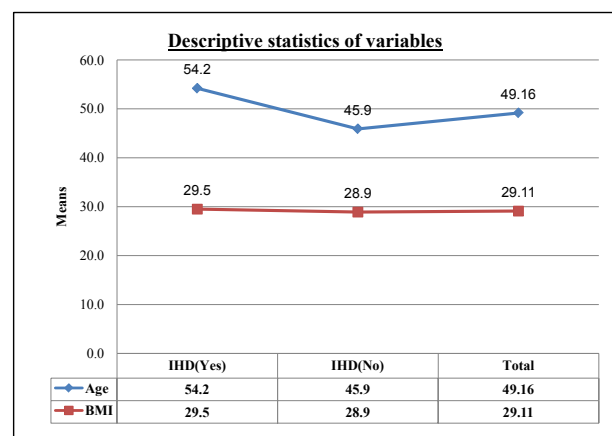
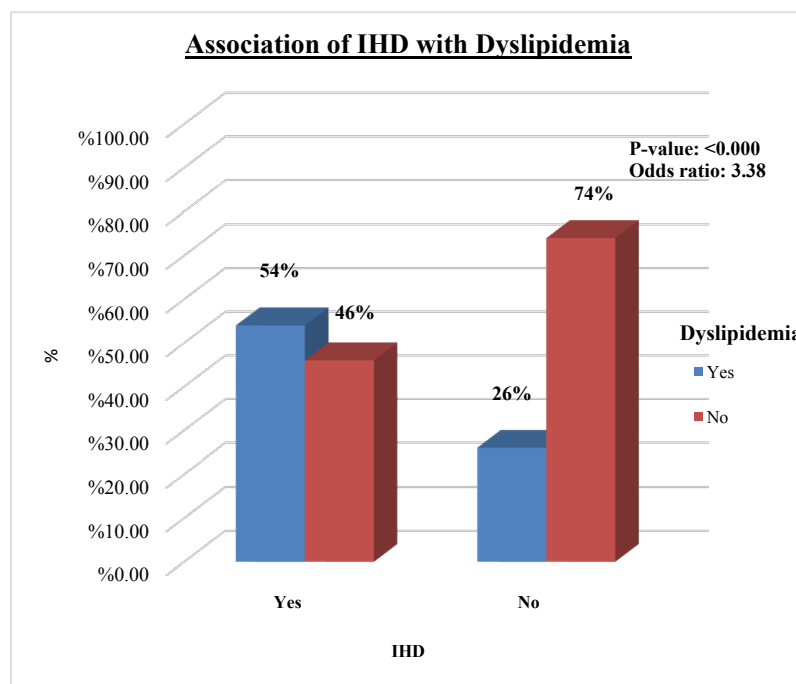


Figure 1: Chart summarizing average age and BMI in IHD vs. non-IHD patients.

**Table 1: Distribution of study variables according to IHD.**

Associated Variables	IHD		Total	P Values	
	Yes	No			
Age groups	30 or less years	0 0.00%	14 14.40%	14 8.80%	0.002*
	31-50 years	25 39.70%	44 45.40%	69 43.10%	
	More than 50 years	38 60.30%	39 40.20%	77 48.10%	
Gender	Female	25 39.70%	45 46.40%	70 43.80%	0.403
	Male	38 60.30%	52 53.60%	90 56.20%	
BMI	Underweight	2 3.20%	11 11.30%	13 8.10%	0.3
	Normal	8 12.70%	9 9.30%	17 10.60%	
	Overweight	15 23.80%	22 22.70%	37 23.10%	
	Obese	38 60.30%	55 56.70%	93 58.10%	
Stage of HTN	Stage 1	11 17.50%	91 93.80%	102 63.70%	<0.000*
	Stage 2	44 69.80%	0 0.00%	44 27.50%	
	Stage 3	8 12.70%	6 6.20%	14 8.80%	
Diabetes Mellitus	Yes	51 81.00%	19 19.60%	70 43.80%	<0.000*
	No	12 19.00%	78 80.40%	90 56.20%	
Smoking	Yes	18 28.60%	11 11.30%	29 18.10%	0.006*
	No	45 71.40%	86 88.70%	131 81.90%	



**Figure 2: Association of IHD with dyslipidemia.**

Table 2: Association of IHD with Dyslipidemia according to patient's characteristics.

Associated variables	Dyslipidemia	IHD		P values	Odds ratio (95% CI)	
		Yes	No			
Age groups	30 or less years	Yes	0(0%)	1(100%)	N/A	N/A
		No	0(0%)	13(100%)		
	31-50 years	Yes	15(65.2%)	8(34.8%)	0.001*	6.75 (2.23-20.44)
		No	10(21.7%)	36(78.3%)		
	More than 50 years	Yes	19(54.3%)	16(45.7%)	0.429	1.44 (0.58-3.54)
		No	19(45.2%)	23(54.8%)		
Gender	Female	Yes	9(56.2%)	7(43.8%)	0.051*	3.05 (0.97-9.62)
		No	16(29.6%)	38(70.4%)		
	Male	Yes	25(58.1%)	18(41.9%)	0.003*	3.63 (1.51-8.67)
		No	13(27.7%)	34(72.3%)		
BMI	Underweight	Yes	0(0%)	4(100%)	0.305	N/A
		No	2(22.2%)	7(77.8%)		
	Normal	Yes	8(66.7%)	4(33.3%)	0.012*	N/A
		No	0(0%)	5(100%)		
	Overweight	Yes	8(80%)	2(20%)	0.003*	11.43 (1.94-67.26)
		No	7(25.9%)	20(74.1%)		
Obese	Yes	18(54.5%)	15(45.5%)	0.046*	2.4 (1.0-5.73)	
	No	20(33.3%)	40(66.7%)			
Stages of Hypertension	Stage 1	Yes	7(26.9%)	19(73.1%)	0.002*	6.63 (1.76-25.04)
		No	4(5.3%)	72(94.7%)		
	Stage 2	Yes	19(100%)	0(0%)	N/A	N/A
		No	25(100%)	0(0%)		
	Stage 3	Yes	8(57.1%)	6(42.9%)	N/A	N/A
		No	0(0%)	0(0%)		
Diabetes Mellitus	Yes	Yes	23(92%)	2(8%)	0.007*	6.98 (1.46-33.41)
		No	28(62.2%)	17(37.8%)		
	No	Yes	11(32.4%)	23(67.6%)	0.000*	26.3 (3.21-215.7)
		No	1(1.8%)	55(98.2%)		
Smoking	Yes	Yes	13(81.3%)	3(18.8%)	0.018*	6.93 (1.29-37.22)
		No	5(38.5%)	8(64.5%)		
	No	Yes	21(48.8%)	22(51.2%)	0.015*	2.55 (1.19-5.44)
		No	24(27.3%)	64(72.7%)		

dyslipidemia in overweight and obese patients. In overweight patients, the OR was 11.45 (95% CI 1.94-67.26) and p-value was 0.003. In the obese population, statistical significance was achieved with a p-value of 0.046 (OR 2.4 (95% CI 1.0-5.73)). A statistically significant correlation was only noted in patients with stage I hypertension (p= 0.002; OR 6.65 (95%CI 1.76-25.03)). Other stages of hypertension did not reach statistical significance. As for diabetes, we noted a statistically significant risk of IHD with dyslipidemia with both diabetics and non-diabetic patient (p=0.007, OR 6.98 (95% CI 1.46-33.41)) in diabetics vs. p= 0.000, OR 26.30 (95% CI 3.21-215.7) in non-diabetics). The IHD risk with dyslipidemia was high in both smoker and non-smoker patient populations with p-values 0.018 (OR 6.93 (95% CI 1.29-37.22) and 0.015 (OR 2.55 (95% CI 1.19-5.44) in smoking and non-smoking patients respectively.

## DISCUSSION

The present case-control study revealed a significant correlation between dyslipidemia and IHD. Besides this correlation, male gender, age (31-50 years), overweight, obesity, stage one hypertension, diabetics or non-diabetics, smokers or non-smokers had significant correlation with IHD in the presence of dyslipidemia. Interestingly, the study did not reveal statistically significant correlation of stages two and stage three hypertension with IHD in the presence of dyslipidemia.

Hypertension and dyslipidemia are leading independent risk factors of CVDs as well as key components of metabolic syndrome which further increase the risk of CV events. Coexistence of hypertension and dyslipidemia poses even more adverse impact on cardiovascular functions through endothelial dysfunction, heightened oxidative stress and accelerated



atherosclerosis [14]. A study from China, conducted by Yu et al. [15] has reported high prevalence of dyslipidemia (68.7%). Similarly, Spannella et al. [16] conducted an observational study in Italy including 1219 outdoor patients, reporting the prevalence of dyslipidemia as high as 91.1% among those who were referred for the management of hypertension. Unfortunately, dyslipidemia is often neglected in hypertensive patients. Jani et al. [17] conducted a prospective cross sectional including 600 patients suffering from hypertension and diabetes. They reported insufficiently treated dyslipidemia in patients with controlled and uncontrolled hypertension as 23% and 67%, respectively. It has been reported that effective treatment of hypertension alone and hypertension plus hypercholesterolemia reduces CVD risk by 20-25% and >50%, respectively [16]. Therefore, proper control of high blood pressure and dyslipidemia significantly reduces the risk of IHD and other CVDs.

Similarly, presence of other risk factors such as male gender, age (31-50 years in the present study), obesity, diabetics and smoking along with dyslipidemia and hypertension adds to the risk of CVDs. For instance, post-MI morbidity, mortality and re-infarction are higher among diabetics as compared to non-diabetics [18]. Like hypertension and dyslipidemia, diabetes is also an independent risk factor of CVD. Therefore, coexistence of these three risk factors intensifies the risk of CV events. The present study has revealed a significant correlation with IHD among those patients with hypertension stage 1 as reported in previous studies [19,20]. Interestingly, Qi et al. [19] and Talaei et al. [20] have reported significant correlation of hypertension stage 1 with CVDs among young and middle-aged patients (<65 years), not in those above 65 years. In the present study, more patients were having dyslipidemia at hypertension stages two and three, posing more risk of developing IHD and its complications. In this context, Wu et al. [21] has reported higher CVD mortality among those patients with hypertension stages two and three as compared to those with hypertension stage one. Proper control of hypertension among young patients at stage one helps reduce cardiovascular risk.

The present study reveals that combination of dyslipidemia and hypertension is a significant

risk for the development of IHD even among non-diabetics and non-smokers. Limitations of the study include single-centered study and small sample size. As dyslipidemia and hypertension are common risk factors for IHD, large sample size from multiple centers could have offered more precise results.

## CONCLUSION

The combination of hypertension and dyslipidemia is a significant risk of IHD for male gender, 31-50 years old, overweight, obese, diabetics or smokers. In this context, risk of IHD can be cut down significantly by optimizing the treatment of hypertension and diabetes, reduction of weight and dyslipidemia, and smoking cessation. In fact, large benefits can be gained by addressing multiple risk factors of IHD simultaneously.

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