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Combined Risks of Hyperlipidemia and Hypertension for Coronary Heart Disease: A Case-Control Study of the Local Population of Bahawalpur, Pakistan

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Abstract

Hypercholesterolemia, being one of the most important risk factors for coronary heart disease, is defined as a total cholesterol concentration of ≥240 mg/dL. Hypertension has become a major public health hazard all over the world due to the serious damage it causes to the body organs and the many complications it induces, including the coronary heart disease. The current study aimed to evaluate the combined risks of correlation between hypertension and hyperlipidemia and their association with coronary heart disease. It included 100 patients diagnosed with hypertension and hyperlipidemia, as well as 100 healthy individuals of the same age and background. A standardized questionnaire was used to collect the family history of patients and control. Blood samples with a volume of 3-5ml were drawn from all patients to analyze the composition of blood serum including LDL (low-density lipoprotein), HDL (high-density lipoprotein), triglyceride, and cholesterol levels. The frequencies of all concerned factors were calculated and the mean values of blood pressure, cholesterol, LDL, and HDL were found to be in the hazardous range in patients. The data were analyzed using the chi-square test and binomial regression statistical analysis. The analysis of risk factors revealed that age, BMI (body mass index), high blood pressure, smoking, and high salt intake had a significant association with the high lipid profile in the patients. The risk of cardiovascular diseases (CVDs) is enhanced in patients with high blood pressure and hyperlipidemia.

Keywords: body mass index (BMI), cardiovascular diseases (CVDs), hyperlipidemia, hypertension, low-density lipoprotein (LDL), high-density lipoprotein (HDL)

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Introduction

Hypercholesterolemia, one of the most important risk factors for cardiovascular diseases (CVDs), is found in 13.1% of the US adult population [1]. It is one of the leading causes of death, worldwide [2]. Cholesterol is an essential lipid molecule for the proper working and functioning of the brain. Any disorder of lipid metabolites is characterized by an elevated or decreased level of cholesterol, low-density protein, high-density lipoprotein, and triglyceride in the plasma, all of them being major causes of CVDs [3, 4]. Some major signs include an enlarged spleen and liver, xanthoma, chest pain, abdominal pain, pimple-like lesions across the body, heart attack, obesity, and diabetes [5].

Hyperlipidemia is characterized by an increased level of cholesterol in the blood. It is mainly caused by smoking, alcohol, hypothyroidism, and estrogen therapy, as well as environmental and genetic factors. A high intake of fats is considered a risk factor that ultimately leads to hypercholesterolemia which induces impairment in several mechanisms, such as renin-angiotensin activity, sodium ions homeostasis, as well as transport, and signals transduction. The rate of blood flow to the heart doesn't remain constant, rather it continues to vary constantly. In this regard, long-term abnormal pressure in the main arteries results in hypertension [6]. It is a major health issue, in addition to obesity and diabetes [7]. If someone regularly has a systolic blood pressure over 140mmHg or more, and/or their diastolic blood pressure is consistently 90mmHg or more, the resulting condition is known as high blood pressure [8].

Hypertension is common in underdeveloped and low-income countries such as Pakistan [9], where more than 80% of the total deaths are due to heart diseases. Hypertension and hyperlipidemia may co-exist in some patients and their co-occurrence poses a high risk of CVDs [10]. In individuals of age between 40 and 90 years, the risk of fatal coronary disease may double with a 20/10 mm Hg rise in blood pressure, which would increase the chances of heart disease by ≥50% [11]. Blood vessel constriction and stiffness due to excessive cholesterol accumulation can lead to blocked arterial circulation. Precipitation of calcium ions in cholesterol promotes the hardening and digitization of plaque. Consequently, the walls of the blood vessels become stiff, brittle,

narrow, and rigid, making blood circulation in the body less effective. The toughening of the coronary arteries results in heart disease [12].

The current study was planned to assess the role of the body mass index (BMI), diabetes, exercise, smoking, and high salt intake in the progression of high blood pressure and hyperlipidemia, their interconnection, and the consequent progression of CVDs in the local population of Punjab, Pakistan. This study is unique in the sense that it assesses dyslipidemia based on four factors including cholesterol, HDL, LDL, and triglyceride, which differentiate it from the previous studies that used only one parameter. We hypothesized that dyslipidemia and hypertension are affected by multifactorial parameters and cholesterol, HDL, LDL, and triglyceride that perform accumulative functioning in the development of these phenotypes.

Materials and Methods

The current research work included 100 patients older than 20 years of age, regardless of their gender, ethnicity, and cast, who were either diagnosed with hypertension and hyperlipidemia, or were under the observation of diagnosis, or taking antihypertensive medication. Children and teenagers were excluded from the current study. One hundred healthy individuals of the same age were also enrolled as the control for comparison. A questionnaire was designed based on risk factors including gender, age, weight, height, body mass index (BMI), family history, blood pressure, smoking, exercise, hypertension, blood sugar level, salt intake, and CVDs to collect the required information from each patient manually, at the time of enrollment and blood sampling.

The automatic blood pressure monitor was used to calculate the blood pressure of the patients. BMI was estimated by using the formula: BMI= kg/m^2. Patients/control were categorized according to the standard lipid profile values given by the World Health Organization (WHO) (Table 1). Blood samples of 3-5ml were drawn from all patients and control individuals. Serum was separated in Eppendorf tubes and was stored at -20^{o}C for further lipid profile analysis. The analysis of the composition of blood serum indicating its LDL, HDL, triglyceride, and cholesterol level was performed according to the standard values given by WHO. The data was entered into SPSS software and evaluated using the chi-square test and

binomial regression statistical test. Variables with a *p*-value <0.05 were considered as significant.

Table 1. Lipid Profile

Lipids Profile	Desirable value	Borderline	High risk
Cholesterol	Less than 200 mg/dl	200-239 mg/dl	240 mg/dl
Triglycerides	Less than 140 mg/dl	150-199 mg/dl	200-499 mg/dl
HDL	60 mg/dl	40-50 mg/dl	Less than 40 mg/dl
LDL	60-130 mg/dl	130-159 mg/dl	160-189 mg/dl
Cholesterol/HDL	4.0	5.0	6.0

Results and Discussion

The current study was conducted to check the correlation between hyperlipidemia and hypertension and its effects on CVDs in the local population of Bahawalpur, Punjab, Pakistan. According to a study, the correlation between these two variables continues to vary all over the world and their combined effects lead to various CVDs [13]. No such study was previously performed on the local population of Bahawalpur and the results are compared with the results of the studies conducted previously on different populations of the world. Gender, age, weight, height, BMI, blood pressure, salt intake, headache, chest pain, fatigue, blurry vision, smoking, exercise, heart problem, and diabetes were all determined as risk factors for developing hypertension, hyperlipidemia, and CVDs. The statistical data supported our hypothesis. Each selected parameter was found to be significantly associated with any one of the four factors (cholesterol HDL, LDL, and triglyceride) of lipid profile, as indicated by the graph.

The frequencies of all these demographic factors were calculated and the results are illustrated in Table 2. The BMI of most patients was above the borderline. Headache complains, chest pain, and blurry vision were observed in most of the cases. Hypertension, along with heart problems and diabetes, was observed in the majority of the patients with hyperlipidemia. Cholesterol, LDL, HDL, and triglyceride with high-risk values were reported in more than fifty percent (50%) of hyperlipidemia patients (Table 1). The comparison of the mean values of blood pressure and lipid profile parameters, such as cholesterol, LDL, and triglyceride indicated a higher mean value in patients as compared to the control group, while HDL indicated a low value in patients (Table 2).

Table 2. Frequency of Different Demographic Factors in Case and Control (N=200)

Characteristics		Case= 100		Control= 100		Total= 200
		N	%	N	%	
Gender	Male	57	57	67	67	124
	Female	43	43	33	33	76
Age	25-40	29	29	28	28	57
	41-55	38	38	34	34	72
	56-70	27	27	26	26	53
	71-85	6	6	12	12	18
Height	140-155	32	32	33	33	65
	156-170	39	39	37	37	76
	171-185	29	29	30	30	59
BMI	18-24.9	12	12	55	55	67
	25-29.9	46	46	38	38	84
	30 and ≥	41	41	6	6	47
BP	101-120	0	0	100	100	100
	121-140	20	29	0	0	29
	141-160	59	59	0	0	59
	161-180	12	12	0	0	12
Smoking	Yes	31	31	28	28	59
	No	69	69	72	72	141
Exercise	Yes	35	35	38	38	73
	No	65	65	62	62	127
Salt intake	High	9	9	9	9	18
	Low	23	23	27	27	50
	Moderate	62	62	56	56	118
	Very Low	6	6	8	8	14
Symptoms	Headache/ Fatigue	43	43	0	0	43
	Chest Pain	22	22	0	0	22
	Blurry Vision	35	35	0	0	35

Characteristics		Case= 100		Control= 100		Total= 200
		N	%	N	%	
Conditions	Nil	0	0	100	100	100
	Hypertension/ Heart Patient	76	76	0	0	76
	Hypertension/ Diabetes	23	23	0	0	23
	Nil	1	1	100	100.	101
Cholesterol	Less than 200	0	0	100	100.	100
	201-239	35	35.0	0	0	35
	240 and above	65	65.0	0	0	65
LDL	60-129 mg/dl	0	0	100	100.	100
	130-159 mg/dl	18	18.0	0	0	18
	160-189 mg/dl	82	82.0	0	0	82
HDL	60 mg/dl	0	0	100	100.	100
	40-59 mg/dl	9	9.0	0	0	9
	Less than 40 mg/dl	91	91.0	0	0	91
Triglyceride	Less than 150 mg/dl	0	0.0	100	100.	100
	150-199 mg/dl	20	20.0	0	0	20
	200-499 mg/dl	80	80.0	0	0	80

Lipid profile parameters including triglycerides, cholesterol, LDL, and HDL were cross-tabulated with age. A significant association of triglyceride with age (p-value = 0.034) was observed, indicating that the high lipid profile value could be dependent on age which remains an important contributor to hypertension, hyperlipidemia, and heart diseases. Indeed, the chances of developing the disease may increase with increasing age. The odd ratio, with a 95% confidence interval, also indicates that the risk of hyperlipidemia increases with increasing age (it was determined to be 1.079, 1.003, and 0.483 times higher in groups two, three, and four respectively as compared to the reference group) (Table 3). Adamu et al. [14] also cited a correlation between lipid abnormalities and age and showed that it was most pronounced among people who were more than 40 years of age.

Table 3. Comparison of Mean Value of Different Hematological Parameters in Case and Control (n=200).

Hematological Parameters	Patients N=100, Mean+ SD	Control N=100, Mean+ SD
Blood Pressure	149.030±11.605	109.65±7.516
Cholesterol	240.57±17.98	113.51±46.91
Low-density L	167.98±14.43	92.04±30.60
High-density L	24.44±9.34	90.21±30.39
Triglyceride	335.61±110.55	113.59±30.22

Obesity has an accelerating effect on cholesterol levels and hypertension and exacerbates these major risk factors for coronary heart diseases. Cross-tabulation of BMI with cholesterol showed a significant association among them with a *p*-value of 0.037. The risk of hyperlipidemia due to BMI indicates that overweight and obese people are 1.172 and 1.125 times respectively more prone to disease progression, in comparison to people with a normal BMI.

A comparison of blood pressure and hyperlipidemia revealed that people with relatively elevated blood pressure showed hyperlipidemia, while others with low or moderate blood pressure were less hyperlipidemic. The chi-square value of blood pressure with lipid profile was found to be significant (*p*-value = 0.035) for LDL. Subsequently, blood pressure was confirmed as one of the most important factors contributing to hyperlipidemia (Table 4). According to various studies, people with high blood pressure usually suffer from hyperlipidemia [14] because hypertension mainly occurs due to factors, such as headache, vision issues, and chest pain [15, 16], which are also important risks factors for hyperlipidemia. It was also observed that high blood pressure leads to high cholesterol levels [17]. Whereas, a 19.1% increased incidence of hyperlipidemia was reported in hypertensive patients by Soomro et al. [18].

Hyperlipidemia is caused by various factors, such as headache, fatigue, blurred vision, and chest pain. When cross-tabulated with dyslipidemia, a

significant value (*p*-value = 0.027) for cholesterol was obtained, thus showing their mutual association. According to Marshall *et al.*, some people with hypertension have problems including headaches, vertigo, tinnitus, and blurred vision [16].

Smokers are 1.155 times more likely to develop hyperlipidemia in comparison to non-smokers and smoking is also a major cause of various CVDs [19]. It affects the amount of lipid in the plasma of both men and women. The results of the current study indicated that individuals who regularly do exercise are 1.138 times less likely to develop CVDs, as compared to the individuals who do not exercise. According to the literature, a sedentary lifestyle contributes to the accumulation of bad cholesterol in the body [20].

The current study also focused on a major parameter which is salt intake. It was found that healthy individuals consume a very low level of salt as compared to the patients. So, individuals with very low salt intake are safe from the disease as compared to the individuals with low, moderate, and high salt intake (OR = 1.136, 1.476, and 1.33, respectively) (Table 4). It was also found that a high level of salt intake results in more pressure on the arteries [21] and leads to hypertension [22]. A positive link between high salt intake with raised blood pressure has been reported also in the literature [23]. Other factors associated with hyperlipidemia include diabetes and heart disease with significant *p*-values for LDL (*p*-value = 0.017) and HDL (*p*-value = 0.005), respectively (Table 4 and Table 5). Similar results were demonstrated by Dalal *et al*. Their study showed that both hyperlipidemia and hypertension are significant contributors to developing coronary heart diseases [10].

Similarly, Iskandar's research showed a positive association between triglyceride and heart diseases [24]. Accordingly, Bao *et al.* found cholesterol, LDL, HDL, and triglyceride levels higher in heart patients as compared to the healthy group [25].

Table 4. Proportion of Lipid Profile Parameters Based on Different Predictors in Cases (n=100)

Characteristics		Triglyceride mg/dl		P-value	Cholesterol mg/dl		P-value	LDL mg/dl		P-value	HDL mg/dl		P-value
		150-199	200-499		201-239	>240		130-159	160-189		40-50	< 40	
Age	25-40	4	25	0.034**	6	23	0.278	4	25	0.631	1	28	0.132
	41-55	11	27		16	22		8	30		4	34	
	56-70	2	25		11	16		4	23		2	25	
	71-85	3	3		2	4		2	4		2	4	
Total		20	80		35	65		18	82		9	91	
BMI	18-24.9	2	14	0.454	10	6	0.037**	3	13	0.535	2	14	0.210
	25-29.9	9	41		16	34		7	43		2	48	
	30 and above	9	25		9	25		8	26		5	29	
Total		20	80		35	65		18	82		9	91	
BP	121-140	6	23	0.554	10	19	0.717	1	28	0.035**	0	29	0.112
	141-160	13	46		22	37		13	46		8	51	
	161-180	1	11		3	9		4	8		1	11	
Total		20	80		35	65		18	82		9	91	
Symptoms	Headache	8	35	0.926ns	15	28	0.027**	7	36	0.804	3	40	0.230
	Blurry Vision	5	17		3	19		5	17		4	18	
	Chest Pain	7	28		17	18		6	29		2	33	
Total		20	80		35	65		18	82		9	91	

Characteristics		Triglyceride mg/dl		P-value	Cholesterol mg/dl		P-value	LDL mg/dl		P-value	HDL mg/dl		P-value
		150-199	200-499		201-239	>240		130-159	160-189		40-50	< 40	
Conditions	heart Patient	16	60	0.093	26	50	0.694	10	66	0.017**	7	69	0.005***
	Diabetes	3	20		9	14		7	16		1	22	
	Nil	1	0		0	1		1	0		1	0	
Total		20	80		35	65		18	82		9	91	

P-value < 0.05 is significant

Table 5. Logistic Regression Analysis of Different Variables

Characteristics		OR (CI)
Age	25-40	Ref
	41-55	1.079(0.538-2.163)
	56-70	1.003(0.475-2.119)
	71-85	0.483(0.159-1.463)
BMI	18-24.9	Ref
	25-29.9	1.172 (0.537-2.560)
	30 and >	1.125 (0.493-2.565)
Smoking	No	Ref
	Yes	1.155(0.629-2.123)
Exercise	Yes	Ref
	No	1.138(0.640-2.025)
Salt Intake	Very Low	Ref
	High	1.33(0.327-5.434)
	Low	1.136(0.344-3.755)
	Moderate	1.476(0.482-4.517)

Conclusion

LDL and HDL cholesterol levels play an important function in the occurrence of CVDs. If the quantity of LDL is increased in the blood, it may result in hypercholesterolemia. The latter may precipitate in the sub-endothelial layer, causing endothelial impairment and malfunctioning of the walls of an artery and leading to the development of atherosclerosis [26]. The situation is worsened if there is also a corresponding decrease in the HDL level.

HDL, being a protective factor, plays an important role in the reverse cholesterol traction (RCT) process. RCT makes possible the return of surplus cholesterol in peripheral tissues to the liver for excretion. A low level of HDL in the blood may reduce the body's immunity from atherosclerosis, resulting in the narrowing of blood vessels and malfunctioning of endothelium. Subsequently, blood supply to the heart is reduced and the constant accumulation of fats injures the artery wall, causing the intensification of atherosclerosis which is strongly associated with CVDs. An increase in the total cholesterol quantity in the blood may result in cholesterol deposits in the walls of arteries, disrupting the endothelial function due to the increased production of oxygen free

radicals. This results in deactivating the production of nitric oxide, which is a major endothelial-relaxing factor. With the long-term increase in total cholesterol and triglycerides, the permeability of the endothelial wall is increased which causes the accumulation of lipoproteins in it, resulting in CVDs [27, 28].

Implications

The prevalence and impact of CVDs is growing all over the world, while both hyperlipidemia and hypertension are significant risk factors for developing heart diseases. To control their spread, awareness seminars should be arranged about the importance of lipid profile measurement. Prevention and treatment plans are crucial at the national level to reduce the burden of disease in Pakistan. This study contributes to our understanding of the relationship between hypertension and hyperlipidemia, major causes behind their occurrence, and the epidemiological data of the two major risk factors of CVDs in patients from Bahawalpur. It also provides the details of the prevalence and the related load of the disease in the local population. Furthermore, it helps to provide pervasive data on the disease that can be used as a baseline for the development of good health facilities and future resource provision.

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