

Original Article

Correlation of Total Cholesterol, LDL-C & HDL-C With Coronary Heart Disease Among Different Ethnic Groups in Northern Pakistan

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ABSTRACT

Background: Coronary heart disease (CHD) is a leading cause of morbidity and mortality in adults, causing angina, MI, and sudden death. Total cholesterol and LDL-C are biochemical markers that increase CHD risk, while HDL-C reduces it. About 7.5 million deaths occur globally. The study aims to establish the association between test parameters like Total Cholesterol, LDL-C, and HDL-C with Coronary Heart Disease (CHD) among different ethnic groups of Pakistani population. High cholesterol, low LDL, and low HDL levels can cause serious cardiac complications.

Objective: The objective is to find out a correlation between increase in blood levels of Total Cholesterol, LDL-C & HDL-C levels with increased risk of Coronary Heart Disease (CHD) in the patients from various ethnic groups of Northern Pakistan.

Methodology: A prospective study was conducted at RIC Rawalpindi's Department of Pathology, collecting blood samples from 200 patients with heart-related complaints diagnosed as having coronary heart disease (CHD). The study examined serum levels of total cholesterol, HDL cholesterol, and LDL cholesterol using biochemical kits. The results were analyzed using SPSS version 23 and collected from both diseased cases and healthy controls.

Results: The study reveals significant variations in lipid profiles in patients with coronary heart disease (CHD) compared to the control group. Total cholesterol and low-density lipoprotein-cholesterol levels were higher in CHD patients, while high-density lipoprotein-cholesterol levels were lower. Out of 200 subjects, 100 were confirmed with CHD and 100 were a control group. Age-related changes were observed in males (82%), females (77%), and males (23%).

Conclusions: This study confirms a strong positive relationship between cholesterol and LDL levels and heart disease, with a higher prevalence in patients over 45 years old, indicating that lipid profile increases with age, making individuals more susceptible to cardiac diseases.

Keywords: Coronary Heart Disease (CHD), Lipid Profiles, Ethnic Groups, Cholesterol, LDL and HDL Correlation, Cardiac Risk Factors, Pakistani Ethnic Health Study

INTRODUCTION

Coronary Heart Disease (CHD) and contributes to more than 7.4 million deaths per year globally, which accounts for nearly half of all deaths from non-communicable diseases. By the year 2020, World Health Organization (WHO) is predicting more than 17.4 million deaths from CVD and 20 million people survive Heart Attack and Stroke every year. (1) Coronary Heart Diseases primarily caused by atherosclerosis, a chronic inflammatory disease of the arteries in which the deposition of cholesterol and fibrous materials in artery walls forms a plaque or lesion. (2)



Key risk factors that associate with the number of atherosclerotic CVD events include the total concentration of cholesterol found in the blood, as well as the cholesterol found in individual lipoprotein subclasses. (3) Serum concentrations of low-density lipoprotein-cholesterol (LDL-C) and high-density lipoprotein-cholesterol (HDL-C) have opposite effects on CVD risk, consistent with the role of LDL particles in the promotion of, and HDL particles in the protection against, atherosclerosis. (4)(5)

The Framingham Heart Study first demonstrated a link between serum cholesterol and heart disease, hypothesizing dietary cholesterol's impact on serum lipids, despite no such association at the time.(6)(7) The hypothesis was supported by animal studies, including Nikolai N. Anchovy's 1913 study on rabbits, which demonstrated that high cholesterol intake led to atherosclerotic plaques.(8) Early studies revealed species-specific differences in atherosclerotic response to large doses of dietary cholesterol, with rats being more resistant than rabbits and guinea pigs.(8) The average intake of dietary cholesterol in U.S. adults is typically between 200–350 mg/day, depending on gender and age group.(9) Eggs, a significant source of cholesterol, account for about a quarter of daily cholesterol intake in the U.S., contributing to both children and adults.(10)(11) Saturated fat increases serum cholesterol, while eggs, low in saturated fat, contribute only 2.5% of total saturated fatty acid intake among U.S. adults.(11)

Early observational studies demonstrated a link between dietary cholesterol and risk for CHD (12) (13); Initial studies failed to account for confounding variables, and recent epidemiological studies show no association between dietary cholesterol and egg intake and CHD risk in the general population. (14)(15)(16)

The occurrence of elevated levels of serum cholesterol in patients with CHD has been known over years. (17)(18)(19)(20) Recent studies on lipoproteins have made significant progress in understanding and managing lipid disorders, which are related to abnormalities in lipoprotein metabolism. (21)(22)(23). Clinically, the concentration of lipoproteins in the plasma is assessed by quantifying the cholesterol moiety of lipoprotein particle, which are sensitive markers for the assessment of Coronary Heart Disease (CHD) risk. (24)(25)(26) The concentration of HDL cholesterol especially HDL2 shows a strong inverse association with CHD. (27)(28)(29)(30) The levels of LDL- cholesterol were consistently raised in patients with CHD as compared to controls in various studies. (31)(32)(33) Significant rise in VLDL cholesterol has been reported in CHD patients in some studies. (34)

Coronary Heart Disease (CHD) is a major cause of mortality and morbidity in Pakistan, with lifestyle factors, diet, environmental factors, and genetic predisposition influencing its progression and development. (35) Global epidemiological studies reveal a consistent correlation between healthy characteristics and the prevalence of CHD in healthy individuals, highlighting the progression of risk factors. (36) The results have drawn attention to the status of risk factors in formative outcomes (37) and heterogeneity of CHD patients. Family history of CHD is highly associated with disease occurrence. (38) Hypertension (39) frequently has a correlation with CHD. Increased serum cholesterol levels (40) are associated with the risk of CHD and decreased levels of low-density lipoprotein (LDL) and high-density lipoprotein (HDL) are important in the progression (41) of CHD. Hypertriglyceridemia is known (42) in the progression of CHD.

According to the guidelines of the American Heart Association, the following values are prescribed for the above-mentioned risk factors for cardiovascular disease: total cholesterol: <200mg/dl, HDL: >40 mg/dl and LDL: <130 mg/dl. (43) Cardiovascular diseases, including ischemic, rheumatic, and cerebrovascular diseases, are influenced by lipid profiles, which include high cholesterol levels, which are strongly associated with heart disease progression.(44)(45) The lipid hypothesis suggests that elevated cholesterol levels in the blood increase the risk of atherosclerosis, heart attack, stroke, and peripheral vascular disease,(46) Bad cholesterol (LDL) and good cholesterol (HDL) are genetically determined, but can be altered by body composition, medications, and diet, (47) and other factors. (48)

Elevated levels of the lipoprotein fractions, LDL, IDL and VLDL, rather than the total cholesterol level, correlate with the extent and progress of atherosclerosis. (50) High levels of HDL cholesterol, despite being within normal



limits, have been linked to increased cardiovascular disease risk, raising doubts about the cardioprotective role of "good cholesterol."(51)(52)

The study aimed to determine the correlation between routine lipid profile tests, including Total Cholesterol, HDL-C, and LDL-C levels, in CHD patients across different ethnic groups in Northern Pakistan. Our study also aims to confirm previous studies in Pakistan and Northern Pakistan, extrapolating findings to our own population, and determine the prevalence of CHD among different ethnic groups.

MATERIALS AND METHODS

The study was approved by the Rawalpindi Institute of Cardiology's ethical committee and conducted in the Emergency and Pathology Department of the tertiary care Cardiac Hospital. The study used a prospective and cross-sectional, descriptive design and was completed in six months from June 2019 to November 2019. The study included 200 patients reporting cardiovascular system complaints at the RIC Emergency Department, with 100 diagnosed with CHD and 100 suspected but not diagnosed as CHD. Informed consent was obtained from each participant.

Patients with suspected coronary heart disease (CHD) were interviewed using a structured questionnaire, including socio-demographic data, history of smoking, exercise, family history of CHD, diabetes mellitus, and hypertension.

This study's inclusion criteria encompassed individuals of all ages and genders diagnosed with CHD, based on clinical symptoms, ECG changes, positive Troponins, CKMB values, and radiological evidence, specifically focusing on Northern Pakistani patients. Exclusion criteria involved individuals not diagnosed with CHD or those from regions outside Northern Pakistan.

In this study, a range of laboratory tests was conducted to evaluate various aspects of Coronary Heart Disease (CHD) in Northern Pakistani patients. These tests included Troponin-I (Trop-I), Creatine Kinase-MB (CK-MB), electrocardiogram (ECG), total cholesterol, low-density lipoprotein (LDL), and high-density lipoprotein (HDL) measurements. At the RIC Emergency Department, patients reporting with suspected CHD underwent essential point-of-care testing, including Trop-I and CK-MB assays, along with ECG recordings to aid in the diagnosis of CHD.

The measurement of Trop-I and CK-MB was performed using the HUBI Cardiac DUO, an immunochromatography-based diagnostic test. This involved adding blood samples, separating cells, and reacting with colloidal gold antibody conjugates. Results were displayed on the HUBI QUAN pro screen. ECGs, which record the heart's electrical activity over time, were used to identify patients with elevated reference values and definitive ECG changes indicative of CHD.

In the laboratory, spectrophotometry was employed as an analytical principle to measure the absorbance of light by chemical substances. Enzymatic analysis, a widely accepted method in medical laboratories, involved color reactions initiated by enzyme-catalyzed reactions. Samples were sent to the lab for testing CK-MB levels in CHD individuals. For the estimation of total cholesterol, the enzymatic end-point method (CHOD-PAP) was utilized. This method involved the hydrolysis of cholesterol esters into cholesterol and fatty acids, followed by oxidation into cholestenone and H2O2. The resulting red quinoneimine dye was measured spectrophotometrically at 540/600 nm.

HDL-cholesterol was estimated using the Beckman Coulter AU System HDL-Cholesterol test, which involved solubilizing free cholesterol and selectively solubilizing HDL-lipoproteins. The absorbance increase was proportional to HDL-C concentration. LDL-cholesterol was measured using the Beckman Coulter AU System LDL-Cholesterol test, which employed a two-reagent homogenous system. The concentration of LDL-C was determined by selectively solubilizing LDL-lipoproteins and measuring the resulting colorless end product. All these tests were carried out with strict adherence to calibration, quality control, and regulatory requirements. The results were



automatically calculated using the BECKMAN COULTER AU 480, a spectrophotometric-based chemical analyzer, ensuring the accuracy of the findings.

We adhered to standard laboratory precautions when handling reagents and disposed of undiluted reagents while flushing waste pipes with water to prevent compound buildup. Local guidelines were followed for waste disposal. Excluded samples had abnormal characteristics or improper storage.

RESULTS

In the present study, lipid profile of patients with CHD, showed significant variation when compared to that of the control group. The Total Cholesterol and Low-Density Lipoprotein-Cholesterol were significantly higher in the CHD patients, whereas the High-Density Lipoprotein-Cholesterol had significantly lowered. Out of 200 subjects under the study, 100 subjects were confirmed with CHD and 100 subjects were regarded as control group without CHD. In our study the control group was consist of 100 subjects out of which 54 (54%) were males and 46 (46%) were females, their laboratory findings gives the normal results as mentioned in Table 1, on the other hand diseased group was consist of 100 cases out of which 71 (71%) were males and 29 (29%) were females, and there was an increase in levels of Total Cholesterol and LDL-C while decrease in the level of HDL-C in the different age groups of subjects as listed in the Table 2.

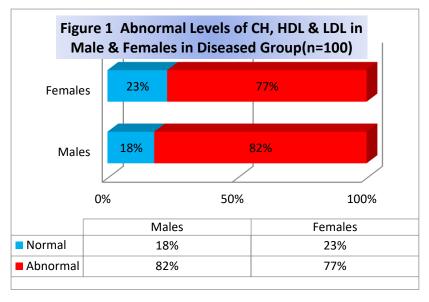
Statistical analysis was performed using the statistical package for social sciences (SPSS) version 23. Statically significant P value was set as <0.01 level. The correlation between total cholesterol and LDL cholesterol is significant at <0.01 level and p value is < 0.001 obtained that indicate a close relationship between total cholesterol and LDL with CHD patients.

TABLE 1: MEAN LEVELS OF CHOLESTEROL, HDL & LDL IN NORMAL PATIENTS OF DIFFERENT AGE GROUPS (n=100)				
AGE GROUPS	CHOLESTEROL	HDL	LDL	
<30 Years	163.21±13.96	42.0±3.07	106.21±9.47	
30-45 Years	165.1±16.07	40.1±2.17	102.21±9.07	
45-55 Years	156.21±15.07	37.21±3.07	98.21±12.07	
55-65 Years	160.21±13.07	38.2±4.07	88.21±16.07	
>65 Years	179.21±9.57	40.21±1.87	108.21±7.07	

TABLE 2: MEAN LEVELS OF CHOLESTEROL, HDL & LDL IN CHD PATIENTS OF DIFFERENT AGE GROUPS. (n=100)				
AGE GROUPS	CHOLESTEROL	HDL	LDL	
<30 Years	191.21±1.07	34.1±2.7	117.1±3.7	
30-45 Years	189.21±18.27	32.2±3.7	121.2±22.27	
45-55 Years	211.21±20.07	31.21±3.8	140.21±36.07	
55-65 Years	220.21±20.27	30.21±3.47	141.1±27.07	
>65 Years	244.21±38.07	28.31±3.87	148.21±19.07	

Out of 100 study subjects, in males 82% cases were detected in which all these parameters shown changes and 18% cases were detected in which all the studied parameters were normal while in case of Females 77% cases were detected in which changes were present and 23% cases were normal as in Figure 1.





MEAN LEVEL OF TOTAL CHOLESTEROL IN CONTROL AND DISEASED GROUP:

The total cholesterol level in control group is normal in all ages while the level of cholesterol increased with age i.e. >30 years of age have mean (191.21±1.07), years have mean (189.21±18.27), 45-55 years have mean (211.21±20.07), 55-65 years have mean (220.21±20.27) and >65 years have mean (244.21±38.07) as listed in the (Table 3).

TABLE 3 MEAN LEVEL CHOLESTEROL IN CONTROL AND DISEASED GROUP ON THE BASIS OF GENDER (n=100)

Age group	Normal Serum Cholesterol	Gender distribution	Serum Cholesterol among CHD Patients	Gender distribution
<30 Years	163.21±13.96	Male:2 (50%)	191.21±1.07	Male: 02 (100%)
		Female: 2(50%)		Female: 0
30-45 Years	165.1±16.07	Male: 14 (51%)	189.21±18.27	Male:08(100%)
		Female:13(49%)		Female: 0
45-55 Years	156.21±15.07	Male:15(44%)	211.21±20.07	Male:22(73%)
		Female:18(56%)		Female:8(27%)
55-65 Years	160.21±13.07	Male: 16(64%)	220.21±20.27	Male:23(74%)
		Female: 9(36%)		Female:08(26%)
>65 Years	179.21±9.57	Male:08(66%)	244.21±38.07	Male:24(80%)
		Female:04(44%)		Female:06(20%)

lable-3: age-wise distribution of serum cholesterol (SC) concentration among normal and CHD subjec

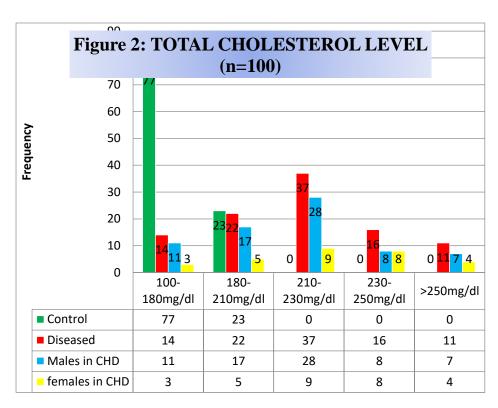
MEAN LEVEL OF HDL CHOLESTEROL IN CONTROL AND DISEASED GROUP:

The HDL level in normal groups remains the normal while decreased in diseased group i.e. <30 years have mean (34.1 ± 2.7) , 30-45 years have mean (32.2 ± 3.7) , 45-55 years have mean (31.21 ± 3.8) , 55-65 years have mean (30.21 ± 3.47) and >65 years have (28.31 ± 3.87) mean values of HDL as listed in the (Table 4)

TABLE 4 MEAN LEVEL HDL-C IN CONTROL AND DISEASED GROUP ON THE BASIS OF GENDER (n=100)

Age group	Normal Serum HDL	Gender distribution	Serum HDL among CHD Patients	Gender distribution
<30 Years	42.0±3.07	Male:2(50%)	34.1±2.7	Male: 02 (100%)
		Female: 2(50%)		Female: 0
30-45 Years	40.1±2.17	Male:14 (51%)	32.2±3.7	Male:08(100%)
		Female:13(49%)		Female: 0
45-55 Years	37.21±3.07	Male:15(44%)	31.21±3.8	Male:22(73%)
		Female:18(56%)		Female:8(27%)
55-65 Years	38.2±4.07	Male: 16(64%)	30.21±3.47	Male:23(74%)
		Female: 9(36%)		Female:08(26%)
>65 Years	40.21±1.87	Male:08(66%)	28.31±3.87	Male:24(80%)
		Female:04(44%)		Female:06(20%)
Table-4: Showing age wise distribution of HDL concentration among normal and CHD patients				





TOTAL CHOLESTEROL:

Figure 2 shows the level of total Cholesterol in control & diseased group and the number of subject that lie in categorized levels of parameter .i.e. in level 100-180mg/dl subjects were in this level in control group while 14 subjects were in this level in diseased group, similarly in level 180-210mg/dl 23 subjects in control while 22 in diseased, in level 210-230mg/dl no subject in control

group while 37 in diseased group, in level 230-250mg/dl no subjects in control group while 16 in diseased group and in level>250mg/dl 11 subjects were present in diseased group.

MEAN LEVEL OF LDL-C IN CONTROL AND DISEASED GROUP:

The LDL-C level is remains normal in the control group while increase in the diseased group with the increase of age .i.e. <30 years of age have mean (117.1±3.7), 30-45 years have mean (121.2±22.27), 45-55 years have mean (140.21±36.07), 55-65 have mean (141.1±27.07) and >65 years of age have mean (148.21±19.07) of total LDL levels as listed in (Table 5).

TABLE 5 MEAN LEVEL OF LDL-C IN CONTROL AND DISEASED GROUP ON THE BASIS OF GENDER (n=100)

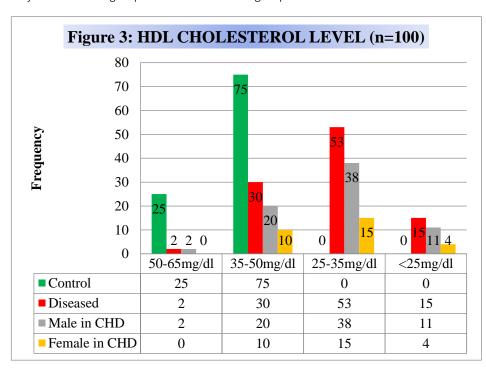
Age group	Normal Serum LDL	Gender distribution	Serum LDL among CHD Patients	Gender distribution
<30 Years	106.21±9.47	Male:2(50%)	117.1±3.7	Male: 02 (100%)
		Female: 2(50%)		Female: 0
30-45 Years	102.21±9.07	Male:14 (51%)	121.2±22.27	Male:08(100%)
		Female:13(49%)		Female: 0
45-55 Years	98.21±12.07	Male:15(44%)	140.21±36.07	Male:22(73%)
		Female:18(56%)		Female:8(27%)
55-65 Years	88.21±16.07	Male: 16(64%)	141.1±27.07	Male:23(74%)
		Female: 9(36%)		Female:08(26%)
>65 Years	108.21±7.07	Male:08(66%)	148.21±19.07	Male:24(80%)
		Female:04(44%)		Female:06(20%)

HIGH DENSITY LIPOPROTEIN:

Figure 3 shows the level of HDL Cholesterol in control & diseased group and the number of subject that lie in the categorized levels of parameter .i.e. in level 50-65mg/dl 25 subjects were in this level in control group while 2 subjects were in this level in diseased group, similarly in level 35-50 mg/dl 75 subjects in control while 30 in



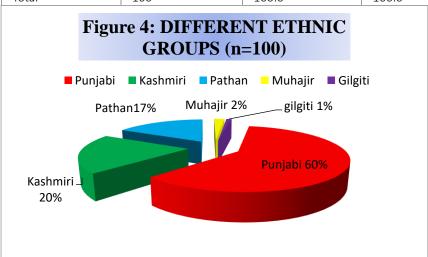
diseased, in level 25-35mg/dl no subject in control group while 53 in diseased group and in level <25mg/dl no subjects in control group while 15 in diseased group.



ETHNICITY:

Table 6 shows that Punjabi are more susceptible for CHD about 60% of total and other ethnic groups have less percentage as compared to Punjabi.

TABLE 6	Frequency	Percent %	Valid Percent	Cumulative Percent
Punjabi	60	60.0	60.0	60.0
Kashmiri	20	20.0	20.0	20.0
Pathan	17	17.0	17.0	17.0
Muhajir	2	2.0	2.0	99.0
Gilgiti	1	1.0	1.0	100.0
Total	100	100.0	100.0	





CORRELATION OF CHOLESTEROL HDL AND LDL IN DISEASED GROUP:

Table 7 shows that there is a strong correlation between cholesterol and LDL also called as direct relationship when one is increase other also increase, this table shows that correlation is significant at 0.01 level. The graphical presentation also shows the relationship between Cholesterol and LDL, HDL has inverse relation with the Cholesterol when cholesterol increase HDL decrease at 0.01 levels.

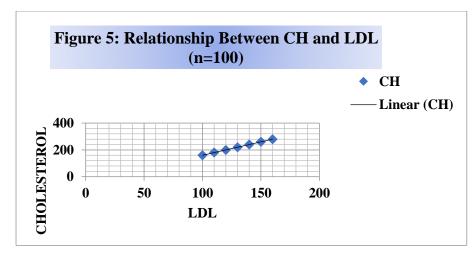
Table 7 Correlations between Total Cholesterol, HDL and LDL in Diseased Group (n=100)

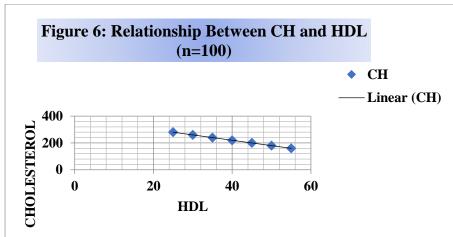
		Ages of Subjects	Total Cholesterol level in CHD Patients	High Density Lipoproteins in CHD Patients	Low Density Lipoproteins in CHD Patients
Ages of Subjects	Pearson Correlation	1	.177	.017	.190
	Sig. (2-tailed)		.078	.868	.058
	N	100	100	100	100
Total Cholesterol level in MI Patients	Pearson Correlation	.177	1	132	.645**
	Sig. (2-tailed)	.078		.191	.001
	N	100	100	100	100
High Density Lipoproteins in MI	Pearson Correlation	.017	132	1	.022
Patients	Sig. (2-tailed)	.868	.191		.832
	N	100	100	100	100
Low Density Lipoproteins in MI	Pearson Correlation	.190	.645**	.022	1
Patients	Sig. (2-tailed)	.058	.001	.832	
	N	100	100	100	100
**. Correlation is signific	ant at the 0.01 level	(2-tailed).			

Table 8 Correlations of Total Cholesterol and LDL In Diseased Group (N=100)

		Total Cholesterol level in CHD patients	Low Density Lipoproteins in CHD Patients
Total Cholesterol level in CHD	Pearson Correlation	1	.645**
Patients	Sig. (2-tailed)		.001
	N	100	100
Low Density Lipoproteins in CHD	Pearson Correlation	.645**	1
Patients	Sig. (2-tailed)	.001	
	N	100	100
**. Correlation is significant at the 0.01 level (2-tailed).			







DISCUSSION

CHD remains a major cause of death in developed countries, with modifying risk factors including plasma cholesterol, affecting mortality rates. (87) The cholesterol-diet-CHD hypothesis suggests that elevated plasma cholesterol concentrations increase the risk of coronary heart disease (CHD), while decreasing cholesterol levels decrease the risk. (88)(89) Epidemiologic studies have linked the intake of high levels of dietary fat rich in cholesterol and saturated fats, with increased plasma cholesterol levels. Therefore, restriction of saturated fat and cholesterol is the cornerstone of dietary therapy to lower down the elevated blood cholesterol levels. (90) In the present study, CHD incidence was more especially those in the age group 51-60 years.

Clinical studies show an inverse relationship between HDL-C levels and atherosclerosis, as HDL enhances reverse cholesterol transport, has anti-oxidative, anti-inflammatory, anti-thrombotic, and vasso-protective effects. (91) The study found a significant decrease in HDL-C levels in patients with coronary heart disease (CHD) compared to controls, indicating an inverse association between HDL-C and cardiovascular risk. (92)(93) Recent study shows increased HDL-C levels 57% lessen CHD risk, but clinical guidelines prioritize LDL-C, non-HDL-C, and HDL-C as secondary targets in prevention, with goals varying by gender. (94)(95) LDL-C is crucial for CHD pathogenesis and lowering it in high-risk patients can reduce atherosclerosis progression, revascularization, and ischemic events, according to the National Cholesterol Education Program. (96)

Studies show a significant increase in TC/HDL-C in men and women aged 51-70, with plasma HDL cholesterol values and TC/HDL ratios being important coronary risk factors.(97) In a study evaluating the prognostic significance of several risk factors on the outcome of CHD in 639 cardiovascular disease-free subjects with heterozygous familial hypercholesterolemia (FH), it was found that a one-unit difference in LDL-C/HDL-C ratio was



associated with a 17% higher risk. (98) This study shows that LDL-C levels eight times more than HDL-C predicts an adverse CHD event, in patients with FH.

Smoking is more common in males due to societal norms and perceived manhood. This leads to a higher prevalence of smoking among males, a key risk factor for cardiovascular diseases (CHD), compared to females in Europe and Pakistan. (99) In the 20th century, 100 million people died the world over due to diseases caused by the use of excess tobacco, and it is projected that by 2030, one of every six individuals will die due to the deadly effects of smoking. Of these deaths, 50% are expected among the middle-age group (35-69 years).(100) The INTERHEART and other studies conducted in Pakistan have shown a linear relationship between the number of cigarettes smoked and CHD. Stress, hypertension, and diabetes increase the risk of MI in males, while females are less prone to these issues. Hypertension is a leading cause of CHD, while diabetes increases heart disease risk.

A Finnish study reveals that diabetic patients without a previous myocardial infarction have a similar risk of infarction compared to those without diabetes. (102) Diabetes increases vulnerability to coronary heart disease (CHD), with males having a higher risk due to hormonal changes. In Pakistan, 5.1% of newly diagnosed diabetics are males and 6.8% women. (103). Society's changing environment leads to dietary habits, with males being more active and resourceful. This leads to weight gain, obesity, and increased BMI, which is directly related to cardiovascular disease (CVD) and ischemic stroke. (104) the all above explains why dynamics of CHD in male population.

A 2008 study by Dr. Maciej Tomaszewski suggests that men's higher risk for heart disease may be due to specific effects of sex hormones. (105). The study found that females have a lower risk of CHD due to hormonal changes, with 78% of cases being male and 22% female. The study found that females are more likely to develop psychological problems and symptoms similar to CHD, leading to a higher number of female cases in suspected individuals. Normal cholesterol levels, not just elevated lipid profiles, also contribute to CHD. The study reveals that age increases the risk of coronary heart disease (CHD), with 87 cases between 40-70, and 69.7% of patients having elevated cholesterol levels. (106) The study analyzed 100 subjects with varying cholesterol and LDL levels, finding a strong positive correlation between HDL cholesterol and total cholesterol. The majority (93%) were diagnosed with CHD, indicating an increase in cases with age. CHD prevalence rates increase with LDL cholesterol level and decrease with HDL cholesterol, with low HDL cholesterol causing greater prevalence.

Our study consists on the people reported with CHD at RIC from Northern Areas of Pakistan and their Ethnicity is Mentioned in Table 6 & Figure 4 .i.e. 60% Punjabi, 20% Kashmiri, 17% Pathan and <1% other ethnic groups are diagnosed with CHD, the main reason behind this is that the people of the Provence Punjab have loss of physical activities, living in the cities and use of fast as well as junk foods, improper balance diet, busy life style all these conditions are more vulnerable to Cardiac diseases due to increase of Lipid profile while in the people of rural area are less prone to CHD due to strong physical efforts, fresh environment, use of green vegetables, climate, and good life style. The majority of the people of Pakistan live in rural areas (60%-65%); however, people are migrating to the large cities. According to a report on the national vision, more people will move to cities than to rural areas, and by 2030 Pakistan will become predominantly urban.(107) Pakistan's people face severe challenges such as lack of safe drinking water, food insecurity, and inadequate quality and affordable primary healthcare services.(108) This results in a poorly developed social protection net; an infrastructure shortfall, mainly in transport, energy, and irrigation; and inadequate delivery of social services.(109)(110) Besides these challenges, the continuous structural changes and dictated policies in Pakistani health systems have led to social inequalities and worsened health statistics in the world.

CONCLUSION

The findings from this study revalidate this scientific observation that there was a significant rise in the levels of TC and LDL-C in the patients that were confirmed with CHD when they were compared to the controls, and the level of HDL-C were low in most of the patients with CHD. It is confirmed by this study s study that Cholesterol and LDL have a strong positive relationship with CHD. As percentage of the disease was more in the age >45 years, it



is concluded that people are more prone to cardiac diseases due to elevation of lipid profile with the advancement of age.

RECOMMENDATION:

It is important to monitor the risk factors of CHD with the passage of age to reduce the occurrence of CHD, the main focus on the monitoring of Lipid profile after every 5 years of age. Modify the lifestyle measures like consumption of a proper diet along with regular physical exercise; and if required, cholesterol lowering therapy (e.g., statins) should be initiated in susceptible populations even though the levels may be well within the internationally desired levels.

REFERENCES

- 1. World Health Organization. Global Status Report on Noncommunicable Diseases 2014. Geneva, Switzerland: World Health Organization; 2014.
- 2. Ross R. Atherosclerosis- an inflammatory disease. N Engl J Med. 1999;340:2115-26.
- 3. Prospective Studies Collaboration. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet. 2007;370(9602):1829-1839.
- 4. Gordon DJ, Probstfield JL, Garrison RJ, Neaton JD, Castelli WP, Knoke JD, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation. 1989;79(1):8-15.
- 5. Law MR, Wald NJ, Rudnicka AR. Quantifying effect of statins on low-density lipoprotein cholesterol, ischaemic heart disease, and stroke: systematic review and meta-analysis. BMJ. 2003;326(7404):1423.
- 6. Dawber TR, Moore FE, Mann GV. Coronary heart disease in the Framingham study. Am J Public Health Nations Health. 1957;47:4–24.
- 7. Mann GV, Pearson G, Gordon T, Dawber TR, Lyell L, Shurtleff D. Diet and coronary heart disease in the Framingham study: I. Measurement of dietary intake. Am J Clin Nutr. 1962;11(3):200-225.
- 8. Anitschkow N. On experimental cholesterin steatosis and its significance in the origin of some pathological processes (1913). Arteriosclerosis. 1983;3:178-182.
- 9. Wang D, van der Horst K, Jacquier E, Afeiche M, Eldridge A. Snacking patterns in children: A comparison between Australia, China, Mexico, and the US. Nutrients. 2018;10(2):198.
- 10. Keast D, Fulgoni V, Nicklas T, O'Neil C. Food sources of energy and nutrients among children in the United States: National Health and Nutrition Examination Survey 2003–2006. Nutrients. 2013;5(1):283-301.
- 11. O'Neil C, Keast D, Fulgoni V, Nicklas T. Food sources of energy and nutrients among adults in the US: NHANES 2003–2006. Nutrients. 2012;4(12):2097-2120.
- 12. Shekelle RB, Stamler J. Dietary cholesterol and ischaemic heart disease. Lancet. 1989;1:1177–1179.
- 13. Kushi LH, Lew RA, Stare FJ, Ellison CR, El Lozy M, Bourke G, et al. Diet and 20-year mortality from coronary heart disease: the Ireland–Boston Diet–Heart Study. N Engl J Med. 1985;312(13):811-818.
- 14. Rong Y, Chen L, Zhu T, Song Y, Yu M, Shan Z, et al. Egg consumption and risk of coronary heart disease and stroke: dose-response meta-analysis of prospective cohort studies. BMJ. 2013;346:e8539.
- 15. Shin JY, Xun P, Nakamura Y, He K. Egg consumption in relation to risk of coronary heart disease and diabetes: a systematic review and meta-analysis. Am J Clin Nutr. 2013;98(1):146-159.



- 16. Virtanen JK, Mursu J, Virtanen HE, Fogelholm M, Salonen JT, Koskinen TT, et al. Associations of egg and cholesterol intakes with carotid intima-media thickness and risk of incident coronary heart disease according to apolipoprotein E phenotype in men: the Kuopio Ischaemic Heart Disease Risk Factor Study. Am J Clin Nutr. 2016;103(3):895-901.
- 17. Goldstein JL, Hazzard WR, Schrott HG, Bierman EL, Motulsky AG. Hyperlipidemia in coronary heart disease I. Lipid levels in 500 survivors of myocardial infarction. J Clin Invest. 1973;52(7):1533-1543.
- 18. Salel AF, Riggs K, Mason DT, Amsterdam EA, Zelis R. The importance of type IV hyperlipoproteinemia as a predisposing factor in coronary heart disease. Am J Med. 1974;57(6):897-903.
- 19. Heyden S, Heiss G, Hames CG, Bartel AG. Fasting triglycerides as predictors of total and CHD mortality in Evans County, Georgia. J Chronic Dis. 1980;33(5):275-282.
- 20. Kannel WB, Dawber TR, Friedman GD, Glennon WE, McNamara PM. Risk factors in coronary heart disease: an evaluation of several serum lipids as predictors of coronary heart disease: The Framingham Study. Ann Intern Med. 1964;61(5_Part_1):888-899.
- 21. Awan ZA, Baseer A. A Study of Serum Triglyceride and Lipoproteins Cholesterol in Coronary Heart Disease Patients. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 1995;45:263-265.
- 22. Awan ZA, Baseer A. A Study of Serum Triglyceride and Lipoproteins Cholesterol in Coronary Heart Disease Patients. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 1995;45:263-265.
- 23. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High-density lipoprotein as a protective factor against coronary heart disease: the Framingham Study. The American journal of medicine. 1977;62(5):707-714.
- 24. Naito HK. The association of serum lipids, lipoproteins, and apolipoproteins with Coronary Heart Disease assessed by coronary arteriography. Annals of the New York Academy of Sciences. 1985;454(1):230-238.
- 25. Shefique M, Mirza WB, Hussain S. Study of lipoproteins in patients of myocardial infarction in BV Hospital. Bahawalpur Pak. J. Med. Res. 1988;27:186-90.
- 26. Shefique M, Mirza WB, Hussain S. Study of lipoproteins in patients of myocardial infarction in BV Hospital. Bahawalpur Pak. J. Med. Res. 1988;27:186-90.
- 27. Pearson TA, Bulkley BH, Achuff SC, Kwiterovich PO, Gordis L. The association of low levels of HDL cholesterol and arteriographically defined Coronary Heart Disease. American journal of epidemiology. 1979;109(3):285-295.
- 28. Gordon T, Castelli WP, Hjortland MC, Kannel WB, Dawber TR. High-density lipoprotein as a protective factor against coronary heart disease: the Framingham Study. The American journal of medicine. 1977;62(5):707-714.
- 29. Anderson DW, Nichols AV, Pan SS, Lindgren FT. High-density lipoprotein distribution: resolution and determination of three major components in a normal population sample. Atherosclerosis. 1978;29(2):161-179.
- 30. Ascherio A, Willett WC. New directions in dietary studies of coronary heart disease. The Journal of nutrition. 1995;125(suppl_3):647S-655S.
- 31. Zilversmit DB. Atherogenic nature of triglycerides, postprandial lipidemia, and triglyceride-rich remnant lipoproteins. Clinical chemistry. 1995;41(1):153-158.
- 32. Awan ZA, Baseer A. A Study of Serum Triglyceride and Lipoproteins Cholesterol in Coronary Heart Disease Patients. JOURNAL-PAKISTAN MEDICAL ASSOCIATION. 1995;45:263-265.



- 33. National Health and Nutrition Examination Survey [PDF]. United States Center for Disease Control. Retrieved 28 January 2012.
- 34. Lecerf JM, De Lorgeril M. Dietary cholesterol: from physiology to cardiovascular risk. British Journal of Nutrition. 2011;106(1):6-14.
- 35. Goudev A, Kyurkchiev S, Gergova V, Karshelova E, Georgiev D, Atar D, et al. Reduced concentrations of soluble adhesion molecules after antioxidant supplementation in postmenopausal women with high cardiovascular risk profiles—a randomized double-blind study. Cardiology. 2000;94(4):227-232.
- 36. Soliman HA, El-Desouky MA, Hozayen WG, Ahmed RR, Khaliefa AK. Hepatoprotective effects of parsley, basil, and chicory aqueous extracts against dexamethasone-induced in experimental rats. Journal of intercultural ethnopharmacology. 2016;5(1):65.
- 37. Lee IM, Sesso HD, Oguma Y, Paffenbarger Jr RS. Relative intensity of physical activity and risk of coronary heart disease. Circulation. 2003;107(8):1110-1116.
- 38. Williams RR, Hunt SC, Heiss G, Province MA, Bensen JT, Higgins M, et al. Usefulness of cardiovascular family history data for population-based preventive medicine and medical research (the Health Family Tree Study and the NHLBI Family Heart Study). The American journal of cardiology. 2001;87(2):129-135.
- 39. Gaze PC. Clinical cardiology—a bedside approach.
- 40. Rifai N, Bachorik PS, Albers JJ. Lipids, lipoproteins and apolipoproteins. Tietz textbook of clinical chemistry.
- 41. Spieker LE, Sudano I, Hürlimann D, Lerch PG, Lang MG, Binggeli C, et al. High-density lipoprotein restores endothelial function in hypercholesterolemic men. Circulation. 2002;105(12):1399-1402.
- 42. Hague W, Forder P, Simes J, Hunt D, Tonkin A; LIPID Investigators. Effect of pravastatin on cardiovascular events and mortality in 1516 women with coronary heart disease: results from the Long-Term Intervention with Pravastatin in Ischemic Disease (LIPID) study. American heart journal. 2003;145(4):643-651.
- 43. Gupta S, Lakhani KK, Munshi H. A study of risk factors in young patients of acute coronary syndrome. International Journal of Contemporary Medical Research. 2017;4:2144-2147.
- 44. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). Executive summary of the third report of the National Cholesterol Education Program (NCEP) expert panel on detection, evaluation, and treatment of high blood cholesterol in adults. JAMA. 2001;285(19):2486.
- 45. Conte JV, Baumgartner WA, Dorman T, Owens SG. The Johns Hopkins Manual of Cardiac Surgical Care: Mobile Medicine Series. Elsevier Health Sciences. 2007.
- 46. Rahilly-Tierney C, Bowman TS, Djoussé L, Sesso HD, Gaziano JM. Change in high-density lipoprotein cholesterol and incident coronary heart disease in apparently healthy male physicians. The American journal of cardiology. 2008;102(12):1663-1667.
- 47. Singh IM, Shishehbor MH, Ansell BJ. High-density lipoprotein as a therapeutic target: a systematic review. JAMA. 2007;298(7):786-798.
- 48. Gaziano TA, Bitton A, Anand S, Abrahams-Gessel S, Murphy A. Growing epidemic of coronary heart disease in low- and middle-income countries. Current problems in cardiology. 2010;35(2):72-115.
- 49. Furberg CD, Goldberg RB, Howard BV, Stein JH, Witztum JL. Lipoprotein Management in Patients With Cardiometabolic Risk: Consensus statement from the American Diabetes Association and the American College of Cardiology Foundation. Diabetes Care. 2008;31(4):811.



- 50. Nazareth IAP, Vernekar SR, Gad RS, Naik GM. A Study of cholesterol percentage in blood tissue in the presence of salt.
- 51. Tanyanyiwa DM, Marais AD, Byrnes P, Jones S. The influence of ApoE genotype on the lipid profile and lipoproteins during normal pregnancy in a Southern African population. African health sciences. 2016;16(3):853-859.
- 52. Lewington S, Whitlock G, Clarke R, Sherliker P, Emberson J, Halsey J, et al. Blood cholesterol and vascular mortality by age, sex, and blood pressure: a meta-analysis of individual data from 61 prospective studies with 55,000 vascular deaths. Lancet. 2007;370(9602):1829-1839.
- 53. National Institutes of Health. National Heart, Lung and Blood Institute. Detection, Evaluation and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III) Final Report [PDF]. 1 September 2002. Retrieved 27 October 2008.
- 54. van der Steeg WA, Holme I, Boekholdt SM, Larsen ML, Lindahl C, Stroes ES, et al. High-density lipoprotein cholesterol, high-density lipoprotein particle size, and apolipoprotein AI: significance for cardiovascular risk: the IDEAL and EPIC-Norfolk studies. Journal of the American College of Cardiology. 2008;51(6):634-642.
- 55. Robinson JG, Wang S, Jacobson T. Meta-analysis of comparison of effectiveness of lowering apolipoprotein B versus low-density lipoprotein cholesterol and non-high-density lipoprotein cholesterol for cardiovascular risk reduction in randomized trials. The American journal of cardiology. 2012;110(10):1468-1476.
- 56. Kronmal RA, Kosinski AS, Mock MB. The relationship between cholesterol level and myocardial infarction or mortality risk in patients with Coronary Heart Disease: a report from the coronary artery surgery study (CASS) registry. Annals of epidemiology. 1992;2(1-2):129-136.
- 57. Lamon-Fava S, Wilson PW, Schaefer EJ. Impact of body mass index on coronary heart disease risk factors in men and women: the Framingham Offspring Study. Arteriosclerosis, thrombosis, and vascular biology. 1996;16(12):1509-1515.
- 58. Segrest JP, Jones MK, De Loof H, Dashti N. Structure of apolipoprotein B-100 in low-density lipoproteins. Journal of Lipid Research. 2001;42(9):1346-1367.
- 59. Campos H. LDL Particle Size Distribution. Arteriosclerosis, Thrombosis, and Vascular Biology. 1992;12(12):1410-1419.
- 60. Kumar V, Butcher SJ, Öörni K, Engelhardt P, Heikkonen J, Kaski K, et al. Three-dimensional cryoEM reconstruction of native LDL particles to 16Å resolution at physiological body temperature. PLoS One. 2011;6(5):e18841.
- Daphale A, Acharya S, Shukla S. Detection of Asymptomatic Coronary Heart Disease (CHD) in Newly detected Type 2 Diabetes Mellitus (DM) by Exercise Treadmill Test. Int J Contemp Med Res. 2017;4:2269-2275.
- Daphale A, Acharya S, Shukla S. Detection of Asymptomatic Coronary Heart Disease (CHD) in Newly detected Type 2 Diabetes Mellitus (DM) by Exercise Treadmill Test. Int J Contemp Med Res. 2017;4:2269-2275.
- 63. Bonow RO, Carabello BA, Chatterjee K, De Leon AC, Faxon DP, Freed MD, et al. ACC/AHA 2006 guidelines for the management of patients with valvular heart disease: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines (writing Committee to Revise the 1998 guidelines for the management of patients with valvular heart disease) developed in collaboration with the Society of Cardiovascular Anesthesiologists endorsed by the Society for Cardiovascular Angiography and Interventions and the Society of Thoracic Surgeons. J Am Coll Cardiol. 2006;48(3):e1-e148.



- 64. Nkomo VT, Gardin JM, Skelton TN, Gottdiener JS, Scott CG, Enriquez-Sarano M. Burden of valvular heart diseases: a population-based study. Lancet. 2006;368(9540):1005-1011.
- 65. Soliman GA. Dietary cholesterol and the lack of evidence in cardiovascular disease. Nutrients. 2018;10(6):780.
- 66. Daphale A, Acharya S, Shukla S. Detection of Asymptomatic Coronary Heart Disease (CHD) in Newly detected Type 2 Diabetes Mellitus (DM) by Exercise Treadmill Test. Int J Contemp Med Res. 2017;4:2269-2275.
- 67. Dubois C, Armand M, Mekki N, Portugal H, Pauli AM, Bernard PM, et al. Effects of increasing amounts of dietary cholesterol on postprandial lipemia and lipoproteins in human subjects. J Lipid Res. 1994;35(11):1993-2007.
- 68. Goldbourt U, Yaari S, Medalie JH. Isolated low HDL cholesterol as a risk factor for coronary heart disease mortality: a 21-year follow-up of 8000 men. Arterioscler Thromb Vasc Biol. 1997;17(1):107-113.
- 69. Assmann G, Cullen P, Schulte H. The Münster Heart Study (PROCAM). Results of follow-up at 8 years. Eur Heart J. 1998;19:A2-11.
- 70. Lamarche B, Despre JP, Moorjani S, Cantin B, Dagenais GR, Lupien PJ. Prevalence of dyslipidemic phenotypes in ischemic heart disease (prospective results from the Quebec cardiovascular study). Am J Cardiol. 1995;75(17):1189-1195.
- 71. Hippisley-Cox J, Coupland C, Vinogradova Y, Robson J, May M, Brindle P. Derivation and validation of QRISK, a new Coronary Heart Disease risk score for the United Kingdom: prospective open cohort study. BMJ. 2007;335(7611):136.
- 72. Robson J. Lipid modification: cardiovascular risk assessment and the modification of blood lipids for the primary and secondary prevention of cardiovascular disease. Heart. 2008;94(10):1331-1332.
- 73. Bibow S, Polyhach Y, Eichmann C, Chi CN, Kowal J, Albiez S, et al. Solution structure of discoidal high-density lipoprotein particles with a shortened apolipoprotein Al. Nat Struct Mol Biol. 2017;24(2):187.
- 74. Huang CX, Zhang YL. The target of regulating the ATP-binding cassette A1 protein (ABCA1): promoting ABCA1-mediated cholesterol efflux in different cells. Curr Pharm Biotechnol. 2013;14(6):623-631.
- 75. Ferri FF. Coronary Heart Disease. In: Ferri's Clinical Advisor 2016. Philadelphia, PA: Mosby Elsevier; 2016.
- 76. Coronary heart disease. National Lung, Heart, and Blood Institute. http://www.nhlbi.nih.gov/health/health-topics/topics/CHD. Accessed Oct. 12, 2015.
- 77. Usatine RP, et al., eds. Coronary Heart Disease. In: The Color Atlas of Family Medicine. 2nd ed. New York, NY: McGraw-Hill; 2013.
- 78. Understanding blood pressure readings. American Heart Association. http://www.heart.org/HEARTORG/Conditions/HighBloodPressure/AboutHighBloodPressure/Understanding-Blood-Pressure-Readings_UCM_301764_Article.jsp. Accessed Oct. 13, 2015.
- 79. Seventh report of the joint national committee on prevention, detection, evaluation, and treatment of high blood pressure. Bethesda, MD: National Heart, Lung, and Blood Institute. http://www.nhlbi.nih.gov/health-pro/guidelines/current/hypertension-jnc-7. Accessed Oct. 12, 2015.
- 80. Wilson PWF. Overview of the possible risk factors for cardiovascular disease. http://www.uptodate.com/home. Accessed Oct. 13, 2015.
- 81. Longo DL, et al. Ischemic heart disease. In: Harrison's Principles of Internal Medicine. 18th ed. New York, NY: The McGraw-Hill Companies; 2012.



- 82. Your guide to lowering your cholesterol with therapeutic lifestyle changes (TLC). National Heart, Lung, and Blood Institute.
- 83. Eckel RH, et al. 2013 AHA/ACC guideline on lifestyle management to reduce cardiovascular risk. Circulation. 2014;129:S76.
- 84. Franzese CJ, et al. Relation of fish oil supplementation to markers of atherothrombotic risk in patients with Coronary Heart Disease not receiving lipid-lowering therapy. Am J Cardiol. 2015;115:1204.
- 85. Omega-3 supplements: An introduction. National Center for Complementary and Alternative Medicine.
- 86. Laman Fava S, Wilson PW, Schaefer EJ. Impact of body mass index on coronary heart disease risk factors in men and women. The Framingham Offspring Study. Arterioscler Thromb Vasc Biol. 1996;16(12):1509-1515.
- 87. 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.
- 88. Werner M, Gabrielson DG, Eastman J. Ultramicro determination of serum triglycerides by bioluminescent assay. Clin Chem. 1981;27(2):268-271.
- 89. BeLue R, Okoror TA, Iwelunmor J, Taylor KD, Degboe AN, Agyemang C, Ogedegbe G. An overview of cardiovascular risk factor burden in sub-Saharan African countries: a socio-cultural perspective. Globalization and health. 2009;5(1):10.
- 90. Yusuf S, Hawken S, Ôunpuu S, Dans T, Avezum A, Lanas F, et al. Effect of potentially modifiable risk factors associated with myocardial infarction in 52 countries (the INTERHEART study): case-control study. The Lancet. 2004;364(9438):937-952.
- 91. Castelli WP, Anderson K, Wilson PW, Levy D. Lipids and risk of coronary heart disease The Framingham Study. Ann Epidemiol. 1992;2(1-2):23-28.
- 92. Gotto AM. Cholesterol intake and serum cholesterol level.
- 93. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for Coronary Heart Disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996;3(2):213-219.
- 94. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for Coronary Heart Disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996;3(2):213-219.
- 95. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for Coronary Heart Disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk. 1996;3(2):213-219.
- 96. Panagiotakos DB, Toutouzas PK. Importance of LDL/HDL cholesterol ratio as a predictor for coronary heart disease events in patients with heterozygous familial hypercholesterolaemia: a 15-year follow-up (1987-2002). Curr Med Res Opin. 2003;19(2):89-94.
- 97. Multiple Risk Factor Intervention Trial Research Group. Mortality rates after 10.5 years for participants in the Multiple Risk Factor Intervention Trial. Findings related to a priori hypotheses of the trial. JAMA. 1990;263(13):1795-1801.
- 98. Greenland P, Knoll MD, Stamler J, Neaton JD, Dyer AR, Garside DB, Wilson PW. Major risk factors as antecedents of fatal and nonfatal coronary heart disease events. JAMA. 2003;290(7):891-897.



- 99. Nishtar S, Bile KM, Ahmed A, Amjad S, Iqbal A. Integrated population-based surveillance of noncommunicable diseases: the Pakistan model. Am J Prev Med. 2005;29(5):102-106.
- 100. Nishtar S. Vision 2030 of the Planning Commission of Pakistan–strategic health imperatives. Heartfile. 2006;5:1-11.
- 101. Kannel WB, Schwartz MJ, McNamara PM. Blood pressure and risk of coronary heart disease: the Framingham study. Dis Chest. 1969;56(1):43-52.
- 102. Roger VL, American Heart Association Statistics Committee and Stroke Statistics Subcommittee. Heart disease and stroke statistics-2011 update: a report from the American Heart Association. Circulation. 2011;123:e18-e209.
- 103. Barolia R, Sayani AH. Risk factors of Coronary Heart Disease and its recommendations in Pakistani context. J Pak Med Assoc. 2017;67(11):1723.
- 104. BMJ 2013;347doi:http;//doi.org/10.1136/bmj.f5446 (Published 01 Oct 2013) Cite this as: BMJ 2013;347:f5446.
- 105. Samani NJ, Erdmann J, Hall AS, Hengstenberg C, Mangino M, Mayer B, et al. Genomewide association analysis of Coronary Heart Disease. N Engl J Med. 2007;357(5):443-453.
- 106. Kronmal RA, Kosinski AS, Mock MB. The relationship between cholesterol level and myocardial infarction or mortality risk in patients with Coronary Heart Disease: a report from the coronary artery surgery study (CASS) registry. Ann Epidemiol. 1992;2(1-2):129-136.
- 107. Nishtar S, Khalid F, Ikram A, Javad A, Jaffer H, Brown K, Badsha T. Protecting the poor against health impoverishment in Pakistan: Proof of concept of the potential within innovative web and mobile phone technologies. World Health Report. 2010;55.
- 108. Krishnadath IS, Jaddoe VW, Nahar-van Venrooij LM, Toelsie JR. Ethnic differences in prevalence and risk factors for hypertension in the Suriname Health Study: a cross-sectional population study. Popul Health Metrics. 2016;14(1):33.
- 109. Blas E, Kurup AS, eds. Equity, social determinants and public health programmes. World Health Organization. 2010.
- 110. Lim SS, Vos T, Flaxman AD, Danaei G, Shibuya K, Adair-Rohani H, et al. A comparative risk assessment of burden of disease and injury attributable to 67 risk factors and risk factor clusters in 21 regions, 1990–2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet. 2012;380(9859):2224-2260.