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Original Article

Regression Methods for Analyzing Risk Factors Causing Cardiovascular Disease in Muzaffarabad AJ&K, Pakistan

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Abstract

Background: The aim of the study was to determine the most likely risk factor of cardiovascular disease (CVD) and to model the prevalence of CVD in patients arriving at Abbas Institute of Medical Sciences hospital, Muzaffarabad Azad Kashmir, Pakistan.
Objective: This paper attempted to identify the significant risk factors associated with CVD in Muzaffarabad. A hospital-based, case- control study was conducted in Muzaffarabad Azad Kashmir, Pakistan, to identify the most significant risk factors that could expose the normal person to CVD as an individual and to predict the increased threat by mutual effect of risk factors like age, blood pressure, pulse rate, family history, diabetes and smoking. A total of 150 cases of coronary artery disease along with 250 controls were studied.
Methodology: Descriptive analysis was done and binary logistic regression carried out with goodness of fit test such as cox and Snell's test, likelihood ratio test and Chi-square test to detect the significant risk factors.
Results: The present analysis shows that for age group 60 and above the risk of CVD is higher as compared to other age groups. It is also projected that people with blood pressure (systolic) >140, pulse rate >120, diabetic and with positive family history are more likely to have cardio-vascular disease.
Conclusion: The present study concludes that in the presence of increased age, pulse rate, systolic blood pressure, diabetes and a family history of CVD there is 0.97 probability for a person to be a CVD patient.
Key words: Cardiovascular disease, binary logistic, case-control study, predicted probabilities.

Introduction

The CVD is a class of diseases; including the heart or blood vessels.[1] A population-based study carried between 1985 and 2009 revealed that in males residing in cities the mortality rate because of CVD was >34%.[2] A risk factor is generally defined as a trait of an individual that relates to the consequent development of a disease. Internationally documented major risk factors for CVD includes age, family history, smoking, obesity, unhealthy diet, lack of physical activity, dyslipidemia, hypertension and diabetes.[3] The other risk factors for CVD are Hyperlipidemea, cold sweating, orthopnea, use of cooking oil and angina.[4] Smoking is a major risk factor for CVD and the second common cause for CVD mortality is hypertension. High blood glucose, lack of physical activity, obesity and elevated cholesterol levels are other leading cause of mortality due to CVD and according to the existing literature smoking has an important part to play.

Smoking is more common among men and in lower socioeconomic classes, appearing concomitantly with other harmful health behavior.[5] According to the British Heart Foundation, smokers are said to have more threat of dying of a heart attack. Those who are less than 40 years of age having history of smoking would have five times greater probability of heart attacks. Males also have a two to five times higher risk of CVD.[6] These factors are the reasons of imbalance in life expectancy for both sexes. In Finland, for instance, life expectancy is 77.5 for males and 83.4 years for females.[7] The effect of smoking on one's CVD risk parameters such as cholesterol and blood pressure (B.P) seems to be clinically less significant for

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Authors Contribution

TK conceptualized the project. IH & SA did the data collection. SM & MF did the literature search. Statistical analysis was also done by TK & SM. MF also did the drafting, revision & writing of manuscript.

people aged 46years.[8] Between 1980 and 1993 the death rate for CVD declined steadily because of improved medical treatments. Approximately 75-80% deaths in adult diabetic patients are due to CVD. One of the independent risks for both men and women is obesity.

A study on the cardio-metabolic and psychological variations following weight loss in a cohort of overweight adults has revealed that hypertension and serum triglyceride levels decreased in weight losers.[9] The fundamental genetic mechanisms may be blamed for hypertension and kidney disease in African Americans. The outcomes of scientific trials showed that the decrease use of sweetened beverages was a major way for decreasing CVD in African Americans.[10] The role of the potential cardio protecting properties of diet is moderately fresh, with most applicable studies completed in the recent past.[11] The special properties of omega-3 fatty acids on serum markers and CVD risk factor have been evaluated. Greater fish oil use has been associated with a decreased CVD risk, however the apparatuses are unclear. Plant-source oil omega-3 fatty acids have also been studied concerning their CVD effect.[12] Diabetes is a strong independent risk factor for CVD mortality in Japanese–American men and women. Hyperglycemia is associated with CVD mortality in diabetic subjects.[13] Sleeping duration can be an important indicator of CVD. A study on a representative sample of US adults has reported that there is an association between both shorter and longer sleep durations and CVD.[14] Pakistan stands in countries having higher risk of CVD in the world. In Pakistan 30-40% of all the mortalities are because of CVD. Nearly 200,000 deaths per year are reported in Pakistan due to CVD. The current study was conducted to identify the risk factors causing CVD and to model the prevalence of CVD in patients arriving at the Abbas Institute of Medical Sciences Muzaffarabad hospital in Pakistan. The logistic regression analysis was done to measure the degree of association of CVD with different risk factors and odd ratios were calculated to observe this association. Cox and Snell R-square and Negelerkerk R-square was used to check the variability in the dependent variable due to independent variable.

Methodology

A sample of 150 patients was selected. Demographic as well as health related information was collected for both Cases and Controls. All computations were carried out in SPSS version 17. For each patient, the phenomenon of CVD was studied against different risk factors namely gender, age, pulse rate, blood pressure, family history of CVD, diabetes and smoking.

Researchers in medical field perform different statistical analysis on the data obtained from patients for a medical study of their interest. The most widely used statistical technique for this purpose is regression analysis introduced by Frances Galton (1822-1911).[15] In this study, we have used different multivariate techniques to fulfill the objectives. We have used Chi-Square, and binary logistic regression.

The logistic regression has been proposed here for use in the analysis of a dichotomous variable. In the logistic regression model the quantity $\pi(x) = E(Y|X)$ represents the conditional mean of Y given x. The specific form of the logistic regression model is:

$$\pi(x) = \frac{e^{\beta_0 + \beta_1 x}}{1 + e^{\beta_0 + \beta_1 x}} \qquad (1)$$

So,

$$g(x) = In\left[\frac{\pi(x)}{1-\pi(x)}\right]$$
$$= \beta_0 + \beta_1 x$$

This transformation is known as logit transformation. The logit, g(x) is linear in parameters.

The probable risk factors among all were identified in logistic regression analysis. At first step, a univariate logistic regression analysis was performed by considering each risk factor as single and independent variable. The significant risk factors were identified based on Wald statistic and likelihood ratio test, Cox and Snell R^2 and Nagelkerke R^2. At the second step, all factors were used in multiple logistic regression model. The significant risk factors were identified based on Cox and Snell R^2, Nagelkerke R^2 and odds ratios. For categorical predictors, first category was considered as the reference and its comparison was made with the rest of the categories. The study sample used in the present research includes patients who visited the hospital (Abbas Institute of medical sciences Muzaffarabad, Pakistan) during 2017. It was a case-control study. The sample consists of 400 patients. A total of 150 patients with significant CVD were regarded as cases whereas 250 patients without significant CVD were taken as controls.

The risk factors for CVD and the scores assigned to them included, gender (male=1, female=0), age (>40= 0, 40-49=1, 50-59=2, 60 and above=3), pulse rate (55-70=0, 71-85=1, above 86=2), systolic (>120=0, 120-140=1, 140 and above=2), diastolic (60-70=0, 71-80=1, 81-90=2, 91-100=3), family history (yes=0, no=1), diabetes (yes=0, no=1), smoking (yes=0, no=1). The criteria for the risk factors identification was based on standard procedures. Sphygmomanometer was used for checking blood pressure (normal range 120/80 mmHg).Pulse was manually checked (radial pulse normal range 72 to 80/ min). Blood sugar was checked by Glucometer (Accu check) (normal range fasting blood sugar <100mg/ dl, 02hrs after meal < than 140mg/dl).

The logistic regression model for the 5 above mentioned indicator variables can be written as:

X_1 = age X_2 =pulse X_3 =systolic X_4 =family history X_5 = diabetes

Results

Results are presented in Tables 1-7. Table-1 show the descriptive statistics of different factors. Table-2 demonstrates Pearson chi-square test used for checking the association between risk factors gender, age, blood pressure, pulse rate, diastolic, family history, diabetes and smoking with disease (CVD) at 5% level of significance.

Table 2: Strength of association between risk factors and cardiovascular disease (CVD).

Factors	*Pearson Chi-square*	*df*	*p-value*
Gender	3.184	1	0.074
Age	49.115	3	0.000
Pulse rate	28.019	2	0.000
Blood pressure	43.446	2	0.000
diastolic	4.030	3	0.258
Family history	59.553	1	0.000
Diabetes	61.110	1	0.000
Smoking	19.045	1	0.080

Table-3 illustrates the Wald test as a test of significance of risk factors according to disease (CVD). Table-4 shows the significance of risk factors checked by Cox and Snell R^2, Nagelkerke R^2 and log likelihood. In second stage multiple logistic regression analysis is carried out to determin the risk factors with CVD.

Table 1: Descriptive analysis of risk factors of cardiovascular disease (CVD).

Factors		*Frequency*	*Percentages*	*Mean*	*SD*
Gender	Male	85	56.7	0.5667	0.49720
	Female	65	43.3		
Age	>40	33	22.0	2.6667	1.17962
	40-49	38	25.3		
	50-59	25	16.7		
	60 and above	54	36.0		
Pulse rate	55-70	29	19.3	2.2267	0.75215
	71-85	58	38.7		
	Above 86	63	42.0		
Systolic	>120	32	21.3	2.2533	0.78737
	120-140	48	32.0		
	140 and above	70	46.7		
Diastolic	60-70	34	22.7	1.3800	0.98764
	71-80	46	30.7		
	81-90	49	32.7		
	91-100	21	14.0		
Family history	Yes	92	61.3	0.6133	0.48862
	No	58	38.7		
Diabetes	Yes	95	63.3	0.6333	0.48351
	No	55	36.7		
Smoking	Yes	55	36.7	0.3667	0.48351
	No	95	63.3		

Table 3: Set of independent variables in equation.

Factors	*Coefficients (B)*	*S.E*	*Wald*	*d.f*	*p-value*
Age	0.607	0.119	25.824	1	0.000
Pulse	0.536	0.173	9.642	1	0.002
Systolic	0.610	0.168	13.234	1	0.000
Family history	1.637	0.270	36.738	1	0.000
Diabetes	1.488	2.268	30.721	1	0.000
Constant	-5.447	0.594	83.967	1	0.000

Table 4: Significance of risk factors in the causation of cardiovascular disease.

-2log likelihood	*Cox and Snell R^2*	*Nagelkerke R^2*
355.023	0.353	0.481

Table 5-7 illustrates odds ratios for multiple logistic regression, the significance of risk factors identified based on Cox and Snell R^2, Nagelkerke R^2 and the predicted probabilities of developing CVD according to the risk factors. The results for association between various risk factors and CVD are provided in appendix. Table-1 presents the percentages, mean and standard deviation (SD) of various risk factors of CVD which are gender, age, pulse rate, Systolic BP, Diastolic BP, family history of CVD, Diabetes and smoking.

Table 5: The odds ratios for multiple logistic regression.

	Model				
Variable	*1*	*2*	*3*	*4*	*5*
Age					
Less than 40	1	1	1	1	1
40-49	1.914	1.893	1.589	1.642	1.867
50-59	3.883	3.650	3.399	2.876	2.867
60 and above	6.940	6.452	5.458	5.862	6.839
Pulse					
55 to 70		1	1	1	1
71 to 85		2.040	1.976	2.156	2.240
Above 86		3.847	3.022	3.323	2.986
Systolic					
<120			1	1	1
120-140			1.874	1.707	1.747
>140			4.128	3.946	3.434
Family history					
No				1	1
Yes				5.618	5.230
Diabeties					
No					1
Yes					4.508

Table-2 shows that Based on Pearson Chi square there is an association between disease(CVD) and age, pulse rate, (systolic) blood pressure family history and diabetes. However, there is no association between disease (CVD) and diastolic BP and smoking. Table 3 presents the results of full set independent variables including age, pulse rate, family history, diabetes and Systolic BP with 1 degree of freedom. Significant results have been obtained for age group with a co-efficient for 0.607 and a Wald test value of 25.824. The coefficient of pulse, systolic blood pressure, family history and diabetes are 0.536, 0.610, 1.637 and 1.488 respectively with Wald test 9.642, 13.234, 36.738 and 30.721 respectively and highly significant.

Table 6: The results of Cox and Snell R-square.

	Models				
	1	*2*	*3*	*4*	*5*
Cox & Snell R^2	0.116	0.163	0.211	0.300	0.355
Nagelkerke R^2	0.159	0.223	0.287	0.409	0.484

The Table-4 displays the values of Cox and Snell R-square, Nagelkerke R-square and log likelihood. The Cox and Snell reveal a 35% variation in dependent variable due to the independent variable. Similarly, the values of Nagelkerke reveals that there is 48% variation in dependent variable due to the independent variable.

The Table-5 presents the odds ratios from multivariate logistic regression model of the likelihood of CVD in the patients. Model1 examines the likelihood of CVD within the age group of the patients. It is observed that the age group 60 and above is 6.940 times more likely to have CVD than the patients who are <40 years. It also shows that the patients with age group 50-59 years is 3.883 times more likely to have CVD than the patients who are <40, the odd ratios of age group as well as pulse rates of the patients is also presented. It is observed that patients with pulse rate (>86) are 3.847 times and patients with pulse rate 71-85 are 2.04 times more likely to have CVD as compared to patients of pulse rate 55-70. The trend of association of age group with the CVD is the same as in model 1. In model 3 there are three variables (age, pulse rate and systolic). The odd ratio reveals that the patients having systolic BP of >140 are 4.128 time more likely to have CVD than the patients with a systolic B.P of 120. Similarly having

Table 7: Predicted probabilities according to risk factors.

Pulse	Age	*(B.P) Systolic Less than 120*				*(B.P) Systolic 120-140*				*(B.P) Systolic Above 140*			
		Diabetes				*Diabetes*				*Diabetes*			
		No		*yes*		*No*		*yes*		*No*		*yes*	
		Family history				*Family history*				*Family history*			
		No	*Yes*	*No*	*Yes*	*No*	*Yes*	*No*	*Yes*	*No*	*Yes*	*No*	*Yes*
55-70	<40	0.0242	0.1133	0.0992	0.3614	0.0437	0.1904	0.1685	0.5102	0.0777	0.3022	0.2717	0.0572
	40-49	0.0436	0.1900	0.1681	0.5094	0.0774	0.3015	0.2711	0.6565	0.1339	0.4428	0.4064	0.7787
	50-59	0.0772	0.3009	0.2705	0.6558	0.1335	0.4420	0.4056	0.7750	0.2209	0.5931	0.5568	0.8659
	Above60	0.1331	0.4412	0.4049	0.7776	0.2204	0.5924	0.5560	0.8655	0.3423	0.7279	0.6974	0.9222
71-85	<40	0.0407	0.1793	0.1584	0.4917	0.0725	0.2867	0.2573	0.6403	0.1258	0.4256	0.3894	0.7662
	40-49	0.0723	0.2861	0.2567	0.6396	0.1255	0.4245	0.3886	0.7656	0.2089	0.5759	0.5392	0.8574
	50-59	0.1250	0.4238	0.3879	0.7651	0.2084	0.5751	0.5384	0.8570	0.3265	0.7136	0.6822	0.9169
	Above60	0.2080	0.5744	0.5376	0.8566	0.3258	0.7130	0.6815	0.9166	0.4708	0.8205	0.7975	0.9529
>85	<40	0.0677	0.2719	0.2434	0.6231	0.1179	0.4073	0.3719	0.7526	0.1975	0.5585	0.5215	0.8485
	40-49	0.1176	0.4066	0.3712	0.7521	0.1970	0.5577	0.5207	0.8481	0.3110	0.6989	0.6672	0.9113
	50-59	0.1695	0.5570	0.5199	0.8477	0.3104	0.6982	0.6059	0.9110	0.4531	0.8098	0.7875	0.9496
	Above60	0.3098	0.6976	0.6652	0.9108	0.4523	0.8093	0.7853	0.9495	0.6032	0.8866	0.8707	0.9719

a systolic B.P of 120 mmHg to 140 mmHg has less chances (1.874) of having CVD In model 4 there are 4 variables i.e., (age, pulse, systolic and family history). Patients who have CVD in their family history have 5.618 times more chances of disease as compared to those who do not have a positive family history. In model.5 there are 5 variables (age, pulse rate, systolic, family history and diabetes). Diabetic patients have greater chance of CVD .Odd ratios for age, pulse, systolic and family history of CVD was increased. This is the indication of strong association between these variables.

Table-6 shows that for model 1, 2, 3, 4 & 5 the Cox and Snell R-square values reveals variation of 11%, 16%, 21%, 30% and 30% respectively in independent variable due to an independent variable. The value of Nagelkerke R-square reveals that for model 1, 2, 3, 4 & 5 there is 15%, 22%, 28%, 40% and 48% variation in the dependent variable due to independent variable.

The results of Table-7 displays that in patients <40 yrs of age, having BP of <120 mmHg, pulse rate 55 to 70, non-diabetic and having no family history of CVD the probability of developing CVD was 0.02426. It can also be seen that as the B.P of the patient increases the probability of CVD also increases. Patients with systolic BP >140, known diabetics and having a CVD positive family history have greater (0.6572) probability of developing CVD, whereas it was lower (0.3614) when the B.P was less than 120. It is also observed that diabetes and, CVD positive family history in relation with B.P played an important role in the potential risk of developing cardiovascular disease. Results shows age as the most determinant factor for the CVD. About 50% & 80% increase in the probability of CVD is noted in patients who were ≥ 60 non-diabetics and having negative CVD family history although the pulse rate was 55 to 70. However an increase (0.2080) in the probability of CVD is observed in patients with pulse rate of 71-85/min. According to Table-7 there is 0.7975 times. probability for CVD in patients who are ≥60 years of age having a systolic BP >140 and non diabetic. The probability of developing CVD in diabetic patients with age less than 40 and a positive CVD family history increased from 0.6231 to 0.7662 when the B.P raised from <120 to >140.

It is also observed that the predicted probabilities were 0.9108 and 0.9719 respectively for diabetic patients with ≥60 years of age having B.P of <120 & >140 pulse rate of >86 and a positive family history of CVD.

Discussion

In the recent past CVD has been widely researched. There are many risk factors associated with CVD. The CVD accounts for >17 million deaths globally each year, of which more than 10% are estimated to be caused by cigarette smoking.[16,17] The risk of heart attack doubles for age 55 and above. The risk of stroke raises up several times, for a person having high blood pressure along with smoking, obesity and high blood cholesterol or diabetes.[18] However, where about one-quarter of all cardiovascular disease deaths occurred in persons who were <70 years of age in the developed world, more than half of these deaths occurred in those <70 years in the developing world.[19,20]

In current study for each patient the phenomena of CVD were studied in relation to different risk factors namely age, gender, pulse rate, blood pressure, family history of CVD, diabetes and smoking. We found that there is a significantly strong association between age, pulse rate, blood pressure(systolic), family history and diabeties. In the past similar results have been reported by other studies. Marcello and Viviane have concluded in their study that diabetes should be regarded solely as the tradional risk factor. Age, blood pressure, & family history were amongst the other conditions that increased the CVD risk.[21] Similar results have also been reported in a hospital based study in Faisalabad region where gender family history, hypertension, diabetes were reported as the risk factors for CVD.[4]

The present research findings also confirmed that diabetes and family history in relation with B.P played a significant role in causing CVD. Martin et al in a review article reported that the major cause of morbidity and mortality in diabetes is cardiovascular disease, which is exacerbated by hypertension.[22]

We have found that there is an association between disease (CVD) pulse rate, (systolic) blood pressure family history and diabetes however there is no association between disease (CVD), diastolic BP and smoking for Muzaffarabad region. Systolic blood pressure has been reported to be more harmful as compared to diastolic by Kannel et al in the data obtained for the Framingham study.[23] In our study no significant association was found between smoking and CVD. Smoking has been frequently reported to be an independent risk factor for CVD in many studies.[5-8,17] The different findings in our study could be due to the use of different criteria for defining cigarette smoking.

The overweight and obesity throughout adolescence are related with a greater risk for CVD. The outcomes of a national revision indicate that US youths carry high prevalence of CVD risk factors, especially those who are overweight or obese.[24]

Finally, on basis of the findings of the present study conducted on a random sample of 400 people we conclude that age, pulse rate, systolic blood pressure, diabetes and a family history of CVD plays an important role in developing CVD.

Conflict of interest: None declared.

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