Understanding Cardiovascular Disease Risk Factors in the Pakistani Population: A Comparative Analysis of Newly Diagnosed versus Previously Diagnosed Patients

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Abstract- cardiovascular diseases (CVDs) stand as the leading cause of mortality worldwide, with approximately 17.9 million deaths attributed to CVD annually. In Pakistan, CVDs accounted for over 16% of deaths in 2020, ranking the country 30th globally with a death rate of 193.56 per 100,000 people. While research predominantly originates from Western countries, the variability in lifestyle, genetics, and living standards among populations underscores the necessity of gathering local data to assess CVD risk factors accurately. Consequently, a cross-sectional study was conducted within the Pakistani population to explore the associated risk factors for CVD. The study encompassed CVD patients as the case group and a healthy cohort from the Pakistani population as the control group. Further categorization of CVD patients into newly diagnosed (NDCVD) and previously diagnosed (PDCVD) subgroups was conducted. Informed consent was obtained from all participants, who underwent a brief interview to complete a questionnaire on personal information and medical history. Following WHO guidelines, intravenous blood samples were drawn from all subjects after 10 to 12 hours of fasting for lipid profile analysis, including total cholesterol (TC), triglyceride (TG) and HDL cholesterol (HDL-C) level. Statistical analysis was performed on the data obtained through the questionnaire and lipid profile analysis. A total of 2,497 participants were enrolled, comprising 715 NDCVD patients, 927 PDCVD patients, and 855 healthy individuals as the control group. Notably, the study unveils a concerning trend with a mean age of 47.5 years among newly diagnosed CVD patients. Significant disparities were observed in smoking habits and BMI across all three distinguished groups. Additionally, newly diagnosed CVD patients exhibited lower physical activity levels, higher consumption of street food, and a higher prevalence of dyslipidemia compared to previously diagnosed CVD patients and the control group. Moreover, there was a notable increase in the proportion of females affected by CVD over time. These findings underscore the imperative for tailored interventions and continued research efforts to address the evolving landscape of CVD within the Pakistani population.

Index Terms- Cardiovascular Disease, Diabetes, Dyslipidemia, Hypertension

I. INTRODUCTION

Cardiovascular diseases (CVDs) are the leading cause of death worldwide, responsible for about a third of all deaths annually [1]. Low- and middle-income countries (LMICs) bear a disproportionate burden of CVDs, with 80% of deaths occurring in these regions [2]. In Pakistan, CVDs accounted for over 16% of deaths in 2020, with a death rate of 193.56 per 100,000 people, ranking the country 30th globally [3, 4].

CVDs can be caused by modifiable factors like diet, smoking, and exercise, as well as non-modifiable factors such as genetics and age[5]. Biomedical risk factors like hypertension, dyslipidemia, and diabetes also contribute significantly to CVD risk [6]. Dyslipidemia involves elevated triglycerides (TG), LDL cholesterol (LDL-C), total cholesterol (TC), or decreased HDL cholesterol (HDL-C) [7]. Normal values are TG<150 mg/dl, TC<200 mg/dl, LDL-C<100 mg/dl, and HDL-C>40 mg/dl [8].

Research predominantly from Western countries informs our understanding of CVD risk factors, but factors like lifestyle, genetics, and standards of living vary between populations. Therefore, it's crucial to gather local data when assessing CVD risk factors for a specific population. This study aims to provide insights into the prevalence and patterns of CVD risk factors among newly and previously diagnosed CVD patients compared to the healthy population in Pakistan. This study also compares CVD risk factors between newly and previously diagnosed CVD patients, offering insights into whether there's any improvement in these risk factors over time. Accurate knowledge and early intervention are essential for reducing the likelihood of CVD in at-risk populations.

II. METHODOLOGY

A. Ethics

This study was approved by the ethical committee of the Institute of Microbiology and Molecular Genetics.

B. Study Design and Subject Selection

A cross-sectional study investigated risk factors for early onset CVD in the Pakistani population. CVD patients formed the case group, while a healthy Pakistani cohort comprised the control group. Patients were categorized into NDCVD and PDCVD subgroups. NDCVD patients presented symptoms and abnormal ECG findings, confirmed by cardiologists, while PDCVD patients had prior CVD incidents and were on lipid-lowering

medication. Participants were randomly selected from hospitals in Lahore, drawing individuals nationwide. Inclusion criteria specified symptoms and diagnostic confirmation by cardiologist for NDCVD and prior CVD incidents for PDCVD. Exclusion criteria included congenital heart disease, familial hypercholesterolemia, malignancy, infections, and pregnancy. Patients on lipid-lowering medication were excluded from the NDCVD and control groups.

C. Data and Blood Collection

Informed consent was obtained from all subjects in the study. A questionnaire covering personal information and medical history was completed through brief interviews with each participant. Intravenous blood was drawn from all subjects following WHO guidelines after 10 to 12 hours of fasting. After blood collection in a gel vial, centrifugation at 4000 rpm for 5 minutes separated the serum for lipid parameter measurement.

D. Estimation Of Lipid Profile

A Microlab 300 chemistry analyser was used to measure lipid profiles, including TG, TC, LDL-C, and HDL-C by using commercially available kits (Human Diagnostics). LDL cholesterol (LDL-C) was measured using the Friedwald formula if TG was less than or equal to 300 mg/dl; otherwise, an enzymatic homogenous assay was used to measure it [9].

E. Statistical Analysis

Data analysis was conducted using Microsoft Excel and SPSS. Information from questionnaires and lipid profiles was presented as percentages and means ± standard deviations. The t-test and one-way analysis of variance (ANOVA) were employed to compare quantitative data between groups, while the chi-square test for independence was used to compare qualitative data. A p-value < 0.05 was considered statistically significant for all analyses.

III. RESULTS

A. Demographic And Biomedical Characteristics of Candidates from Each Distinguished Group

In this study, 2,497 participants were enrolled, including 715 NDCVD patients, 927 PDCVD patients, and 855 healthy controls. NDCVD patients were younger (mean age 47.5 ± 12.2 years) compared to PDCVD patients (mean age 57.4 ± 11.0 years) and controls (mean age 46.4 ± 12.8 years). NDCVD patients had higher male representation (59.7%) than females (40.3%), while PDCVD patients had 66.5% males and 33.5% females, and controls had 55.4% males and 44.6% females. NDCVD patients had higher BMI (28.8 ± 6.1 kg/m2) compared to PDCVD patients (27.8 ± 5.9 kg/m2) and controls (27.9 ± 6.5 kg/m2). NDCVD patients were less physically active and consumed street food more frequently. Both CVD patient groups exhibited higher rates of diabetes, hypertension, and family history of CVD compared to controls. Smoking prevalence was also higher in CVD patients compared to controls. Significant differences were observed among groups in various demographic and clinical characteristics. See Table 1 for details.

B. Details Of Lipid Profile of Individuals Having Dyslipidemia from Each Distinguished Group

NDCVD patients exhibited higher levels of lipid parameters compared to PDCVD patients and controls. Mean TG, TC, and LDL-C levels were significantly elevated in NDCVD patients compared to the other groups. HDL-C levels were similar among groups, but PDCVD patients had a significantly lower HDL-C level compared to controls. The TC/HDL-C ratio was highest in NDCVD patients, indicating unfavorable lipid profiles. Significant differences were observed in TC/HDL-C ratios among the three groups. See Table 2 for a detailed comparison of lipid profiles.

C. Percentage Of Individuals Having Dyslipidemia from Each Distinguished Group

A large proportion of NDCVD patients exhibited dyslipidemia compared to PDCVD patients and controls. Among NDCVD patients, 73.4% had increased TG levels, 46.6% had hypercholesterolemia, 40.8% had elevated LDL-C levels, and 60.7% had lower than desirable HDL-C levels. Moreover, 57.5% of NDCVD patients had a Total Cholesterol/HDL-C ratio above desirable levels. In comparison, fewer PDCVD patients and controls showed dyslipidemia. See Table 3 for detailed percentages of dyslipidemia among the groups.

IV. DISCUSSION

The rising incidence of CVD is a global concern, specifically affecting younger populations due to various risk factors like genetics, sedentary lifestyles, and poor diet. This study offers real-time insights into the risk factors associated with cardiovascular diseases (CVD) within the Pakistani population. In Pakistan, there's a lack of comprehensive studies comparing risk factors among NDCVD and PDCVD patients. This study aimed to fill this gap by dividing CVD patients into two groups to understand current risk factors better. Notably, the mean age of NDCVD patients was 47.5 years, indicating a departure from the typical onset age and suggesting longer disease burden potential. The study also found no significant age difference between NDCVD patients and the control group, highlighting that CVD can affect individuals of any age. Conversely, PDCVD patients, despite their prior CVD experience, had an average age of 57.4 years, which is also relatively a younger age for previous CVD patients, indicating a shift towards earlier instances of CVD in Pakistan.

BMI is commonly used to estimate body fat and assess the risk of CVD. However, it doesn't directly measure body fat but rather evaluates fitness levels based on weight and height. Its relationship with CVD risk varies among populations. Some studies support BMI as a strong predictor for CVD, while others challenge its independent predictive capability [10, 11]. In the current study, BMI didn't show a notable difference between CVD patients and control groups. Surprisingly, all groups fell into the obese category, suggesting BMI alone might not reliably predict CVD in Pakistani population. This highlights a concerning trend of obesity prevalence in Pakistan.

A sedentary lifestyle increases the risk of CVD. Current research highlights lower physical activity levels in NDCVD patients compared to controls, indicating its role as a risk factor. Regular exercise positively impacts heart health by improving various functions like myocardial contraction and endothelial function, controlling blood pressure and diabetes, regulating blood lipid levels, and managing weight [12, 13]. It also reduces stress,

which is beneficial for heart health [14]. Many previous studies suggest higher physical activity reduces CVD risk [15, 16]. According to current study, patients with previous CVD diagnoses tend to have higher activity levels, likely due to medical recommendations. However, many remain inactive, facing barriers like physical discomfort or work commitments. Healthcare professionals need to educate CVD patients about the importance of exercise for their health.

Unhealthy food consumption is a significant risk factor for onset of CVD. Among the groups studied, a higher percentage of NDCVD patients reported consuming more street food, which often contains high levels of trans fats, saturated fats, sodium, and added sugars—key contributors to heart disease risk [17]. These foods are linked to diabetes, obesity, high blood pressure, and harmful cholesterol levels, all increasing the risk of CVD. Ultra-processed foods, including street food, are associated with higher morbidity and mortality rates due to CVD [18]. Interestingly, PDCVD patients showed a decrease in street food consumption, likely as a conscious effort to reduce complications. This behavior change aligns with findings from previous research [19].

Current study also showed a significant difference in diabetes prevalence between NDCVD patients and the control group, with a higher percentage of diabetic individuals in the former. Diabetes and CVD are intricately linked due to factors like endothelial dysfunction, inflammation, and insulin resistance [20]. High blood sugar levels can damage blood vessels and increase the risk of atherosclerosis and elevated lipid levels, further elevating the risk of CVD [21, 22]. Complications like microangiopathy and cardiac autonomic neuropathy contribute to the onset of CVD in diabetic individuals [23]. Oxidative stress, triggered by hyperglycemia, exacerbates inflammation and fibrosis, accelerating CVD progression [24]. The bidirectional relationship between CVD and diabetes was evident, with a higher prevalence of diabetes among PDCVD patients. Stress was identified as a potential instigator of diabetes in CVD patients, triggering hormonal changes and inflammation that contribute to insulin resistance. Understanding these connections sheds light on how CVD can lead to diabetes and vice versa. Additionally, dyslipidemia, particularly low levels of high-density lipoproteins (HDL-C), increases diabetes risk among CVD patients, as observed in the study.

High blood pressure is also a significant risk factor for the onset of CVD globally, as evidenced by the current study. Compared to healthy individuals, both NDCVD and PDCVD patients have a higher percentage of hypertensive individuals. Hypertension increases the workload on the heart, damaging blood vessels over time and raising the risk of plaque buildup and atherosclerosis, which can hinder blood flow to vital organs [25]. Genetics also play a role, with specific variants linked to higher blood pressure levels and increased risk of CVD [26]. In Pakistan, the prevalence of hypertension has increased over the years, with a significant percentage of the population affected, highlighting the importance of addressing this risk factor [27, 28].

The study found no significant difference in smoking habits between NDCVD patients and the control group, but a notably higher percentage of PDCVD patients had a history of smoking. However, it's important to note that smoking rates in Pakistan have declined over time, and societal stigma around smoking may affect the accuracy of self-reported habits. Family history of CVD showed a significant difference between CVD patients and the healthy population, with both newly and previously diagnosed CVD patients demonstrating a strong family history of CVD compared to controls. The family history of CVD, especially in younger individuals, is a strong predictor of future early onset CVD episodes. Relatives of CVD patients have a heightened risk of developing CVD, emphasizing the importance of ongoing efforts to reduce risk factors in these individuals. Previous research, including studies in the Pakistani population, supports this association [29].

Dyslipidemia, characterized by imbalanced lipid parameters like TG, TC, and LDL-C, is a significant risk factor for the onset of CVD. NDCVD patients exhibited significantly elevated levels of TG, TC, and LDL-C compared to the control group. This elevation in lipid levels is often associated with sedentary lifestyles, poor dietary habits, and lack of physical activity, where excessive calorie intake exceeds the body's ability to burn. High consumption of sugars and saturated fats contributes to increased TG and cholesterol levels [30]. Elevated TG levels, especially prominent among NDCVD patients, can lead to lipid deposition in blood vessels, forming plaque and narrowing arteries. This increases the risk of cardiovascular events like heart attacks and strokes. Furthermore, high TG levels can affect blood clotting factors, promoting clot formation and increasing the risk of clot-related complications [31]. Previous research has consistently linked elevated TG levels to an increased risk of cardiovascular disease [32]. The current study also highlights elevated TC, including high levels of LDL-C, and suboptimal levels of HDL-C as risk factors for the onset of CVD in NDCVD patients. LDL-C, known as the primary risk factor for CVD, promotes atherosclerosis, the underlying pathology of CVD. Lowering LDL-C levels with statins has been shown to significantly reduce CVD risk [33]. While no significant difference in HDL-C levels was observed between NDCVD patients and the control group, both groups exhibited relatively low HDL-C levels, which is common in the Pakistani population. The TC/HDL ratio, an indicator of cardiovascular health, was notably elevated in a large percentage of NDCVD patients, indicating a higher risk of CVD. A high TC/HDL ratio, associated with elevated LDL-C and decreased HDL-C, contributes to atherosclerosis development. Previous studies have demonstrated that a high TC/HDL ratio is a strong predictor of cardiovascular events, emphasizing its importance in early onset CVD management.

The TG, TC, and LDL-C levels fall within normal ranges, likely due to lipid-lowering medications. However, their HDL-C levels were notably lower compared to both newly diagnosed CVD patients and the healthy control group. This decline in HDL-C could be attributed to aging, as HDL-C production tends to decrease with age [34]. Additionally, it may be linked to metabolic issues, tissue inflammation, insulin resistance, and abnormal triglyceride metabolism [35]. Lower HDL-C levels could worsen cardiovascular disease progression in PDCVD patients. In the control group, lipid parameters remained within normal ranges, highlighting the importance of maintaining optimal lipid levels to reduce cardiovascular disease risk.

V. CONCLUSION

The present study reveals a robust association between cardiovascular diseases and factors such as physical activity, diabetes, hypertension, and family history of CVD within the Pakistani population. Surprisingly, smoking and BMI did not emerge as significant predictors of CVD risk in our analysis, suggesting the influence of other variables specific to this demographic. Additionally, our findings underscore a notable shift in the age of onset for CVD patients in Pakistan, with an average diagnosis age of 47.5 years, indicating a trend towards earlier manifestation. Furthermore, the rising incidence of CVD among females presents additional complexities for public health initiatives.

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Table 1: Baseline characteristics of the population under study. Categorical variables are expressed as percentages; Continuous variables are expressed as the mean ± SD; p is the statistically significant value calculated through t test and chi square test.

Variables	NDCVD Group	PDCVD Group	Control Group	P Value NDCVD vs Control	P Value PDCVD vs Control	P value NDCVD vs PDCVD vs Control
Number	715	927	855			
Ages	47.5 ± 12.2	57.4 ± 11.0	46.4 ± 12.8	.082	.000	.000
BMI (kg/m^2)	28.8 ± 6.1	27.8 ± 5.9	27.9 ± 6.5	0.67	.604	.001
Male	59.7% (n=427)	66.5% (n=616)	55.4% (n=474)	.088	.000	.000
Female	40.3% (n=288)	33.5% (n=311)	44.6% (n=381)			
Physically Active	39.6% (283)	51.2% (475)	46.7% (399)	.005	.054	.000
Street Food Intake	62.5% (447)	34.7% (322)	32.8% (280)	.000	.567	.000
Diabetic	34.1% (244)	44.4% (412)	20.6% (176)	.000	.000	.000
Hypertensive	60.3% (431)	63.1% (585)	50.6% (432)	.000	.000	.000
Smoking	15% (107)	17.2% (159)	12.2% (104)	.105	.003	.012
Family history (1st degree) of CVD	53.8% (353)	57% (528)	39.5% (337)	.000	.000	.000

Table 2: Blood lipid levels of the NDCVD and PDCVD patients and controls under study. Continuous variables are expressed as mean ± SD. P is the statistically significant value calculated through t test and ANOVA test.

Variables	NDCVD Group	PDCVD Group	Control Group	P Value NDCVD vs Control	P Value PDCVD vs Control	P Value ANOVA
TG <150 mg/dl	241.9 ±127.7	145.9 ±42.9	130.8 ±44.7	.000	.000	.000
TC < 200 mg/dl	204.9 ±95.8	155.5±42.5	163.1 ±36.5	.000	.000	.000
LDL-C <130 mg/dl	124.5 ±51.1	94.5 ±37.2	102.9 ±31.3	.000	.000	.000
HDL-C > 40 mg/dl	39.3 ±15.1	38.1 ±11.2	40.5 ±9.3	.074	.000	.000
TC / HDL-C Ratio < 5.0	5.5 ±2.8	4.3 ±1.1	4.2 ±1.1	.000	.043	.000

Table 3: Percentages of subjects under study with dyslipidemia.

Variables	NDCVD Group	PDCVD Group	Control Group
TG	73.4% (525)	47.1% (437)	31.8% (272)
TC	46.6% (333)	15.9% (147)	14.7% (126)
LDL-C	40.8% (292)	17.5% (162)	20.0% (171)
HDL-C	60.7% (434)	64.1% (594)	49.0% (419)
TC/ HDL-C Ratio	57.5% (411)	22.3% (207)	15.6% (133)