Genetic risk factors of CVD in the Pakistani population. A systematic Review:

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Abstract- The primary reason for death, is cardiovascular diseases (CVDs), responsible for 17.7 million deaths annually worldwide**.** The incidence of CVDs is likewise very high in Pakistan. The pathogenesis of CVD is complex, and numerous risk factors, including predisposition to genes, are implicated. CVDs may have polygenic or monogenic genetic causes. Additionally, there are variations in the genetic propensity to heart problems among various global populations. The study aims to concentrate on the genetic risk factors for CVDs in the population of Pakistan.

A literature search was carried out using current studies on the presence of familial risk variables for heart disease in the electronic databases Medline, PubMed, Web of Science, Google Scholar, and the World Health Organization (WHO) website. Furthermore, an extensive search for published literature was carried out. According to the research, population-specific genetic risk factors like lipoprotein (a) and population-specific gene-modulating variables may exist.

In descending order, coronary heart disease, hypertension, atherosclerosis, heart failure, and aneurysm have the highest number of detrimental genetic variations causing common CVDs. This study gives an extensive understanding of the harmful mutations that cause heart disease in the Pakistani population

Index Terms- Cardiovascular disease, Genetic variation, Polygenic, Monogenic.

I. INTRODUCTION

The most prevalent chronic disorders tend to be linked to the heart, especially coronary artery diseases, arterial hypertension, and type 2 diabetes mellitus (T2DM). According to estimates from 2012, the leading cause of death worldwide is cardio-vascular disease (CVD), which is accountable for over 31% of all fatalities and is now considered the number-one killer in the world. Compared to advanced economies, developing countries such as Pakistan currently bear a larger proportion of the total incidence of CVD. [1] The World Health Organization reports that during 2000 and the year 2016, 11.473 million disability-adjusted life years (DALYs) resulting from CVDs hit Pakistan; these DALYs made up 30.84% of the nation's overall load of non-communicable illnesses.[2] The forecasts for world health indicate that it will continue to be the leading cause of death in 2030[3]. Empirical research indicates that the genesis of cardiovascular disease (CVD) is heavily impacted by fundamental genetic and physiologic elements, such as physiological susceptibility, body composition, and environmental modifications resulting from migration[4,5.] The genetically inherited factor is induced by complicated gene-gene interaction, increasing the chance of developing cardiovascular diseases[6]. Numerous studies show that the genetic makeup of CVDs is extremely varied[7] and is divided into monogenic and polygenic groups. Monogenic involves the mutation in a single gene whereas polygenic involves a mutation in multiple genes responsible for different forms of CVDs such as myocardial infarction, hypertension, dilated cardiomyopathy, coronary artery disease, stroke, and hypercholesteremia.

With a populace of over 130 million, Pakistan is a growing country. The National Health Survey of Pakistan (NHSP) reports an increase in coronary heart disease-related deaths[8.] Many studies concerning the genetic risk factors of CVDs have been conducted. However, the current systematic review was planned to investigate the prevalence of genetic risk factors that lead to CVD in the Pakistani population.

Definitions of Cardiovascular diseases and Genetic risk factors:
Cardiovascular diseases:

The term "cardiovascular disease" (CVD) refers to a group of conditions that affect the heart or blood vessels. Fatty deposit accumulation in the arteries is usually associated with a higher possibility of blood clots. Cardiovascular diseases comprise coronary artery disease (also known as coronary heart disease), cerebrovascular disease (stroke), peripheral arterial disease, hypertension, rheumatic heart disease, congenital heart disease, cardiomyopathies, cardiac arrhythmias, deep vein thrombosis, and pulmonary embolism[9].

Genetic risk factors:

The likelihood that a person carries a certain disease-associated mutation or is affected by a genetic abnormality is their genetic risk[10.] The pathophysiology of cardiovascular disorders is influenced by a number of variables, including hereditary and environmental factors. The majority of CVDs are caused by the extensive interactions of several genes at numerous loci. Some genetic variants linked to CVDs are MTHFDIL, PSRCI, MIA3, SMAD3, CDKN2A, APOC3, SLC9A3R1, PLA2G7, CYP2F1, TREH, A3GALT2, NRG4 which plays a key role in conferring the susceptibility of CVDs.

II. METHODOLOGY

The Preferred Report Items for Systemic Reviews and Meta-Analysis (PRISMA) standards were followed by us when conducting the systematic processing[11.] Databases like ResearchGate, PubMed, and Science Direct were investigated for the literature search. Additional records were found through

searches on Google Scholar. A list of keywords such as "Genetic risk factors of CVD in Pakistani population", "Genetic disorders of CVD in Pakistan", "Risk of genetic burden of CVD in Pakistani population" and "Genetic factors involved in CVD in Pakistani population" was utilized to acquire the relevant data. We only comprised published papers on genetic risk factors of CVD in Pakistan ranging from 2017-2022. Given the scope of this systematic review, we have reinstated the inclusion of peer-reviewed papers.[12] Only English-language-published articles on the Pakistani population from 2017-2022 were chosen. Finally, after thoroughly reviewing the procedures, 13 publications were chosen as having met the study criteria the best (Figure). To translate studies to each other, integrate translations, and express syntheses a meta-ethnographic technique was adopted.[13]

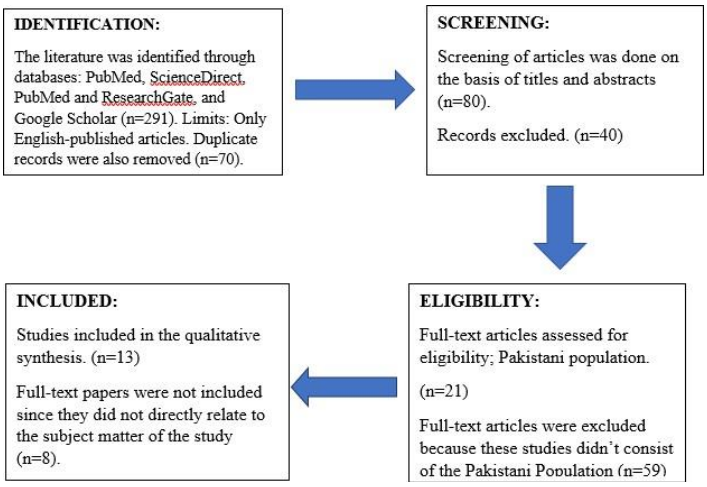

Figure: Flow chart for PRISMA13-compliant study selection for cardiovascular diseases (CVD).

III. RESULT AND FINDINGS

Our search yielded 291 studies of which 70 were duplicates and removed. We screened 80 abstracts of which 40 were irrelevant leaving 21 studies that we assessed for eligibility. Of those 8 studies were not included since they were not related to the subject of study directly. A total of 13 studies were utilized for data extraction.

We provide Table 1 demonstrating our included 13 studies showing genetic risk factors of CVDs in the Pakistani population.

IV. DISCUSSION

Genetic study of cardiovascular disease in Pakistan:

Pakistan, the fifth-largest nation in the world, experiences significant population fluctuations. It has serious health care problems. In Pakistan, consanguineous weddings are prevalent and may contribute to hereditary problems such as cardiovascular disorders. According to estimates, one in five middle-aged adults may have asymptomatic coronary artery disease. An investigation evaluating the prevalence of coronary artery disease in rural Peshawar districts found that myocardial infarction was 11.2% common in our local community[14]. As per one study, there are 3.4/1000 infants with diverse congenital cardiac abnormalities.[15] Limited genetic research on cardiovascular disorders has been conducted in Pakistan, despite the country's high prevalence of these illnesses. Approximately 5% of the cases in the INTERHEART trial (15152 cases and 14820 controls), which examined the relationship between socioeconomic and metabolic variables and myocardial infarction, were from Pakistan.[16] Following a recent investigation by the Pakistan Risk of Myocardial Infarction Study (PROMIS) of the full exomes of 4,793 patients and 5,710 controls, 49,138 rare-frequency (minor allele frequency 1%) projected loss-of-function (pLoF) mutations in 1317 genes were found. Numerous mutations in lipid-metabolizing genes, including PLA2G7, CYP2F1, TREH, A3GALT2, NRG4, APOC3, and SLC9A3R1, were discovered to be important contributors to the susceptibility to myocardial infarction in this study.[17] Through genome-wide association studies, the PROMIS, and other associations also identified variations in many genes to be linked with coronary heart disease and myocardial infarction.[18]Additionally, there are distinct screening reports of a single gene, a limited percentage of genes, or a small number of SNPs that have already been linked to some serious cardiovascular disorders including coronary artery disease,[19,20]myocardialinfarction,[21,22]hypercholesteremia[23],hypertension[24], cardiomyopathies.[25,26]

IV. CONCLUSION

This review concludes by providing a thorough picture of harmful mutations for heart diseases in the Pakistani population. Reducing the modifiable risk factors, such as maintaining a healthy lifestyle, can lessen the impact of this genetic tendency, which is an unchangeable risk factor.

APPENDIX

Abbreviations-

CVDs- cardiovascular disease
WHO- World Health Organization
DALYs- disability-adjusted life years
T2DM- type 2 diabetes mellitus
NHSP- The National Health Survey of Pakistan

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