

**Ischemic heart disease**  
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Ischemic heart disease (IHD) is the main cause of disability and increased health-care expense worldwide, leading to mortality and morbidity in most countries. Coronary Artery Disease(CAD) is multifactorial disease, its cause may be interactions between genetic and environmental factors. Many studies referred to that 40% to 60% CAD occurrence had been caused by the role of genetic factors. However, all these studies have not fully explained the genetic factor role in CAD. Survival after myocardial infarction is the most difficult problem in different societies, but it has been increased in these years by revascularisation techniques, for example: percutaneous coronary intervention (PCI).

Heart disease is a catch-all phrase for a variety of conditions that affect the heart's structure and function. Coronary heart disease is a type of heart disease that develops when the arteries of the heart cannot deliver enough oxygen-rich blood to the heart. It is the leading cause of death in the United States. Coronary heart disease is often caused by the buildup of plaque, a waxy substance, inside the lining of larger coronary arteries. This buildup can partially or totally block blood flow in the large arteries of the heart. Some types of this condition may be caused by disease or injury affecting how the arteries work in the heart. Coronary microvascular disease is another type of coronary heart disease. It occurs when the heart's tiny blood

vessels do not work normally.( The National Heart, Lung, and Blood Institute .

Globally, IHD is ranked the first main cause of death and leads to about 8. million deaths in 2013 . In 2012, IHD was the major cause of deaths in middle- and high-income countries,it had been responsible for about more than 40% of all dead cases in middle-income countries and more than 30% in high-income countries. In 2020, it is detected that coronary artery disease is the leading cause of death, beyond infectious diseases. Myocardial infarction (MI) and heart failure are responsible for the majority of the morbidity and mortality linked with ischemic heart disease . Angina due to CAD affects around 112 million people worldwide . It is estimated that between 4% and 10% of persons which suffer from CAD at 5 years. Although the prevention of ischemic heart disease has become an important , fatal coronary disease is the first manifestation of IHD.

These genetic causes of IHD had been not completely explained. Many biological and genetic factors result in the progression of IHD. In highly risk persons, there is an association between gene polymorphisms and higher risk of IHD occurrence. The cumulative effect of these small variation leads to predictable (MI) and IHD risk. For good treatment and preventing disease can be done by better genetic studies. LDLR locus has many genetic variants, the strongest association was presented between part of this gene and with LDL-cholesterol (LDL-C) has been proved in various countries. Strong correlation is presented between rs2228671 in exon 2 LDLR with LDL-C concentration; lowered concentration of LDL-C is associated with T allele of this snp with lowered IHD risks. The rs688 within exon 12 of LDLR gene is associated with high LDL-C concentration(T allele) and also splicing activity. At last, many genome studies prove that G allele of rs1122608 in intron 30 of SMARC1 gene

adjusted to LDLR gene is correlated with increased concentration of LDL-C with high occurrence of MI.

As a risk factors, studies consider either only biomarkers or with combination with other risk factor to decide if they correlate with occurrence of disease. At the other side, now days new risk factors approved in addition to previous factors that include :molecular genetics immunology, biophysical causes, imaging for detect probable exposing CAD. Lipid concentration in blood, including total cholesterol, LDL cholesterol, HDL cholesterol, and triglycerides, has been considered constituent of cardiovascular risk prediction. Premature IHD is detected by concentration of factors for example increased LDL cholesterol, increased blood pressure, DM, decreased HDL cholesterol, cigarette use and family history. However, numerous risk scores are appeared depending on studies for relative power of importance for patients risk factors. The important prediction is made by Framingham who has done the main prediction that is used as a risk score in IHD for 10 next years for principle prevention.

Coronary artery disease (CAD) is a a result of the linking between various genetic and environmental factors. Studies have tried to find recent risk factors in order to discover new drugs. In this side, mutations that exposed the LDL receptor which led to hypercholesterolemia is the cause of LDL and statin, this shows premature (MI) cause the taking of LDL decreasing drugs that lower IHD risk. PCSK9 has a role in excrete LDL cholesterol by lowering liver binding ability and destroy LDL receptor. The evidence of IHD is lower in persons with low LDL concentration caused by loss-of-function mutations in PCSK9. In hypercholesterolemia patients, there is benefit from drug that inhibit PCSK9 so decrease LDL. However, studies discovered PCSK9 monoclonal antibody proved that significantly

decreasing of LDL. Also studies discovered that remove evidence of disease by harmacogenomic.