

# [Coronary rates associated with cad have shown an](https://assignbuster.com/coronary-rates-associated-with-cad-have-shown-an/)

Coronaryartery disease (CAD) is a complex trait caused by a number of genetic andenvironmental factors. CAD remains a leading cause of death in most developingcountries. According to estimates by the World Health Organization (WHO), nearly seven million people worldwide die of CAD each year equally among menand women, with most of these deaths occurring in both high- and low incomecountries 1. The prevalence of CAD worldwide is rapidly rising.

Over the past twenty years, CAD has become the leading causeof death in Kingdom of Saudi Arabia (KSA) and has reached epidemic proportions. Mortality rates associated with CAD have shown an exceptional increaseparticularly in fast developing economies like the KSA. The maximum increase ofcoincided with fast economic growth and urbanization that promotes sedentarylife style, high energy fat food, smoking, low intake of fruits and vegetablesand mainly developing of oxidative stress. These factors have undoubtedlycontributed to the epidemic of CAD in KSA 2. More than 80% of sudden cardiacdeaths are caused by atherosclerotic CAD.

Atherosclerosisis characterized by the buildup of fatty lesions, inflammation, and scarring ofarterial walls with oxidative stress as a primary contributing factor. Atherosclerosisis an inflammatory disease. According to “ response to retention hypothesis”, the whole sequence of events is found to be initiated by the retention ofmodified Low density lipoprotein (LDL) 3. The oxidative modifications of LDLin the arterial wall may play major role in the development of atherosclerotic lesions. Oxidative stress is known to increase the formation of oxidized LDL. So manystudies suggested that LDL acts as a key event in the genesis ofatherosclerosis 4.

Epidemiological, pharmacological, genetic and clinical studies implicated that the developmentof atherosclerosis is closely associated with so many extrinsic and intrinsic risk factors, including age, hypertension, obesity, smoking, lack of exercise, diabetes and dyslipidemia have beenidentified. Atherogenic dyslipidemia is characterized by abnormal levels ofcholesterol, triglycerides and LDL; however a low level of highdensity lipoprotein (HDL) is a risk factor for the development of CAD andstroke 5. Several authors areindicated that development and progression of CAD is related to free radicalprocesses. Lipid peroxidation is theoxidative degradation of lipids. It is the process in which free radicals” steal” electrons from the lipids in cell membranes, resultingin cell damage, disruption of proteins and other cell components, which ispotentially harmful because it’s uncontrolled. A lot ofoxygenated compounds, particularly aldehydes such as Malondialdehyde (MDA) areproduced during the attack of free radicals to membranes, lipoprotein andpolyunsaturated fatty acids 6.

Thus monitoring of lipidprofiles and lipid peroxidation in the blood provides usefulinformation for the prognosis of CAD patients. Theparaoxonases (PON) are enzymes involved in oxidative stress, in theatherosclerosis process and, consequently, in vascular disease. The PON gene familyin mammals includes 3 members; PON1, PON2 and PON3 are basically lactonaseswith one of the broadest known substrate specificities. All 3 PONs metabolise5- hydroxy cicosate traeomic acid 1, 5 lactone and 4- hydroxy docos ahexanoicacid which are derived from arachidonic acid. PON1 and PON3 are found in manytissues, as well as in circulation, associated with HDL-C, while PON2 isexclusively intracellular.

All PONs share approximately 70% identity at thenucleotide level and 60% identity at the aminoacid level and are locatedadjacent to each other on chromosome 7 (7q21. 3 — 22. 1) in humans 7, 8. Humanserum PON1 is a 44- kDa (355 amino acids) calcium dependent glycoprotein, predominately expressed in the liver that circulates bound to HDL particles. PON1 is an esterase that catalyzes the hydrolysis of multiple organophosphates, including paraoxon, diazoxon, sarin and soman and arylesters such as phenylacetate.

PON1 became the focus of intense research both at phenotypic andgenetic levels subsequent to the identification of its antioxidant properties, particularly to protect LDL from oxidative damage 9. Themost studied PON1 gene polymorphism result from amino acid substitutions atpositions 192 (Glutamine (Q) – Arginine (R) in the coding region of the gene. Alleles at the 192 (Q and R allele) loci of the PON1 codon have been associatedwith enzyme activity and concentration respectively.

The QQ- genotype exhibitsa low PON activity (low activity phenotype), while RR- genotype exhibits a highPON activity (high activity phenotype). However, there is also marked variationin enzyme activity between individuals of the same genotype 10.  PON1 position 192 R isoform binds with HDLwith a 3 fold lower affinity than the Q isoenzyme and consequently exhibitsreduced stability, lapolactonase, arylesterase activity. It has been suggestedthat the Q allele, which is more abundant than the R allele, is responsible forthe protective effect against atherosclerosis, whereas the R allele has beenrelated to CAD because of less protection against LDL. These differences in theproperties of PON1 192 Q/R isoenzyme provide the basis for the contribution of192 Q/R polymorphism to the susceptibility to atherosclerosis 11. So many authorsrevealed that PON1 Q192R polymorphism are an important risk for MI and CADpopulations 12, 13. Contrastingly, some studies reported that no suchassociation between Q192R polymorphism and an elevated atherosclerosis risk 14.

Moreover, several studies have indicating that it is an important to determinethe phenotype, not just the genotype, when studying the atherosclerosis 15, 16. Thusin this case control study, we assess the lipid profile, lipid peroxidationproduct MDA, the distribution and frequency of PON1 Q192R polymorphism and theconcerned phenotype (arylesterase activity) was analyzed with the risk of CAD andhealthy controls in the population of the central province of Saudi Arabia.