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## A Review on HDL-cholesterol Alterations in Metabolic Syndrome

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**Abstract:** The metabolic syndrome increases the risk of many diseases. There are many investigations on the role and alterations of High-Density Lipoprotein (HDL)-cholesterol in different diseases. HDL-cholesterol is an important component of metabolic syndrome. Low HDL-cholesterol has been shown among subjects with metabolic syndrome. Low levels of HDL-cholesterol are collaborated with elevated risk of cardiovascular disease, coronary heart disease, myocardial infarction, stroke and Alzheimer disease. The increased prevalence of metabolic syndrome and its relation with low levels of HDL-cholesterol accentuate its diagnostic importance and medical care. The aim of present study was to review HDL-cholesterol alterations in metabolic syndrome.

**Key words:** HDL-cholesterol, metabolic syndrome, alterations

### INTRODUCTION

Metabolic syndrome is one of the most health problems in the world. There are many different definitions for metabolic syndrome. It is described by some of metabolic abnormalities, such as abdominal obesity, hypertension, glucose intolerance, low level of High-Density Lipoprotein (HDL) and high triglyceride (TG) level (Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001). Studies have shown that the prevalence of the metabolic syndrome changes from 7 to 84% (Balkau *et al.*, 2002; Isomaa *et al.*, 2001). It has been also indicated that the prevalence of metabolic syndrome among adult population changes from 8 to 24.2% and 7 to 46.5% in males and females worldwide, respectively (Gupta *et al.*, 2003; Ford *et al.*, 2002; Balkau *et al.*, 2003; Ramachandran *et al.*, 2003a). The prevalence of the metabolic syndrome was 33 and 21% in adult Mexican American and adult white American, respectively (Meigs *et al.*, 2003). According to the National Cholesterol Education Program's Adult Treatment Panel III (NCEP/ATP III) diagnostic criteria for the metabolic syndrome, the prevalence of metabolic syndrome were approximately 25% and up to 45% in the United States in population older than 20 and 50 years, respectively (Ford *et al.*, 2002). There are evidences that prevalence of metabolic syndrome alters among males and females and different ethnic groups (Park *et al.*, 2003). The prevalence of metabolic syndrome was high in many European countries (Switzerland, Spain, the Netherlands, Italy, France, the UK and Denmark). Studies have indicated that the prevalence of metabolic syndrome in subjects without diabetes and age fewer than 40 years old

was 14-41% (Balkau *et al.*, 2002). Study of Buckland *et al.* (2008) have shown that the prevalence of metabolic syndrome was 24.8% in subjects with age ranges 18-74 years old (Ranging from 2.5 to 51.1% in subjects with age ranges 18-24 to 65-74 year olds, respectively) (2008). Studies in India and Iran have shown that the prevalence of metabolic syndrome among adult subjects changed from 33.7 to 41% (Azizi *et al.*, 2003; Delavari *et al.*, 2009; Ramachandran *et al.*, 2003b). There are many different studies on the alterations of HDL-cholesterol. Studies have indicated that HDL-cholesterol (one of metabolic syndrome components) shows the protection effect against atherosclerosis. The Framingham study in 1976 is shown that there were collaboration between the levels of HDL-cholesterol and the increased cardiovascular morbidity (Gordon *et al.*, 1977). Some other studies have shown that there were no collaboration between low HDL-cholesterol and coronary and cerebrovascular diseases (Goldbourt *et al.*, 1997; Tanne *et al.*, 1997). There are evidences that low HDL-cholesterol is in association with the metabolic syndrome and type 2 diabetes patients. Cardiovascular disease may consider in these patients with low HDL-cholesterol (Watson *et al.*, 2003). The aim of this review is to discuss HDL-cholesterol alterations in metabolic syndrome.

### EPIDEMIOLOGY OF LOW HDL-CHOLESTEROL

Low HDL-cholesterol is associated with insulin resistance, hypertriglyceridaemia. HDL-cholesterol exchanges to atherogenic lipoproteins (LDL-cholesterol) which is important in patients with type 2 diabetes or the metabolic syndrome (Drexel *et al.*, 2005; Krauss, 2004). Studies have shown that 1 in 4 and about 1 in 12 in man

and woman had low HDL-cholesterol in the UK, respectively (Patel *et al.*, 2004). Study on middle-aged Dutch men was shown that one fourth of them had very low HDL-cholesterol (Verschuren *et al.*, 1994). The Turkish people is also indicated low HDL-cholesterol (Soysal *et al.*, 2005). The majority and half of the man and woman subjects in Turkey were shown low HDL-cholesterol, respectively (Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults, 2001). It has been reported that the prevalence of low HDL-cholesterol in Mexico and Brazil was high (Lorenzo *et al.*, 2005; Passos *et al.*, 2005). Study on Mexican population has shown that the prevalence of low HDL-cholesterol among men and women were 46 and 29%, respectively (Aguilar-Salinas *et al.*, 2001). It has been reported that there was an elevation in the prevalence of low HDL-cholesterol by from 2 to 3% during 7 years (Lorenzo *et al.*, 2005; Marjani *et al.*, 2012a, b) has revealed that HDL-cholesterol was low (lower than 50 mg dL<sup>-1</sup>) among Fars and sistanee women with metabolic syndrome (Marjani *et al.*, 2012a, b). Study on the US general population has shown that there is a fast elevation in the prevalence of low HDL-cholesterol among American women (Ford *et al.*, 2004). In a study from 1988 until 1994, it has been shown that low HDL-cholesterol was observed in nearly one-third of US men and women. In a continue study from 1999 until 2000, it has indicated that the prevalence of low HDL-cholesterol was elevated by 0.4 and 3.7% in men and women, respectively. The prevalence of Low HDL-cholesterol was from 33 to 34% and from 39 to 40% among men and women, respectively. It has been revealed that generally, the prevalence of low HDL-cholesterol was 33 and 40% among men and women, respectively (Bruckert, 2006).

#### **SIGNIFICANCE OF HDL-CHOLESTEROL IN DIFFERENT DISEASES**

High-density lipoprotein cholesterol (HDL-C) is known as a good cholesterol. It is in direct association with the ability of HDL particles. These particles carry the extra cholesterol molecules from non-hepatic cells to liver. Studies have revealed that low HDL cholesterol and hypertriglyceridaemia are related to myocardial infarction/stroke in patients with metabolic syndrome (Ninomiya *et al.*, 2004) and High fasting glucose and low HDL cholesterol may cause coronary heart disease (Anderson *et al.*, 2004). Study of Sacco *et al.* (2001) has shown that the function of HDL cholesterol levels indicated as a significant risk factor for stroke (Sacco *et al.*, 2001; Voight *et al.*, 2012) has indicated that there is an association between elevated HDL cholesterol levels and decrease risk of myocardial infarction

(Voight *et al.*, 2012), but Onat *et al.* (2009) reported that high HDL cholesterol levels cannot defend versus risk of a number of diseases such as coronary heart disease or diabetes in general (Onat *et al.*, 2009). Some other studies have revealed that there is an association between low level of HDL cholesterol and risk of cardiovascular and coronary heart disease (Castelli *et al.*, 1986; Ordovas *et al.*, 1986). In a population based study from the Copenhagen City Heart Study (CCHS) and the Copenhagen General Population Study, have been reported that low HDL cholesterol levels were not associated with elevated risk of myocardial infarction, inspite of available data which indicate a correlation (Haase *et al.*, 2012). The Framingham Heart Study has indicated that there were contrary association between HDL cholesterol and the prevalence of coronary artery disease in both genders (Gordon *et al.*, 1977). In men and women, low HDL-cholesterol is a good prognoses for coronary artery disease. This relation is more important and effective in women than men (Gordon *et al.*, 1989). The effect of HDL-cholesterol level in relation to coronary artery disease is depended on the concentrations of HDL-cholesterol (Wilson *et al.*, 1998).

Study of Stampfer *et al.*, 1991 have been shown that patients with low HDL-cholesterol and low total cholesterol concentrations indicated 33% higher risk of coronary artery disease when compared them to subjects with high total cholesterol and high HDL-cholesterol levels (Stampfer *et al.*, 1991). Robins *et al.* (2001) have revealed that the most important factor in reduction of the coronary artery disease was HDL-cholesterol (2001), if risk factors such as diabetes, hypertension, smoking, age and body mass index corrected. The population study of Bezafibrate Infarction Prevention (BIP) revealed that 42% of men and women with coronary artery disease had HDL-cholesterol levels lower than 35 mg dL<sup>-1</sup> (Anonymous, 1992). Genest *et al.* (1992) showed that 40% of patients with premature coronary disease had low HDL-cholesterol levels and only in 10% of patients, HDL-cholesterol levels were high. Study of Rubins *et al.* (1995) on men population at Veteran Affairs Medical Centers in United States indicated that 38 and 63% of subjects had HDL-cholesterol levels lower than 30 and 40 mg dL<sup>-1</sup>, respectively. They have also reported that HDL-cholesterol levels in coronary artery disease patients were lower than those patients without this disease. Many different studies have revealed that there are an association between diabetes and the risk of cardiovascular disease in both genders. A population-based study of Howard *et al.* (1998) indicated that there were important contrary differences among subjects with and without diabetes (men and women) for

HDL-cholesterol levels. In the United Kingdom Prospective Diabetes Study, it has been exhibited that type 2 diabetes patients with coronary artery diseases showed a high relation with HDL-cholesterol levels. They found that elevation of HDL-cholesterol levels can decrease coronary artery disease in type 2 diabetes patients (Patel *et al.*, 2004). Study of Marjani and Moujerloo (2011) has been shown that HDL-cholesterol levels were lower among type 2 diabetes patients with metabolic syndrome when compared to subjects without metabolic syndrome (Marjani and Moujerloo, 2011).

Study of researchers at University of Columbia has indicated that there are a contrary relation between subjects with high levels of HDL cholesterol and develop of Alzheimer disease. They have reported that people with HDL cholesterol higher than 55 mg dL<sup>-1</sup>, showed almost 60% decreased risk of Alzheimer disease when compared with subjects whose HDL cholesterol lower than 39 mg dL<sup>-1</sup>. Their results have been shown that there is an association between high HDL-cholesterol levels and lower prevalence of Alzheimer disease (Reitz *et al.*, 2010).

Marjani and Moghasemi (2012) has been reported that there is low HDL-cholesterol level among postmenopausal women with metabolic syndrome. It has been indicated that following menopause, decrease and increase of HDL-cholesterol levels were seen (Jensen *et al.*, 1990; Do *et al.*, 2000). Many studies have shown that HDL-cholesterol levels either decrease partly (Matthews *et al.*, 1989; Torng *et al.*, 2000, 2002) or remain stable (Kannel *et al.*, 1976) following menopause. Some other studies showed an elevation of HDL-cholesterol levels in Korean and Iranian people after (Azizi and Ainy, 2003; Kim *et al.*, 2000). Kreisberg and Kasim (1987) showed that decrease in HDL-cholesterol levels is associated with coronary heart disease risk factors among postmenopausal women.

Study of Mojerloo *et al.* (2012) has been shown that the prevalence of metabolic syndrome among hemodialysis patients was high (56.3%). It was higher among women when compare with male hemodialysis patients. Their results were in agreement with the findings of other studies (Hsu *et al.*, 2006; Williams and Feidhlim Woods, 2006; Bakker *et al.*, 2007). Stolic *et al.* (2008) and Young *et al.* (2007) have been indicated that about 30 and 69.3% of hemodialysis patients showed progressed metabolic syndrome, respectively (2008 and 2007). Mojerloo *et al.* (2012) have revealed that abdominal obesity and low HDL cholesterol levels were the highest risk of metabolic syndrome components among hemodialysis patients (Mojerloo *et al.*, 2012).

## CONCLUSION

Low levels of HDL-cholesterol are collaborated with elevated risk of many diseases such as cardiovascular disease, coronary heart disease, myocardial infarction, stroke and Alzheimer disease. A low levels of HDL-cholesterol are associated with high levels of triglyceride, high body mass index (overweight), low physical activity and type 2 diabetes mellitus. HDL-cholesterol is one of the most important characteristic components of metabolic syndrome. The increased prevalence of metabolic syndrome accentuates its diagnostic importance and medical care.

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