

Nayab Batool Rizvi · Saeed Ahmad Nagra

# Minerals and Lipids Profiles in Cardiovascular Disorders in South Asia

Cu, Mg, Se, Zn and Lipid Serum Profiles  
for the Example of Patients in Pakistan

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ISBN 978-3-642-34248-6      ISBN 978-3-642-34249-3 (eBook)  
DOI 10.1007/978-3-642-34249-3  
Springer Heidelberg New York Dordrecht London

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# Preface

Cardiovascular disorders are on the rise in developing countries, and SARC countries are no exception to it. Data on any aspect of these disorders, with reference to local living conditions, is very scarce. The work presented here is part of a doctoral study, and the findings primarily focus on the aim of providing an insight about the prevalence of some of the serum minerals and lipids profiles present in various cardiovascular disorders. The data presented and discussed in this book pertains to Pakistan but can serve as a base line, or reference, for future studies in the country, as well as the surrounding continent. It is expected that data presented here may pave the way to more advanced research regarding cardiovascular problems for researchers/clinicians wishing to proceed in this direction.

The linguistics of the book has been kept very simple for easy comprehension so that researchers, clinicians, and even students may be void of any problem. Detailed tables and figures have also been included, which provide, at a glance, a true idea of the prevalence of serum minerals and lipids profiles in countries such as Pakistan. Our findings have been presented as observed, and it is hoped that the book will prove to be of great importance to the habitants of South Asian countries.

We hope that the users of this book will find it appealing and reliable. Any suggestions for improvement will be most welcome.

Lahore, 2012

Nayab Batool Rizvi  
Saeed Ahmad Nagra



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# Chapter 1

## Introduction: Minerals

### 1.1 Introduction

Cardiovascular diseases (CVD) are a group of disorders of the heart and blood vessels and include coronary heart disease (CHD), cerebrovascular disease, raised blood pressure (hypertension), rheumatic heart disease, angina, peripheral arterial disease, atherosclerosis, congenital heart disease, heart failure, and deep vein thrombosis (WHO 2009). Cardiovascular disease is the leading cause of death worldwide accounting for about 40 % of global mortality and 10.3 % of the global burden of disease. The incidence of CVD has risen greatly in low- and middle-income countries (Yusuf et al. 2001). Among cardiovascular disease, CHD is the most common heart disease, responsible for 40–60 % of all deaths and is invariably associated with atherosclerosis (thickening of the arteries). Atherosclerosis is a major cause of CVD that develops slowly over decades. In atherosclerosis, narrowing of the vessel's lumen may lead to obstruction and to its clinical manifestations, such as myocardial infarction (MI) (Lefant and Savage 1995). Although women do not suffer from this problem as frequently as men, but it is numerically more significant in the case of older women. It has been reported that the risk of CHD is more in postmenopausal women (Miller 1990). Angina pectoris is one of the several expressions and one of possible manifestations of coronary heart disease. It is precipitated when the oxygen demands of the myocardium exceeds the available arterial oxygen supply. The major modifiable risk factors for CVD include high blood pressure (hypertension), high total cholesterol, obesity, physical inactivity, unhealthy diet, diabetes mellitus (DM), and homocysteine levels (Mackay and Mensah 2004). The more risk factors a person has, the greater the likelihood of developing CVD. Risk of CHD is two- to threefold higher in persons having type II diabetes as compared to general population (Fox et al. 2004). In diabetes, cardiovascular disease affects both men and women to the same extent (Uusitupa et al. 1993). It has been observed that women with diabetes, regardless of menopausal status, have a four- to sixfold higher risk of developing CVD, whereas men with diabetes have a two- to threefold increased risk of CVD compared to

women and men without diabetes (Legato et al. 2006). Individuals having DM also face the risk of developing atherosclerosis due to the disturbances in the lipid metabolism (Adlerberth et al. 1998). Furthermore, high-density lipoprotein cholesterol (HDL cholesterol) that is commonly regarded as protective is decreased in diabetic patients. Diabetes mellitus acts as an independent risk factor for several forms of CVD, and it has been estimated that approximately 65 % of CVD-caused deaths are of the persons with DM (Geiss et al. 1995). Diabetes accounts for 6 % of total global mortality, with 50 % of diabetes-associated deaths being attributed to CVD (International Diabetes Federation 2008).

Hypertension is another important risk factor and the main cause of mortality for cardiovascular disease (Whelton 1994). It is reported that 50 % of cases of CVD were caused by elevated blood pressure. Women with CHD are at two- to threefold increased risk of developing hypertension (Wenger 2003). Hypertension affects 8–14 % of the population worldwide, and its prevalence is especially high in diabetic persons (Howard et al. 1996). Hypertension depends on factors such as obesity, physical inactivity, excessive alcohol consumption, sodium and potassium intake, and psychological stress.

Lipids and lipoproteins are well-known risk factors for CHD. Increased levels of triglyceride (TG), total cholesterol (TC), LDL cholesterol, and decreased levels of HDL cholesterol are documented as risk factors for atherogenesis as HDL cholesterol is associated with cholesterol removal from peripheral tissues. Excessive caloric intake, with high component of fat, is associated with an increased serum level of total cholesterol (TC) and LDL cholesterol (Shekelle et al. 1981) and hence increases the risk of CVD. The role of various minerals, in relation to various risk factors such as DM, hypertension, and MI, is discussed in the subsequent lines.

Human health depends on a delicate balance among reactions within the organism in which nerve, muscle, blood, bone, endocrine, and visceral tissues are continually renewed. Vital exchanges that constantly occur involve many enzymatic systems activated by minerals or trace elements (Speich et al. 2001). Most of the minerals in our diet come directly from plants or indirectly from animal sources. A well-balanced, low-fat, antioxidant vitamin-rich diet is one of the important elements of secondary prevention of CVD (Waśkiewicz et al. 2008). Nutrition is strongly associated with socioeconomic conditions, health status, and functional capacity. A wide range of trace elements has been linked with one or another aspect of CVD, some being regarded as beneficial to the heart and blood vessels and others directly or indirectly harmful (Shaper et al. 1979).

## 1.2 Copper

Copper (Cu) may play a role in cardiovascular disease through its involvement in the coagulation cascade (Linder and Hazegh-Azam 1996). Heart, brain, kidney, and skeletal muscles are considered as important sites where copper is present in

substantial concentrations. Only a small fraction of copper occurs in the free form. In the body copper shifts between the cuprous ( $\text{Cu}^{1+}$ ) and cupric ( $\text{Cu}^{2+}$ ) forms, though the majority of the body's copper is in the cupric form. Three nonspecific mechanisms of damage implicated in cardiovascular defects of copper deficiency include peroxidation, glycation, and nitration (Aliabadi 2008). Copper deficiency has been linked to MI, severe tachycardia, and also sudden death due to rupture of the heart. Study shows that Cu deficiency can occur in the presence of homocysteine, especially elevated levels of homocysteine. Homocysteine chelates copper, decreasing its availability to cells (Linnebank et al. 2006). Cardiovascular patients with copper deficiency show several characteristics such as abnormal electrocardiograms, decreased myocardial copper, glucose intolerance, hypercholesterolemia, hyperuricemia, necrosis of myocardial cells, and sudden death. Copper deficiency may also lead to abnormal vessel wall formation and other pathological changes, which may lead to cardiovascular disorders (Vlad et al. 1993).

### 1.3 Magnesium

It is estimated that magnesium (Mg) is needed for more than 300 biochemical reactions in the body. It helps maintain normal muscle and nerve function, keeps heart rhythm steady, supports a healthy immune system, and keeps bones strong. It also helps regulate blood sugar levels, promotes normal blood pressure, and is known to be involved in energy metabolism, protein synthesis, and phosphorylation reactions, such as muscle insulin tyrosine kinase (Suarez et al. 1995). Of all the cardiovascular risk factors, Mg now takes first place as judged by the accumulation of epidemiological, pathophysiological, clinical, and experimental data. It has been reported that there is an inverse association between dietary magnesium intake and incidence of CVD (Al-Delaimy et al. 2004). It is also reported that increased oxidative stress during magnesium deficiency leads to protein peroxidation, in the early stages and progression of atherosclerotic lesions (Mazur et al. 2007). Magnesium is needed for the electrical stability of the myocardium and prevention of irregular arrhythmias by regulating the flux of cellular potassium levels across cell membrane and transmembrane potentials (Vitale 1992).

It has also been estimated that magnesium may reduce the risk of CHD as a result of inhibiting platelet function, smooth muscle contraction, and by reducing free fatty acids in circulation (Teragawa et al. 2000). Oral magnesium supplementation lowers systolic and diastolic blood pressure and thus prevents the development of hypertension (Kh et al. 2000). Studies have indicated the effects of magnesium deficiency in the hormonal system which controls blood pressure. Magnesium deficiency might affect blood pressure values, leading to hypertension. Various studies also show an inverse association between magnesium (serum and dietary) and blood pressure values (Ma et al. 2006).

## 1.4 Selenium

One of the major roles of selenium along with zinc and copper in the body is to act as a cofactor of key antioxidant enzymes, namely superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) and selenoproteins (Nayak et al. 2001). Selenium (Se), an essential component of the antioxidant enzyme GSH-Px, functions as an antioxidant scavenging  $H_2O_2$  and by reducing lipid hydroperoxides to their subsequent less reactive end products. It is an essential trace mineral involved in protection against oxidative damage via selenium-dependent GSH-Px and other selenoproteins. Selenomethionine and selenocysteine are two selenium-containing amino acids that have been detected in proteins (Rayman 2000). The major selenoproteins in plasma is selenoproteins P (SeIP). SeIP provides more than 50 % of the total plasma selenium (Mostert 2000). Selenium modulates the cellular response to oxidative stress, inducing a faster restoration of the endogenous antioxidative defense system against the production of reactive oxygen species. Selenium deficiency has been implicated in the development of CVD. It has been observed that low Se levels have a casual effect in the development and deterioration of CHD, but it is unknown whether this is due to Se-mediated reduction in lipid peroxidation, inhibition of inflammation, or an improved lipid profile in the blood (Ravn-Haren et al. 2008). By shifting prostaglandin synthesis from prostacyclin to thromboxane, low selenium may increase platelet aggregability and vasoconstriction. Adequate selenium intake therefore helps to maintain adequate nitric oxide concentrations and reduce LDL-cholesterol oxidation. Selenium may also protect the cardiovascular system from toxic metals that have been implicated in atherogenesis, such as mercury, cadmium, and arsenic, by preventing metal-induced oxidative damage or by forming inactive complexes with metals (Feroci et al. 2005). An inverse correlation has been reported between the appearance of some cardiopathies and low Se levels in the environment, diet, and blood (Navarro-Alarcon and López-Martínez 2000). High concentrations of serum selenium predict reduced levels of oxidative stress and subclinical cyclooxygenase-mediated inflammation. Therefore, the association between selenium, oxidative stress, and inflammation may be related to the cardiovascular protective properties of selenium (Helmersson et al. 2005). Measurement of selenium and plasma homocysteine concentrations in elderly humans showed that blood Se levels should be considered as a potential factor to lower total plasma homocysteine, and there exist an independent inverse association between serum Se and plasma homocysteine (Gonzalez et al. 2004). Selenium deficiency has also been associated with a higher incidence of MI and increased mortality rates from CVD. Some studies in diabetics suggest that selenium supplementation may help to prevent vascular complications and that diabetic patients may be deficient in selenium relative to healthy persons (Rajpathak et al. 2005).

## 1.5 Zinc

Zinc (Zn) is another micronutrient with known antioxidant activity. Zinc is an important component of biomembranes and an essential cofactor in a variety of enzymes (Powell 2000). Zinc plays an important role in the synthesis and function of insulin and is capable of modulating insulin action, and it improves hepatic binding of insulin. It has been observed that people with diabetes have lower serum levels of zinc. Study shows that low serum Zn levels are an independent risk factor for CHD mortality. Studies have also shown that serum zinc level is lower in diabetic patients than in nondiabetic subjects due to increased urinary zinc excretion (Chausmer 1998). Zinc supplementation shows antioxidant properties in the case of diabetics (Roussel et al. 2003) and hence decreases lipid peroxidation. Low serum/plasma zinc concentrations in people with established atherosclerosis indicate that low zinc levels are associated with atherosclerosis (Lissa et al. 2006). Zn supplementation reduces accumulation of cholesterol in the aorta and reduces a number of markers of cholesterol and lipid oxidation (Jenner et al. 2007).

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