Introduction

Human body is dependent on many dietary constituents for its survival. To keep this wonderful machine of human organism functioning, it requires many inorganic elements in addition to water, fat and protein which are the major components. Along with the principal components, these elements also must be supplied in the diet. Quantity required range from grams/day in case of sodium, potassium, chloride to milligrams/day in case of calcium, magnesium and finally, to the few micrograms/day in case of trace elements such as selenium and chromium.

The role of minerals and trace elements in the normal metabolism of various biological species is a well studied one and ample information is available regarding the deficiency and excess content of minerals and trace elements in the health and disease process. A lot of emphasis has been given by the scientists regarding the role of sodium, potassium, calcium, chloride and trace elements like iron and zinc, but somehow magnesium has not got its due share of importance regarding its role in spite of the fact that more than 300 enzymes require magnesium as a co-factor for their role, not only that it is the most abundant cation in the body, and the most abundant cation in the intra cellular fluid. In relation to its role as a co-factor of enzymes, magnesium has wide spectrum of functions including membrane functions, as an antagonist to calcium and many structural functions.

Every mineral and trace element having their role in the various activities of the cell, their excess and deficiencies play a significant role in the malfunctioning of the cell, which ultimately affects the overall function of the organ transforming a state of normal physiology into a pathological one.

Health professionals involved in the day to day management of patients naturally are more concerned regarding the mortality than morbidity. Minor alterations in the levels of some of the elements due to their clinical consequences attract the immediate attention of the attending physician, that makes them to find out their levels and based on the level, the immediate remedial action. Some other elements which are as important as any other in the cellular function but their excess or deficiencies cause subtle effects
which do not draw the attention of the attending physician, as their clinical consequences are not immediately seen or visible. Unfortunately, these ignorant or negligent aspects of the health professional may prove detrimental in the long run as the levels of these elements further come down to such a level that can be categorized as chronic deficiency affecting the various functions of the cell leading to development of a disease or aggravation of existing illness.

Magnesium is one such an element, which has escaped so far the attention of the clinicians and not found its rightful place in the electrolyte panel of estimations carried out in various clinical laboratories across the world. But in recent years there is plethora of studies available reporting the role of long term deficiency of magnesium in the causation and aggravation of various diseases like diabetes, hypertension, Ischemic Heart Disease and cardiac arrhythmias.

Two reasons can be attributed for the development of nutritional deficiencies. One is, inadequate supply of variety of foods in the diet, and the second reason is disease process that interferes with the absorption and metabolism of the nutrients. Some reasons are under the control of man/woman, some reasons are beyond his/her control. Deficiencies occur in both privileged section and under-privileged section. In the under-privileged section, the deficiency of both principal nutrients and accessory elements occur due to out of reach to these people. In the privileged section, they are within the reach of both the principal nutrients as well as accompanying elements. It is easy to understand the reasons behind the deficiency in the under-privileged section, whereas the reasons behind the deficiency in privileged section may be due to two reasons. The predominant reason is self made, and other reason may be due to existence of some sort of disease.

One must probe the reasons why there has been an increasing trend in both vitamins and mineral deficiencies in the modern era. It is possible due to the changing lifestyle and dietary habits, dependence on more and more refined food items and purified drinking water supplies. In recent years apart from deficiencies of other elements and vitamins, the deficiency of magnesium has also been on the rise and the role of magnesium deficiency in the causation and aggravation of various diseases like
cardiovascular disorders and diabetes has prompted us to take up the aspect of role of magnesium in diabetes and cardiovascular disorders.

Amount of magnesium available to man/woman is dependent upon the composition of food and type of drinking water supplies. Magnesium is rich in vegetables as it is component of chlorophyll. Though dietary supplies contribute maximally to the body magnesium, nevertheless one cannot undermine the magnesium available through consumption of drinking water. Out of the daily intake of 300 mg of magnesium per day, drinking water with rich magnesium content can contribute up to 1/3rd of this daily requirement, as the average daily intake of water is 1 to 2 liters. Water has got the capacity to take care of daily intake of magnesium to a major extent in the absence of adequate supply through the dietary means. The importance of magnesium present in water is that, it is easily available in comparison to dietary magnesium, where the available content may vary due to various factors like cooking and other factors which are prevalent in gastrointestinal tract during the digestion of food.

Water is an essential component for sustenance of life. Often we forget that the water cycle and the life cycle are one. Lot of emphasis has been given in the recent years regarding the water supplies. Experts in this field say that, in future water will acquire such an importance in the daily life of mankind that may be in future the main issue for the wars may be water though two third of the world is covered with water. Still the existing water supplies are not fulfilling the requirements of the world population. As estimated, 17% of the world’s population does not have access to the safe drinking water. Only 51% are within the reach of some centralized system of water supplies.

Lack of safe drinking water and adequate sanitation leads to the death of more than 1.6 million children under the age five. Even in the developed countries there are no regulations for the natural potable water supplies as well as bottled water. Though in some countries there are regulations, but there is no such monitoring policy to check the adherence to these regulations. In India also there is existence of standards for drinking water supplies. Due to lack of effective monitoring, these standards are hardly followed.
The general perception of safe drinking water is, water without pathogenic microbial and as obvious anthropogenic or the chemical contaminants. There is a lack of information and regulation in the desirable mineral content present in any source of water including potable or bottled water all over the world. Naturally, lack of awareness has led to the shortfall in the development of regulation to keep the desirable content of minerals in the drinking water.

In India, the awareness of the importance of minerals and other beneficial constituents in drinking water has been in existence over 1000 years. In Vedas of ancient India water is mentioned of having the desirable qualities like Sheetham (cold to touch), sushishi (clean), sivam (should have nutritive value, requisite minerals and trace elements), Istham (transparent), vimalam lahu and shadgunam (its acid base balance should be within normal limits) (Sadgir and Vamanrao 2003). In spite of the details regarding good drinking water in Indian literature, in the modern era people tend to neglect such information and adapt such a lifestyle which will bring harmful effects. Looking into the failure of the commercial suppliers of water filters and the suppliers of bottled water to bring the awareness regarding the contents of water and the maintenance of standards laid down in their products, has led us to take up the first leg of our study, on the drinking water supplies available to the people residing in both urban and rural areas of Surat.

In this phase of study, we have included 557 subjects including normal healthy controls and subjects afflicted with disorders like juvenile onset diabetes, maturity onset diabetes subjects with various cardiovascular diseases and diabetes with cardiovascular disorders. Subjects belonged to both rural and urban areas, information regarding their dietary habits, habits of smoking and alcohol have also been taken up. Information regarding water supplies, type of filter used and the levels of total hardness, calcium and magnesium hardness were also carried out. The basic purpose of this study was, to know the role of magnesium, its availability, deficiency status and consequences of deficiency in health and disease. Magnesium is known to perform many functions. These functions include, as co-factor of enzymes, in membrane transport, in myocardial contractility, synthesis of insulin, storage of catecholamines and release of PTH and also the
reproductive functions. Subclinical deficiency of magnesium is quite common. This may be due to mechanisms like redistribution, reduced intake, increased gastrointestinal loss and renal loss.

Deficiency of magnesium is known to cause hypocalcaemia, hypokalemia, demineralization of bone, neuromuscular manifestations, manifestations of central nervous system and cardiovascular manifestations like arrhythmias, congestive heart failure, hypertension, digitalis toxicity, atherosclerosis and diabetes.

The second leg of our study was focused on the determination of normo and hypomagnesaemic status in the subjects based on the analysis of serum magnesium levels. In this part of our study serum magnesium levels were assessed and the status of magnesium was determined and based on the levels of serum magnesium subjects were categorized into normo and hypomagnesaemic subjects. This categorization was done in each groups whether they were healthy controls or afflicted with either juvenile diabetes, or maturity onset diabetes, or with cardiovascular diseases or diabetes with cardiovascular diseases.

There has been increasing prevalence of diabetes mellitus all over the world. India today leads the world with over 32 million diabetic patients and this number is projected to increase to 79.4 million by year 2030. The rise in incidence of diabetes is not only an urban phenomenon, but also becoming a rural phenomenon, as the incidence of diabetes has risen from 2.2% in 1989 to 6.36% in 2003 in rural Indian population. Magnesium has got well established role in carbohydrate metabolism. Magnesium is involved in the membrane transport of glucose, insulin secretion and binding activity of insulin. Many workers commented that hypomagnesaemia can be a consequence, or a cause of diabetic complications. Both types of diabetes are known to cause magnesium deficiency and it is also well known that, diabetes mellitus is most common metabolic disorder associated with magnesium deficiency. Looking into the importance of magnesium and the consequences of hypomagnesaemia in the causation of diabetes mellitus, we have included 124 subjects belonged to both types of diabetes mellitus and the status of magnesium and their drinking habits, habits like alcohol, smoking and pattern of various
other parameters that determine liver function, renal and cardiac function as well as lipid profile and the body mass index and the status of blood pressure were taken up.

The incidence of cardiovascular disorders is on rise. Persistent presence of hypertension which affects approximately one billion individuals worldwide is a challenge to the health professionals, as people with hypertension have got the higher frequency of development of cardiovascular disorders.

The role of magnesium in cardiovascular physiology is well known. Being a calcium antagonist, it modulates vasomotor tone, blood pressure and peripheral blood flow. Magnesium also lowers the systemic vascular resistance, dilation of coronary arteries and reduces platelet aggregation. There is an association between magnesium deficiency and development of ventricular arrhythmias, torsa de pointes, supraventricular tachycardia and enhanced sensitivity to digoxin. In case of myocardial infarction lower levels of magnesium has been reported. The most worrisome is magnesium deficit and setting of congestive heart failure, which affects more than 4 million Americans and the setting of hypertension which affects more than one billion people around the world.

Moderate deficiency of magnesium may result in flattening of the T wave, shortening of the ST segment and possible prolongation of the PR and QRS intervals. In addition to all the electrocardiographic changes, the T wave may invert and U waves may become pronounced with prolonged deficiencies in severe magnesium deficiency. The observed changes in ECG are similar to those observed in potassium depletion, and the changes may therefore be secondary to hypokalemia, which is commonly seen in magnesium deficiency.

Cardiovascular diseases like ventricular arrhythmias, torsade de points, supraventricular tachycardia and enhanced sensitivity to digoxin have been reported to be associated with magnesium deficiency. There has also been epidemiological and experimental evidence linking magnesium deficiency and atherosclerotic cardiovascular diseases.
Cardiac arrhythmias are well known to be associated with magnesium deficiency. The arrhythmias that occur in magnesium deficiency may be either atrial or ventricular. Supraventricular arrhythmias such as premature atrial complexes, atrial tachycardia, atrial fibrillation, and junctional arrhythmias have also been reported. (Hollifield, 1987). The relationship between magnesium deficiency and arrhythmias associated with acute myocardial infarction seems to be complex. The frequency of ventricular arrhythmias occurring post-myocardial infarction also appears to be increased in hypomagnesaemic patients.

In the myocardial cells, magnesium is involved in regulating the potassium influx through other potassium channels. These channels normally allow potassium to pass more readily inward than outward (inward rectification). Magnesium appears to regulate the outward movement of potassium in myocardial cells. In the absence of magnesium, potassium is transported equally well in both directions. Therefore, in the absence or a deficiency in myocardial magnesium, can lead to a reduced amount of intracellular potassium due to a less efficient Na, K-ATPase system and the loss of inward rectification. The resting membrane potential partially determined by intracellular potassium concentration, less negative resting potential results due to decrease of the concentration of potassium leading to prolongation of the QT interval and enhanced vulnerability for ventricular arrhythmias.

For more than 60 years, the relationship between magnesium and the heart – specially, the influence of lower levels of magnesium on cardiac rhythm has been studied. Magnesium has an essential role in normal cardiac electrophysiology, and inadequate concentrations of this cation contribute to a variety of cardiac arrhythmias as mentioned earlier. Magnesium deficit in the setting of congestive heart failure (CHF), which affects some 4 million Americans, and in the setting of hypertension, which affects more than 30 million, is particularly worrisome. Approximately 4 to 7 lakhs of people are newly diagnosed with CHF every year. Patients with CHF have a very high propensity for ventricular arrhythmias, which are an important cause of death in this group and majority of people are linked to hypomagnesaemia.
There have been reports regarding development of digoxin toxicity in the hypomagnesaemic and magnesium depleted patients though the serum levels are normal. Association of hypomagnesaemia with digitalis toxicity may be due to a number of mechanisms. Enhancement of digitalis toxicity in the hypomagnesaemic subjects is due to the depletion in intracellular potassium, which is common observation in magnesium deficiency. Another mechanism may be due to reduced sodium-potassium Na, K-ATPase activity in myocardial cells with magnesium deficiency. The relationship between magnesium and blood pressure has been studied for decades. An inverse relation between magnesium and blood pressure has been reported and magnesium supplementation has also been found to be useful in reducing blood pressure. Of course there are some studies that did not corroborate these findings.

The possible relationship between hypertension and magnesium deficiency is an important consideration because these two often coexist in high proportions in populations such as diabetics and alcoholics.

Development of atherosclerosis in the hypomagnesaemic subjects is another potential cardiovascular complication. Substantial body of epidemiological and experimental evidence linking magnesium deficiency and atherosclerotic cardiovascular disease is available. A number of experimental studies have suggested that magnesium deficiency may play role in the pathogenesis of atherosclerosis. Magnesium deficiency may contribute to the progression of atherosclerosis by causing hypercholesterolaemia, hypertriglyceridaemia due to disturbances in lipid metabolism. Other features which are reported are increased aggregation of platelets and hypertension.

Coronary artery disease (CAD) is one of the important causes of death in India. 25% of global deaths due to CAD were from India. By year 2015, India will have the largest CAD prevalence in the world. An inverse relationship has been reported between magnesium intake and cardiovascular risk. A number of epidemiological studies have reported the relationship between mineral content of water, water hardness and incidence of cardiovascular disease. In relation to the water hardness, low levels of magnesium have been implicated in the causation of sudden death. It is a well established fact that, cardiovascular diseases are often associated with diabetes mellitus. Subjects with long
term diabetes mellitus are likely to suffer from hypertension and many other cardiovascular complications.

There has been an association between the disturbances in various biochemical parameters especially, lipid profile and enzymes pertaining to cardiac tissue in the cardiovascular disorders. Diabetic subjects with abnormal blood glucose leading to the disturbance in carbohydrate metabolism, have more likely chance of abnormal lipid metabolism also. The abnormal lipid metabolism in diabetic subjects may act as precipitating factors leading to the development of atherogenesis and ultimately leading to cardiovascular complications. The third leg of our study focused on status of magnesium in cardiovascular disorders and diabetes with cardiovascular disorders to find out the extent of normo and hypomagnesaemia and changes in various biochemical parameters pertaining to liver function, renal function, cardiac function, lipid profile, body mass index and status of blood pressure.

Magnesium is not included in the routine electrolyte panel in many laboratories across the world. These lacunae lead to the lack of detection of the deficiency of magnesium in the general population who are visiting hospitals as well as in hospitalized patients. The prevalence of hypomagnesaemia in general patients ranges from 11-49% but it is 20-44% in the patients admitted in intensive care unit. Also another interesting finding is that, mortality rate of the intensive care patients is two folds in the hypomagnesaemics compared to normomagnesaemics. The serum levels of magnesium are found to be lowest in patients admitted in intensive care unit. The fourth leg of our study is based on the patients admitted in intensive cardiac care unit with complications like diabetes mellitus and cardiovascular disorders.

There has been plethora of reports regarding the pattern of various biochemical parameters pertaining to the determination of functional aspects of liver, kidney and cardiac tissue. A number of reports are available regarding the serum levels of uric acid, phosphorous, calcium, magnesium and anthropometric parameters like body mass index in the populations residing in various parts of the India but very few reports are available regarding the status of these parameters in the different age groups and genders in the population residing in and around the city of Surat. The final leg of our study included
the assessment of various biochemical parameters in the different age groups and genders in the subjects either belonged to the group of healthy controls or afflicted with various disorders like juvenile diabetes or maturity onset diabetes mellitus or cardiovascular disorders or diabetes with cardiovascular disorders.

The present study is first of its kind conducted in the population residing in and around the city of Surat to explore the various aspects of magnesium in health and disease, an important cation which received less priority from the health professionals but has immense role in the normal physiology and pathology. It is no doubt that this cation has been grossly neglected and knowing its status would help the clinician in his endeavor to treat the patients afflicted not only with diabetes or various cardiovascular diseases but also various bone and neuromuscular diseases. Analysis of this element is not complex and can easily be included in the current electrolyte panel without putting much burden to the exchequer. A small effort has been attempted to draw the attention of the health professionals regarding the importance of this element, though it is a small step but we believe in the often quoted Chinese proverb which says that “a journey of thousand mile starts with a single step”.