CHAPTER I
INTRODUCTION

The human body is a very complicated system consisting of millions of cells organized uniquely and functioning dynamically together. Any condition that impairs the organization or functioning of a cell can lead to a disease condition. Every disease condition has a cause and it displays a cycle of onset or beginning; course or time-span of afflictions and at the end it disappears or partially disables or kills the victim. Many diseases like Diabetes Mellitus, Coronary Heart Diseases, and Cancer has been threatening to the mankind from the very beginning to the present century.

The term diabetes has been derived from the Greek word “διαβήτης”, diabetes meaning syphion was coined by Aretaeus of Cappadocia. Thomas Willis added the word mellitus “μελίτοείσ”, from the Latin meaning "honey", a reference to the sweet taste of the urine. This sweet taste had been noticed in urine by the ancient Greeks, Chinese, Egyptians, Indians, and Persians. The Indian physician Susrutha in 500AD also mentioned the sweet taste of diabetic urine and classified it as Medhumeha advising exercises to "cure" it (Dwivedi and Dwivedi, 2007).

Clinically diabetes is defined as the most common endocrine disorder of carbohydrate metabolism characterized by hyperglycemia and glucosuria which deepens on deficiency of insulin, leading to micro and macro vascular complications that substantially decreasing the quality of life and increasing the morbidity and mortality rates. Diabetes is diagnosed when fasting plasma glucose concentration values are equal to or exceed 7.0 mmol/l (whole blood greater than or equal to 6.1mmol/l or a random venous plasma glucose concentration equal to or greater than 11.1 mmol/l) (WHO, 2006). In all forms of diabetes, the body's ability to convert food into energy is impaired due to impaired insulin
production and insulin action and leads to symptoms which develop gradually as fatigue, frequent urination, excessive thirst and hunger, weight loss, blurred vision, and slow-healing wounds or sores.

WHO (2006) classified diabetes on the basis of insulin requirement as Insulin Dependent Diabetes Mellitus (IDDM-type I) and as Non-Insulin Dependent Diabetes Mellitus (NIDDM-type II). Other types of diabetes include Malnutrition – Related Diabetes Mellitus (MRDM), Gestational diabetes mellitus (GDM), Impaired Glucose tolerance (IGT), Statistical risk classes that include patients with previous and potential abnormality of glucose tolerance and Diabetes related to other conditions and syndromes like pancreatic disease, hormonal or endocrine etiology, drugs or chemicals induced conditions, abnormalities of insulin or its receptors, or due to certain genetic syndromes.

Type 1 diabetes is also known as insulin-dependent diabetes. It is an auto-immune condition in which the immune system of the body (that protects the body against infection and disease) turns against itself. As a result most, or all, of the insulin-producing cells of the pancreas are destroyed and the pancreas is not able to produce enough insulin. It is seen among those aged less than 40 years of age. There are different kinds of insulin treatments available. Insulin is usually injected 1-4 times per day depending on the type of insulin (quick-acting or slow-acting), the daily routine of the person, the frequency, timing and quantity of exercise taken.

Type 2 diabetes also referred to as non-insulin dependent diabetes occurs when the body does not produce enough insulin or the insulin produced does not work properly (this is known as insulin resistance). Type 2 diabetes usually develops in middle-aged people (over the age of 40) and later life, but has been seen in younger adults and also recently amongst teenagers.

Type 2 diabetes accounts for 90 to 95 percent of all diagnosed cases and occurs more frequently in older people while Type 1 diabetes, which accounts for 5 to 10 percent of cases, usually strikes children and young adults. A third form, gestational
diabetes, develops in some women during pregnancy (LeRoith et al., 2008).

Diabetes Mellitus was once referred to as the ‘disease of prosperity or modernization’ has now become a common problem with serious consequences. It is a silent disease and the fastest growing threat to public health across the globe to both developing and developed nations; and indeed the most challenging health problems in the twenty first century and beyond. Vital statistics of WHO (2006 and 2007) shows an increasing trend in the diabetic population from 124.7 million in 1995 to 153.9 million in 2000 and currently at 220 million (WHO 2011) and is expected to grow in geometric proportions by 2030 affecting 366 million people. About two-third of the diabetic population reside in the developing countries (diabetesindia.com 2005).

Health situation in South East Asian region analysed by WHO (1997 and 2007) shows that 20 percent of the global diabetic population resides in this region and is likely to triple from 27.6 million in 1995 to 79.5 million in 2025; and has emerged as a public health problem.

India is the threshold of far reaching changes that is poised to join the ranks of the developed nations. With its urbanization trends and economic development, the country is also experiencing an Epidemiological Transition. Infectious diseases which were the bane of India are making way for a new crop of non-communicable diseases called ‘life style diseases’. Changing demographic profile, technological advances, sedentary life style and faulty diets have contributed much to it. A high level of glucose intolerance was found among young adults of rural and urban India, highlighting an urgent need for preventive action to avert a public health catastrophe in India (Raghupathya et al., 2007).

As India crowns the glory of being the ‘diabetic capital’ of the world; it is predicted that by 2025, India will harbor more than 60 million diabetic patients, i.e., one out of four individuals will be an Indian diabetic in the world (diabetesindia.com 2005). According to
the IDF (2009) Diabetes Atlas 4th edition, India has the second highest number of people with Diabetes at 5 crore (50 Million) adults. In addition to this, 4 crore (40 million) Indians have impaired glucose tolerance (IGT), which means they are at high-risk of developing Type 2 Diabetes.

Diabetic mortality in India is 1/6 of the total deaths that occurs worldwide. Indians are genetically predisposed to the disease; about 1.6 million cases are diagnosed every year while tens of millions remain undiagnosed (Pillai, 2006). A study conducted by Misra and Naval, (2004) points out that 11.2 percent of males and 9.9 percent of females in India are diabetic; overall prevalence being 10.3 percent.

The prevalence of diabetes in India according to WHO (2007) is 62.47 per 1000 population and is predominantly more among urban population; around six percent between 30 and 39 years, thirteen percent between 40 and 49 years and one-fifth of the population above 70 years of age. The prevalence of diabetes in Metropolitan cities in India is 11.6 percent in New Delhi, 9.3 percent in Mumbai, 11.7 percent in Bangalore and 16.6 percent in Hyderabad; whereas the global prevalence is more than 15 percent (Mageshwari and Minitha, 2004).

A series of recent population-based medical studies have revealed that Kerala is on the fast track to become an ‘ailment society’. With a sedentary lifestyle and high intake of saturated fat, the society is increasingly getting vulnerable to creeping maladies that are claiming an increasing number of young lives. Unless ‘Malayalis’ took a look at their diet and limbered up a bit, the state could be in for real shocks on the health front.

It is estimated that there are about 1.5 million diabetics in Kerala. The figure could be higher because of the absence of any established population based health screening programmes, there could be a lot of undetectable cases in the community says Dr.V.Mohanan Nair, CEO of the Indian Institute of Diabetes. Less
than 50 percent of the patients may have the classic symptoms of diabetes, while the rest are mostly non-symptomatic (Maya 2005).

Kutty et al., (2000) found that the overall prevalence of type 2 diabetes in 30-64-years of age at Neyyattinkara Taluk of Thiruvananthapuram district in Kerala was 9.2% among men, 7.4% among women, and 8.2% for all persons. Mortality rates are twofold higher in diabetics compared to the non-diabetic subjects. Effective prevention of diabetes mellitus is a long-term programme, which includes activities targeted against all ages from foetal life to elderly and needs to be culturally socially and economically appropriate. As the incidence of diabetes on the rise among the younger population, Kerala state might have to deal with an entire generation of chronic diabetes in the next 10-15 years.

Diabetes is scary as it leads to threatening complications lowering the life expectancy by a decade mainly due to kidney failure, lower-limb amputations, blindness and heart attacks. Younger individuals of the productive age group are mostly affected leaving a grave repercussion to the family and country. Diabetes today is not a problem associated with an individual but it is a large public health problem, growing tremendously year after year. The second leading cause of death in India among NCDs is due to diabetes accounted for 1.75 lakh deaths. The right diet combined with other suitable measures is a powerful tool which could keep this silent malaise at bay. Diet counseling with regulated life style, produces significant increase in the awareness on food that enhances good blood glucose control, proper selection of food, quantity of food consumed and factors lowering the risk of complications.

Managing diabetes has become easy with modern technology. But treatment has become high-tech, sophisticated and moneyed affair, handled only by diabetologists using the latest type of insulin and devices like the insulin pen or pump, all of which are prohibitively expensive. The staff reporter of the online edition of India’s National Newspaper, reports that the physicians of
Thiruvananthapuram have appealed to the government to evolve a financial aid scheme for the treatment of children with Type 1 diabetes (The Hindu, 2010). Children having Type 1 diabetes require a lifetime's supply of insulin, the expense of which is unaffordable for most parents.

According to WHO (2006) for a low-income Indian family with a diabetic adult, a quarter of the income is devoted to diabetes care. Treatment cost per person has gone up from around Rs.3000/- in the early 1990's to Rs.14,000/- annually. India presently has an annual estimated treatment cost of Rs.10,000 to 12,000 crore for diabetes which is likely to witness a scaling up to as much as Rs.1,26,000 crore by 2025. Direct cost includes cost of routine treatment, monitoring, laboratory and hospital cost; while indirect costs include lower productivity arising from absenteeism and disability. Many of the burdens of diabetes occur in the productive mid-life period and will therefore adversely affect workforce, productivity and economic development. Accurate estimation of these burdens, their risk factors, and time trends would help better to inform policy makers to monitor change in public health intervention.

In Kerala Scenario we need to adopt a preventive, public health approach to diabetes; promoting commonsense management of the disease, with cheap first-line drugs. Effective prevention of diabetes is a long term programme, which includes activities targeted against all ages from foetal life to elderly and needs to be culturally and socio-economically appropriate. Soman, (2004) echoes his view that life style intervention and education programmes, with a thrust on moderate diet, regular physical activity and tobacco abstinence should be implemented at the community level. The stress should be on community-based early screening programmes for diabetes, hypertension and cholesterol.

Although obesity and physical inactivity are known to be major risk factors for type 2 diabetes, recent evidence suggests that oxidative stress may contribute to the pathogenesis of type 2 diabetes by increasing insulin resistance or impairing insulin
secretion (Montonen et al., 2004). Hyperglycemia induces the overproduction of oxygen free radicals and consequently increases the protein oxidation and lipid oxidation. A significance difference in the mean plasma concentration of total antioxidant status was observed in type I (IDDM patients). Diabetes is an altered metabolic state of oxidation-reduction and that it is convenient to give therapeutic interventions with antioxidants (Ramakrishna and Rama, 2007).

Many recent studies have revealed that antioxidants are capable of neutralizing free radicals and are effective in preventing diabetes in animal models reducing the severity of complications. Antioxidants are substances that fight against oxidation and inhibit reactions of free radicals in our body, which causes major health hazards. They are highly essential chemicals which include vitamin A, E and C, β carotene, zinc, selenium, glutathione peroxidase, superoxide dismutase, and melatonin (Chandrasekhar, 2009; Akbar et al., 2011). Antioxidants are useful radio-protectors and play an important role in preventing many human diseases including diabetes. The present study also measures the antioxidant status of diabetic and non diabetic subjects and the clinical importance of determining the antioxidant status consists of identifying patients with increased risk of diabetes and nutrient deficiency.

Dietary antioxidants have been hypothesized to have a protective effect against the development of diabetes by inhibiting per-oxidation chain reactions. It seems plausible that a sufficient intake of antioxidants plays an important role in protection against type 2 diabetes. Serum tocopherol levels were associated with lower risk of type 1 or type 2 diabetes. Some prospective studies have shown that higher vegetable and fruit consumption may lower the risk of developing diabetes, suggesting that antioxidants in the diet may have a synergistic effect (Montonen et al., 2004).

The overall activity of antioxidants and antioxidant enzymes are used for monitoring and optimizing antioxidant therapy. The depletion of antioxidant induced by oxidative stress is eliminated by
release of stock organ antioxidants, mainly from liver and adipose tissue and the induction or activation of antioxidant enzymes. Plasma from healthy subjects showed significantly higher antioxidant status compared with plasma from diabetic patients. The antioxidant status of plasma, reflect an antioxidant response since ROS generation was rapidly down-regulated by the presence of plasma which is 3.3-fold in diabetic patients and 5.8-fold in healthy subjects. It confirms the lower antioxidant activity of plasma from diabetic patients (Medina et al., 2007).

There can be no innovation in nutrition unless a change occurs to the composition of people’s diets which have the potential to improve antioxidant status and thereby health and wellbeing. The present study aims to measure the significance of supplementing a natural antioxidant spirulina to rule out its anti-diabetic effect. Nutritional or dietary supplements come in a variety of assortments and often contain minerals, vitamins, and sun dried herbs. The purpose is to give something extra in addition to the nutrients from regular food.

According to the Dietary Supplement Health and Education Act (DSHEA) of 1994, a dietary supplement is a product that contains substances like vitamins, minerals, foods, botanicals, amino acids and is intended to supplement the usual intake of these substances. Dietary supplements are found in pill, tablet, capsule, powder or liquid form and are meant to be taken by mouth (Jegtvig, 2006).

In this health conscious age, the blue-green algae, Spirulina is the nature’s most nutritious wholesome organic food with proven beneficial therapeutic properties. It is fast emerging as a whole answer to the varied demands due to its impressive nutrient composition which can be used for therapeutic uses.

Spirulina is a primitive organism originating some 3.5 billion years ago that has established the ability to utilize carbon dioxide dissolved in sea water as a nutrient source for their reproduction. Spirulina is a photosynthesizing cyanophyte (blue–green algae) that
grows vigorously in strong sunshine under high temperatures and highly alkaline conditions (Habib et al., 2008). In 1967, Spirulina was established as a “Wonderful Future Food Source” in the International Association of Applied Microbiology (Sasson, 1997). While no organism fulfilled its promise of cheap protein to combat malnutrition in the underdeveloped and developing countries; spirulina continued to give rise to research and increasing production, reflecting its perceived nutritional assets.

Spirulina provides highest amount of good quality protein (65-71%), various vitamins, and minerals including chelated minerals along with pigments like phycocyanin. It contains B-complex vitamins, gamma-linolenic acid and the super antioxidants, beta-carotene, vitamin E and trace elements. The United Nations world food conference declared spirulina as “the best for tomorrow”, and it is gaining popularity in recent years as a food supplement (Anitha and Chandralekha, 2010). The spirulina’s ability as a potent anti-viral, anti-cancer, hypocholesterolemic and health improvement agent is gaining attention as a nutraceutical and a source of potential pharmaceutical (Layam and Chandra, 2006).

Spirulina or Arthrospira the blue-green alga became famous after it was successfully used by NASA as a dietary supplement for astronauts on space missions. It has the ability to modulate immune functions and exhibits anti-inflammatory properties by inhibiting the release of histamine by mast cells. Multiple studies investigating the efficacy and the potential clinical applications of Spirulina in treating several diseases suggest that this alga may improve several symptoms and may even have anticancer, antiviral and antiallergic effects (Karkos et al., 2008).

Inspite of the intensive research into the aetiology and pathogenesis of diabetes many aspects remain as a mystery. The problems of diabetic population are highly complex. There is every reason to suppose that diabetes will remain as a threat to public health in this century and beyond. Although there are a number of drugs available on the market for diabetes mellitus, long time use
may cause a number of side effects. Hence, a large number of studies are in progress to find natural sources, which are effective in reducing the intensity of diabetes. After taking in to account the importance of Antioxidants and its natural source spirullina, the investigator aims to confine the study to assess antioxidant status of diabetic subjects and to measure the anti-diabetic effect of the supplement.

Currently enormous research interest is centered worldwide about the search for newer, cheaper, and safer natural supplements which can effectively normalize the metabolic derangement underlying the onset of clinical diabetes. Kerala has the highest level of morbidity and hospitalization rate in India. The emerging high morbidity level in the state needs special attention since the state health system is not healthy enough to meet the new phenomenon. Keeping the above facts as the basis the present study entitled ‘Antioxidant Status of Subjects with Diabetic Mellitus’ was undertaken with the following objectives.

**Aims and Objectives:-**

1. To study the socio-economic, dietary and life style pattern of diabetic patients.
2. To assess the health and clinical status of diabetic patients.
3. To analyse the antioxidant status of NIDDM, IDDM and Non-diabetic subjects and assess the impact of food supplementation on the antioxidant status of diabetic patients.

**Hypothesis:-**

\[ H_1: \text{Supplementation of Spirullina + lime juice will increase the antioxidant status of diabetic patients.} \]

\[ H_0: \text{Increase in plasma antioxidant status will decrease blood sugar and cholesterol.} \]