INTRODUCTION
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Diabetes Mellitus (DM) has become a pandemic, most common non communicable disease with a global prevalence of 171 million in year 2000 as per World Health Organization (WHO), which is predicted to be 366 million by the year 2030. As per the WHO projection 32 million of diabetics are in India alone making it a country with highest incidence of the disease. With the increasing prevalence, 80 million Indians are expected to be affected by diabetes up to the year 2030.\textsuperscript{1} \textbf{Diabetes is the leading cause of death, disability and economic loss worldwide.}\textsuperscript{2} Two major concerns are that much of the increase in diabetes will occur in developing countries due to, population growth, ageing, unhealthy diets, obesity and sedentary life styles, and that there is a growing incidence of type II DM-which accounts for 90\% of all cases at a younger age. The number of deaths attributed annually to diabetes is around 3.2 million.\textsuperscript{1} Diabetes has become one of the major causes of premature illness and death in many countries, mainly through the increased risk of cardiovascular disease (CVD). The impact of the world wide explosion of type II DM will remain centered in developing countries, since by the year 2025, 75\% people with diabetes will be in the developing countries as compared to 62\% in 1995, a majority in Indian subcontinent (59\%) and China (68\%).\textsuperscript{3,4}

\textbf{Asian Indians are more prone to type II DM} at a younger age and premature cardiovascular disease.\textsuperscript{5}

The increasing incidence & prevalence of diabetes is putting lot of financial, social & health care burden with decreasing productivity of Indian population. \textbf{Diabetes mellitus being a multi factorial disease, total prevention is impossible.} Understanding the patho-physiology of this \textbf{major silent killer} and its association with various measurable
biochemical parameters may provide further insight in development and progression of diabetes. The present goal worldwide is to understand the factors causing progression and multi organ damage caused by diabetes as a metabolic syndrome. The kinetic factors and the biochemical parameters governing the natural course of the disease may provide vital information in monitoring as well as taking preventive measures to delay the progress of the disease and reduce the burden of morbidity and mortality.

Hyperglycemia has been identified as the major factor for development of diabetic micro vascular complications including retinopathy and nephropathy. Micro-vascular disease or microangiopathies has recently been a focus of discussion and various trials (Diabetes Control and Complications Trail [DCCT] & United Kingdom Prospective Diabetes Study [UKPDS]) have established that good glycemic control inevitably lead to significant reduction in microvascular complications in type I and type II DM.

Type II DM is a heterogeneous disorder characterized by impaired insulin secretion, insulin resistance and increased glucose production. The chronic hyperglycemia of diabetes is associated with long term damage, dysfunction and failure of various organs. The metabolic dysregulation associated with diabetes mellitus causes secondary patho-physiologic changes in multiple organ systems that impose a tremendous burden on the individual with diabetes and on health care system.

Duration of diabetes mellitus and degree of glycemic control are the best predictors of development of retinopathy, hypertension is also a risk factor. Proteinuria in individuals with diabetes mellitus is associated with markedly reduced survival and increased risk of CVD. Diabetic nephropathy is usually first recognized as proteinuria. Urinary albumin excretion may be then, an indicator of renal disease in type II DM patients and in fact may reflect a state of generalized
vascular damage occurring throughout the body. Individuals with diabetic nephropathy almost always have diabetic retinopathy. Therefore being the most common metabolic disorder diabetes has become a leading cause of morbidity and mortality in humans by its long term complications.\textsuperscript{10,11}

**Acute inflammation** is the immediate and early response to an injurious agent. Type II DM is frequently associated with an inflammatory status, there is a **cytokine associated acute phase reaction**, part of the innate immune response.\textsuperscript{12-14} The **dyslipidemia** common in type II DM (hypertriglyceridemia and low serum levels of High Density Lipoprotein [HDL] cholesterol) is also a feature of natural and experimental acute phase reaction.\textsuperscript{15,16} Acute phase proteins (APP) are synthesized in liver and their release occurs in response to circulating **cytokines produced during inflammation**. APP together with systemic features of fever and leucocytosis is termed acute phase response.\textsuperscript{17} **Ceruloplasmin** an APP is considered to be elevated after inflammation, trauma and in a variety of neoplastic states. It is a plasma protein that functions as a copper transporter and causes oxidation of various amines, oxidation of ferrous to ferric ion for subsequent uptake by transferrin and as an antioxidant against lipid peroxidation.\textsuperscript{18,19}

Another important inflammation sensitive protein is **C-reactive protein (CRP) synthesized by liver that predicts coronary heart disease risk**. It is a classic and an exquisitely sensitive APP that shows a strong and independent association with risk of coronary heart disease (CHD) and other athero-thrombotic events. It is thought to represent the state of chronic low grade inflammation of the arterial vessel wall at atherothrombotic sites.\textsuperscript{20,21}

**Sialic acid** is a generic term for a family of acetylated derivatives of neuraminic acid it is an **essential component of glycoproteins and glycolipids**. It is located in the terminal non reducing ends of carbohydrate
chains being linked to other sugars most commonly galactose and N-Acetyl galactosamine. It acts as a cofactor of many cell surface receptors e.g. insulin receptor and is positively associated with most of the serum acute phase reactants. In human plasma large quantity of sialic acid is found as a component of orosomucoid, alpha-1-antitrypsin, haptoglobin, ceruloplasmin, fibrinogen, complement proteins and transferrin.22,23 Some of these sialylated glycoproteins are called acute phase reactants and such substances rapidly increase in concentration after the onset of an inflammatory reaction or injury. Hypothesis has also been made that a cytokine induced acute phase response is an integral part of the pathophysiology of type II DM which leads to an elevated serum sialic acid level.23,24

Excess nourishment and sedentary life style leads to glucose and fatty acid overload which in turn produces reactive oxygen species. Antioxidants work together in human body against the reactive oxygen species (ROS). ROS cause lipid peroxidation & oxidation of some specific proteins, thus affecting many intracellular & inter cellular systems. Impaired antioxidant defense mechanism with increase oxidative stress has been proposed as the root cause underlying development of insulin resistance, beta cell dysfunction and type II DM.25,26 It is also implicated in long term micro and macro vascular complications of diabetes. Reactive oxygen species initiate chain reaction leading to decrease nitric oxide (NO) availability, increased markers of inflammation and chemical modification of lipoprotein.26,27 Oxidative stress can be measured monitoring the changes in blood malondialdehyde (MDA) levels, which is a marker of lipid peroxidation. MDA levels are raised with increased oxidative stress.28 The efficiency of counter mechanism of antioxidant system can be accessed by studying the levels of super oxide dismutase (SOD) an endogenous agent & exogenous potent antioxidant agent in the form of vitamin C.29,30
Type II DM is frequently associated with an inflammatory status; there is a cytokine associated acute phase reaction, part of the innate immune response. The relationship between low grade inflammation and diabetic complications are still unclear. Whether imbalance between oxidants & antioxidant system aggravates the complications & what is their relation with the acute phase reactants in such diabetic patients, needs to be further explored. Therefore the present study “Association of markers of acute phase response to serum total sialic acid levels in type II DM patients with and without nephropathy and its correlation with the antioxidant levels” was undertaken to evaluate and establish the role of sialic acid and APP in type II DM along with the status of oxidants & antioxidant system & their correlation with micro vascular complications. Correlation between complications, acute phase reactants & decrease antioxidant levels may further help in establishing newer simpler parameters to monitor progression of diabetes and support the role of exogenous antioxidants in prevention & delaying of complications in diabetics.