IV. DISCUSSION

Diabetes is a mundane problem and India is the leading partner to this disease. It is the single most important metabolic disease, widely recognized as one of the leading causes of death and disability worldwide. Diabetes has become an epidemic in India. The prevalence of Type-1 and Type-2 diabetes are known to be multifactorial disorders, triggered by a combination of genetic (inheritance) and environmental factors (diet and lifestyle). Diabetes pandemic reaches its peak in India with the highest prevalence. A rapid alarming rate of prevalence of diabetes is noticed in the entire globe.

Diabetes is a syndrome characterised by disordered metabolism and abnormally high blood sugar (hyperglycaemia) resulting from insufficient levels of the hormone insulin. Once it was considered as a disease of affluent and elderly, but now there is a transition from affluent to ordinary and elderly to young and middle aged people with severe morbidity and mortality.

Despite tremendous achievements and advancements in the field of medicine, adequate literacy, growing knowledge on diabetes, this disease is marching towards its peak in an unstoppable speed. It has already taken a new avatar in wreaking a havoc to mankind. This killer evil ramifies the globe without bias, handicaps the victims with different kinds of morbidities, there by generating immense revenue loss to the entire world, and when the complications reach its maximum, it will be fatal.
Of the three types of diabetes (i.e) Type-1, Type-2 and gestational diabetes, Type-1 diabetes is the most severe type of diabetes requiring daily insulin injections on a life long basis. The etiology of Type-1 diabetes is still obscure. Several genetic factors have been identified for the disease, although environmental factors also play a crucial role in Type-1 diabetes.\textsuperscript{292, 293}

There are four stages in the natural history of Type-2 diabetes. First stage at birth, where glucose homeostasis is normal, but individuals are at risk for Type-2 diabetes because of genetic polymorphisms (diabetogenic genes). Decrease in insulin sensitivity emerges probably as a result of a genetic predisposition and life style (environmental), which are initially compensated for by an increase in beta cell function, so that glucose tolerance remains normal in the second stage.

In the third stage, as a result of further deterioration in beta cell function and increase in insulin resistance, fasting plasma glucose can increase due to an increase in basal endogenous glucose production, but the patient is still asymptomatic. Finally in the fourth stage, as a result of further deterioration in beta cell function, both fasting and post-prandial blood glucose levels reach clearly diabetic levels and the patient becomes symptomatic.\textsuperscript{294}

Type-1 diabetes (or) D. insipidus is characterized by the passing of great quantities of urine, which is almost colourless. The disease is most often nervous in origin; and injury to the nerve centres in the brain and spinal cord, excessive emotionalism, overwork, etc., may all bring on the complaint. D. mellitus (or) Type-2 diabetes is the most common form and serious of the two,
where there is sugar present in the urine. In the ordinary course of events, when starches are digested in the small intestine, the resultant glucose (sugar) is carried by the blood to the liver, and only a small amount is allowed to remain in the blood at any one time. In D. mellitus, however more than this minimum amount of sugar remains in the blood, and the kidney gets rid of as much of the excess as they can be excreting in the urine.23

Around 70 percent Indians residing in rural areas are without basic amenities.291 Lack of quality healthcare and awareness, minimum facilities and increasing disease related complications in these areas facilitate the Type-2 diabetes as more violent one.295

Most of the population based studies on diabetes in the globe centre around the urban population.15, 16, 18, 19, 296-298 Such studies in the rural agrarian communities are very scarce to evaluate the level of metabolic syndrome, prediabetes, diabetes and its damage control mode.

The main objectives of the present epidemiological studies on diabetes in a rural agrarian population are: (i) to assess the prevalence of Type-2 diabetes mellitus on different socio-demographic characteristics of the population. (ii) to understand the various known and unknown risk factors in the survey group (iii) to find out the impact of habitat(s) on the incidence of diabetes (iv) to identify how far the disease is noticed in this physically active (agrarian) group and (v) to evaluate the role of individual, environment and heredity on the incidence of diabetes.
Socio-demographic factors on diabetes

The first multicentric study on diabetes in India was done by the Indian Council of Medical Research (ICMR) between 1972-1975, and the disease prevalence was 3.0% in rural and 1.3% in urban areas.68 Most of the population based rural studies on diabetes in rural India shows 3.8%69, 1.9%70, 1.5%71, 5%72, 4.9%73 and 1.9%65 disease prevalence. But, higher rate of diabetes prevalence has been observed from the recent studies with 9.3%74 and 13.2%.80 A similar observation (8.12% disease prevalence) has been found in the present study too.299

Gender and diabetes

The prevalence of diabetes seems to be more or less the same in both genders.300 Some of the population based studies have reported that the prevalence was higher in females.15,301 A similar prevalence of diabetes in males and females are noticed in most of the population based studies.18,302,303 Recent studies reveal a higher prevalence of diabetes in males than in females.62,304 Our study too supports this view.299 In the present study it is found that, male patients have out numbered females. In males the disease prevalence is around 9.84%, where as in females it is 6.31%. It is also well evident from the study that, out of 37 villages, the percentage incidence of diabetes is slightly higher among females than in males in four villages. It is also evident from the study that the incidence of the disease is increasing towards the plain from the hilly areas as well as from the coastal (near) areas, may be due to the food habits of the people which is
explained by a hypothetical flow diagram. It corroborates a recent study.

**Age and diabetes**

The age at the onset of diabetes is at a younger age (i.e) 45-65 years in the developing countries than the developed countries. Indians are thought to develop diabetes at a very young age at least 10-15 years earlier than the whites and other groups. The age specific prevalence of Type-2 diabetes has been observed by many studies. Our study also coincides with the previous findings. The minimum age of T2DM cases in the present study is 19 years. The sudden pick up of the disease in the last two decades pronounces that, there has been a rapid transition of agrarian to urban lifestyles due to the increase of money flow, enhanced buying capacity and the availability of a variety of stuffs. In addition, fast food culture and sedentarianism are thought to be the main driving forces for the diabetes epidemic in the present physically active agrarian group.

The present findings reveal that there are two peaks of diabetes, one is in the age group 50 – 54 years and the other is seen in the group 70 – 74 years. Apart from that the disease pattern is more or less same in the male and female population. It is also clear from the study that the disease starts slowly at the age of 19 years and gains momentum at the age of 40 years in both sexes.
Respondents (5000) settled in 37 villages at a stretch of more than 40 km on road

- near the coast
  - limited access to the town
    - evoke moderate level of life-style changes + heredity + environmental impact
      - pronounces low level of incidence of diabetes
- in the plains
  - having close access to the town
    - enhances abrupt level of life style changes + heredity + environmental impact
      - pronounces high level of incidence of diabetes
- in hilly areas
  - limited access to the town
    - evoke moderate level of life-style changes + heredity + environmental impact
      - pronounces low level of incidence of diabetes

**Fig. 14. hypothetical flow diagram explains the prevalence of Type-2 diabetes in the study areas.**
Socio-economic status and diabetes

The direct\textsuperscript{306, 307} and the indirect\textsuperscript{308} relationship between socio-economic status and diabetes have been reported in many studies. An inverse relationship with 1:2:4 ratio of prevalence of diabetes in the poor, middle and upper class is noticed in the present study. The findings imply the transmission of disease from the rich to the poor ($r=0.94$).\textsuperscript{299}

The prevalence of diabetes in all sectors disproves that, diabetes is not only a disease of affluent people, but also it is common to all sectors and this is confirmed by previous studies. Studies from Cuttack has proved that, it could also occur in malnourished people.\textsuperscript{309} It is evident that in the last two decades, there has been a marked increase in the prevalence of diabetes among urban Indians.\textsuperscript{310}

The subjects in the higher socio-economic group had a higher risk of developing diabetes, where as an inverse relationship between socio-economic status and diabetes is noticed and the prevalence of diabetes is higher in the lower socio-economic groups.\textsuperscript{308} This paradox is mainly due to differences in the stage for epidemiological transition between developing and developed nations.\textsuperscript{311}

Hereditary onset of diabetes

Studies reveal that the prevalence of Type-2 diabetes increases approximately two to four fold when one or both parents are affected.\textsuperscript{83, 84} Different populations based studies reveal an excess maternal transmission of T2DM.\textsuperscript{83, 85, 86, 312} It is true in our
study also\textsuperscript{299} \((r= -1.0)\), the maternal transmission percentage is 24.14 and the paternal transmission is 19.95%. Diabetes is more likely to develop when there are other diabetic members in the family and it is 53.2% in the present study.

**Obesity and diabetes**

Obesity is an independent risk factor for diabetes, hypertension, cardiovascular disease, chronic kidney disease and so on.\textsuperscript{313} Excessive weight has become one of the major health problems among middle and upper class people throughout the globe. Its etiology is multifactorial. Excess body weight is the sixth most important risk factor contributing to the overall burden of disease worldwide.\textsuperscript{314}

Despite having lower prevalence of obesity as defined by BMI, Asian Indians tend to have greater waist circumference and waist to hip ratios\textsuperscript{315} thus having a greater degree of central obesity. Further, they have more visceral fat for any given body mass index,\textsuperscript{316} and for any given body fat and greater insulin resistance.\textsuperscript{102}

Studies shown that Asian Indians have an increased risk for developing Type-2 diabetes and related metabolic abnormalities compared to other ethnic groups.\textsuperscript{317, 318} Even though the prime reason(s) are obscure, certain specific bio-chemical and clinical characteristics known as “Asian Indian Phenotype” is thought to be one of the major triggering forces contributing to the increased predilection towards diabetes.\textsuperscript{319}
The positive role of obesity on T2DM is explained by many researchers.\textsuperscript{320, 321} Conversely, approximately 66\% of our study subjects are overweight or obese. The significance of waist-hip ratio on the incidence of T2DM is explained by some researchers.\textsuperscript{322, 323} The present study reveals a positive correlation of $r = 0.91$ between the non-diabetics and diabetics. The diabetes prevalence was more in patients with $>9.91$ waist-hip ratio.

Obesity is identified as a nutritional disorder, still continuing to be one of the most important, yet preventable health hazard. It has now become an important health problem in developing countries particularly in India, which is currently experiencing a rapid epidemiological transition. The consequences of industrialization and urbanization which lead to rise in standards of living, also promote weight gain and obesity rates begin to rapidly rise thus posing a growing threat to the health of people. There is a paucity of nation-wide data on the prevalence of obesity in India. Studies on obesity reveal that the prevalence of obesity ranges from 10 – 50 percent.\textsuperscript{324}

Rapid lifestyle changes in the past five decades trigger the incidence of new age diseases like Type-2 diabetes, obesity, hypertension, metabolic syndrome and heart disease. The invasion of fast food culture changed the lives of traditional indigenous communities, resulting in the surge of diabetes and related metabolic disorders.

The rise of diabetes in different ethnic groups including Africans and Asian Indians can be explained by Neel’s “thrifty genotype hypothesis”.\textsuperscript{325} This hypotheses proposes that some
genes are selected over previous millennia to allow survival in times of famine by efficiently storing all available energy during times of feast. However, these very genes lead to obesity and Type-2 diabetes when exposed to a constant high energy diet. In virtually all populations, higher fat diets and decreased physical activity and sedentary occupational habits have accompanied the process of modernization which has resulted in the doubling of the prevalence of obesity and Type-2 diabetes in less than a generation.

**Hypertension and diabetes**

Blood pressure is evoking a tremendous impact on the health of man. Hypertension is the primary preventable cause of the two major causes of mortality: coronary artery disease (CAD), and cerebrovascular disease (CVD).\textsuperscript{326} It increases the risk for CAD by two fold that of CVD seven fold and congestive heart failure four fold.\textsuperscript{327, 328} India leads the world with the largest number of diabetic subjects and is also projected to have the maximum number of cardiovascular deaths 15 years from now.\textsuperscript{8, 329, 330} Obesity is considered to be a major risk factor for hypoertension.\textsuperscript{331}

Risk estimates indicate that atleast two thirds of the prevalence of hypertension can be attributed to obesity.\textsuperscript{332} It is an important risk factor for the development and worsening of many complications of diabetes.\textsuperscript{333} The present findings reveal that, there is no sharp difference between the various forms of hypertension and the incidence of diabetes ($r = 0.95$ for non-diabetics Vs diabetics).
Lifestyle and diabetes

Several lifestyle factors affect the incidence of T2DM. Diet plays a tremendous role in the management of diabetes because, it is important to keep the blood sugar within a normal range. Various strategies have been proposed to prevent the development of metabolic syndrome. These include increased physical activity (such as walking 30 minutes everyday) and a healthy, reduced calorie diet. There are many studies that support the value of a healthy lifestyle as above. However, one study stated that these potentially beneficial measures are effective in only a minority of people, primarily due to a lack of compliance with lifestyle and diet changes.

Many reports have shown that the incidence of diabetes is lower in vegan or vegetarians. The present study also supports this view. Vegetarian diet may be effective in managing Type-2 diabetes. Polyunsaturated fatty acids (PUFA) content for less than 10 percent of the total calories and an essential fatty acids (EFA) content of at least 3 percent of the total calories is advisable for the management of diabetes. Protein intake of 0.8 kg. is recommended, so as to contribute 12-20 percent of the total calories. Vegetable proteins are preferred due to their high fibre content and absence of saturated fat that is present in animal proteins.

Sedentary lifestyle is a medical term used to denote a type of lifestyle with no or irregular physical activity. A lack of physical activity is one of the leading causes of preventable death worldwide. One report says the prevalence of diabetes was
almost three times higher in individuals with light physical activity compared to those having heavy physical activity.\textsuperscript{61} The positive role of physical activity on diabetes is well known from the present study with a positive correlation (r=0.75) between the diabetics and non-diabetics.\textsuperscript{299} Several prospective studies have shown that measures of lifestyle modification help in preventing the onset of diabetes.\textsuperscript{346, 347}

Alcohol may increase TG levels and blood pressure. It also increases impotence, retinopathy and possibly peripheral neuropathy, hypertriglyceridemia, ketoacidosis and worsens diabetic control.\textsuperscript{348} The ill-effects of alcohol\textsuperscript{348} and smoking\textsuperscript{349} on diabetes have been discussed. A positive correlation (r = 0.96) between non-diabetics Vs diabetics with different habits including drinking alcohol has been noticed in the present study also.\textsuperscript{299} Studies show that cigarette smoking is associated with a small increase of the risk of Type-2 diabetes.\textsuperscript{350, 351}

In the present study Type-2 diabetes affects all socio-economic groups but, is generally more frequent in lower socio-economic groups. The results of the present study confirm that diabetes prevalence has increased over time. The increase in diabetes prevalence is associated with increasing socio-economic inequality measured by social class and educational level. Diabetes incidence has increased disproportionately among lower socio-economic groups. Poverty, age and lack of knowledge about diabetes are the potential factors especially in the lower socio-economic classes. These may be the prime reasons for the diabetes related morbidity and mortality in the present study groups.
An increase in T2DM incidence may be due to the main risk factors like family history, sedentary lifestyle, obesity, higher smoking rate, heavy alcohol intake, unhealthy diet, etc. One study shows that first born children are having high risk of developing Type-2 diabetes.\textsuperscript{352} But there is no sharp differences between the orders of birth and the percentage prevalence of diabetes in the study present, whereas a positive correlation ($r=0.93$) was observed between diabetics Vs non-diabetics.

There are many controversial reports on the prevalence of T2DM among ‘ABO’ blood group individuals.\textsuperscript{187, 189, 190, 353-356} But one report reveals the presence of T2DM among ‘A’ and ‘O’ blood group individuals.\textsuperscript{191} It is true in our study also.

**Diabetic complications**

Diabetic complications are due to pathologic changes that involve small and large blood vessels, cranial and peripheral nerves, the skin and the lens of the eye. Macrovascular complications involve damage to the large blood vessels of the brain, heart, and extremities. Microvascular complications of diabetes include retinopathy and nephropathy and are thought to be a result of an abnormal thickening of the basement membrane of the capillaries.

Diabetic retinopathy consists of microaneurysm, hemorrhages, exudates and retinal edema, as well as proliferation of newly formed vessels in some cases. Retinopathy may result in the loss of vision. The prevalence of retinopathy is strongly related to the duration of diabetes. After 20 years of diabetes nearly all patients
with Type-1 diabetes and >60% of patients with Type-2 diabetes have some degree of retinopathy. It is the leading cause of blindness in the western world.

Microvascular and macrovascular complications are responsible for the majority of morbidity and mortality associated with diabetes mellitus and prevention of these complications is the main objective of management of diabetes.\textsuperscript{357} The organs affected in microvascular complications are eye (retinopathy), kidney (nephropathy) and peripheral nerves (neuropathy) whereas macrovascular complication affects heart (coronary), brain (cerebral) and foot (peripheral).

Differential prevalences of retinopathy such as 34.1%\textsuperscript{358}, 26.8%\textsuperscript{359}, 22.6%\textsuperscript{360}, and 17.6%\textsuperscript{361} have been reported by many authors. The present study shows only 9.6% prevalence of retinopathy in diabetics. Diabetic polyneuropathy presents with sensory disturbances. Later on, motor disturbances can occur in more severe conditions, leading to distal weakness and atrophy of the muscles of the lower leg and foot. Accordingly, inability to walk on heels is used to identify diabetic subjects with this more severe degree of diabetic polyneuropathy.\textsuperscript{362}

Diabetic neuropathy is amongst the commonest of the long term complications of diabetes affecting between 20-66% of all patients.\textsuperscript{362, 363-365} Several studies have documented a high prevalence of neuropathy in diabetic patients, but the present study shows only 4.68% diabetic neuropathy cases, where the duration and the level of hyperglycemia are found as the important determinants of this complication. Neuropathies are creating
considerable health burdens on patients and can be difficult to treat.\textsuperscript{366}

A common complication of Type-2 diabetes is microalbuminuria (i.e) protein being excreted in the urine due to kidney damage by chronic inflammation. Studies showed 8.9\%\textsuperscript{367} and 2.2\%\textsuperscript{368} prevalence of diabetic nephropathy, the incidence of this complication was 5.42\% in the present study. The urinary marker, albuminuria is reported by many authors.\textsuperscript{368,369} Albuminuria and proteinuria are detected in our diabetic subjects, proteinuria has been reported in a previous study also.\textsuperscript{370}

Classic signs and symptoms of diabetes including polyuria, polydipsia, polyphagia, weight loss, head-ache, tachycardia, palpitation and blurred vision are common in most of the patients.\textsuperscript{371} These problems are also found out in our subjects. Other life threatening complications like diabetic foot problems, erectile dysfunction in males is also noticed in our diabetic cases.

\textbf{Biomarkers and diabetes}

Biomarker is anything that can be used as an indicator of a particular disease state or some other physiological state of an organism. A biomarker is a parameter that can be used to measure the progress of disease or the effects of treatment. Biomarker is a “characteristic that is objectively measured as an indicator of normal biologic processes, pathogenic processes or pharmacologic responses to a therapeutic intervention”.\textsuperscript{372}

Biomarkers are characteristic biological properties that can be detected and measured in parts of the body like the blood or
tissue. They may indicate either normal or diseased processes in the body. It has been used in preclinical research and clinical diagnosis for a considerable time.\textsuperscript{373}

Cholesterol is a biomarker and risk indicator for coronary and vascular diseases and that C-reactive protein (CRP) is a marker for inflammation, serum LDL cholesterol, BP, etc. Safety molecular biomarkers have been used for decades both in pre and clinical research. Most common safety tests are: for liver function (E.g) transaminases, bilirubin, ALP; kidney function (E.g) serum creatinine, creatinine clearance, cystatin-C; cardiac muscle injury (E.g) CK-MB.\textsuperscript{373}

**Conventional biomarkers for diabetic control**

**HbA1C**

Haemoglobin (Hb) is the oxygen carrying pigment that gives blood its red colour and also the predominant protein in RBCs. About 90% of Hb is HbA (the ‘A’ stands for adult type). Although one chemical component accounts for 92% HbA, approximately 8% of HbA is made up of chemically slightly different minor components like A1c, A1b, A1a1 and A1a2.

HbA1C levels depend on the blood glucose concentration (i.e) the higher the glucose concentration in blood, the higher the level of HbA1C. Levels of HbA1C are not influenced by daily fluctuations in the blood glucose concentration but reflect the average glucose levels over the past 6-8 weeks. Therefore HbA1C is a useful indicator of how well the blood glucose level has been controlled in the recent past and may be used to monitor the effects of diet,
exercise and drug therapy on blood glucose in diabetic patients. In healthy non-diabetic patients the HbA1C level is less than 7% of total Hb.

HbA1C below 7% is desirable, as tight glycemic control reduces complications from diabetes, particularly diabetic microvascular complications, which significantly increase morbidity and mortality. People with diabetes who have HbA1C levels within the range have a significantly lower incidence of complications from diabetes, including retinopathy and diabetic nephropathy.\textsuperscript{374, 375} The presence of more HbA1C level in the fasting serum of our diabetic subjects reveals the poor glycemic control in this survey groups (p value = <0.01).

**Glucose**

Large epidemiological studies have consistently shown that patients with diabetes have a two to fourfold increased risk of cardiovascular disease (CVD) relative to non-diabetic patients.\textsuperscript{376} Studies also suggest that in patients with diabetes the degree of glucose elevation is directly related to cardiovascular risk. In addition to LDL cholesterol and blood pressure, glucose appears to be a continuous cardiovascular risk factor.\textsuperscript{377} It is true in our study also.

Possible explanations for the glucose-cardiovascular disease association include direct toxic effect of glucose on cellular function and structure, indirect effects owing to insufficient insulin secretion to maintain normoglycaemia, and a long history of insulin resistance and hyperinsulinaemia prior to glucose elevations.\textsuperscript{377, 378} Dysglycaemia (fasting glucose > 75 mg/dL) may be associated with
multiple cardiovascular risk factors like hypertension, dyslipidaemia, obesity and renal damage could be a simple marker of increased risk. However, it should be further confirmed with large scale studies.

Most investigations believe that excellent blood glucose control decreases the risk of retinopathy. However there have been important dissensions in some diabetic individuals whose blood sugar control was found to be good, and a few with no complications when controlled poorly.\textsuperscript{379} Some reports say non-diabetic individuals from families with several diabetic members, exhibiting retinopathy in distinguishable from diabetic retinopathy.\textsuperscript{380} Reports say glycemia may not be directly related to retinopathy or other diabetic complications.\textsuperscript{381, 382} The incidence of retinopathy is only 9.6% in the present study. However, the possible functional role of glucose on retinopathy should be confirmed by large scale studies only.

**Lipid**

Cholesterol and triglycerides (TGs) circulate in the blood as a complex with proteins called lipoproteins. There are several different types of lipoproteins: high density lipoprotein (HDL), intermediate density lipoprotein (ILDL), low density lipoprotein (LDL), and very low density lipoprotein (VLDL). Lipoprotein lipase (LPL) is the enzyme that breaks down TGS. It is functionally impaired or found in low levels in many Type-2 diabetic cases. LPL can “bridge” lipoproteins and the surface of cells, leading to an increase in the cellular uptake of lipoproteins.\textsuperscript{383}
Diabetes carries an exceptionally high burden of disease, including a higher mortality from cardio-vascular disease, liver, and kidney disease where LDL-C interacts with risk factors of the metabolic syndrome to magnify the risk of CVD. Type-2 diabetic people have high levels of LDL-C and TGs. An enhanced level of these parameters are detected in our diabetic cases also. LDL-C is a type of lipoprotein that carries cholesterol in the blood. It’s level is used to predict the risk of developing heart disease. Lifestyle changes including decreasing the amount of saturated fat in the diet, achieving and maintaining desirable body weight and getting regular exercise will adequately lower LDL-C.

Dyslipidemia appears to be a critical role in the development and progression of diabetic microvascular disease. Specifically elevated levels of VLDL-TG appear to be intimately involved in driving retinopathy and albuminuria. Increased levels of LDL are implicated in the progression of retinopathy, neuropathy and nephropathy and attenuated levels and function of HDL are clearly linked to retinopathy. The most important components of dyslipidemia are on elevated VLDL and total TGs and a decreased HDL concentration in the serum. Similar trends have been detected in the fasting serum of our diabetic subjects.

HDL levels are often reduced in direct proportion to the increase in TGs in insulin resistant states and are decreased in patients with Type-2 diabetes. HDL are known to be associated with a spectrum of vasculoprotective, cardioprotective and antiatherogenic properties. A sharp decrease of HDL levels are detected in our diabetic subjects than their respective controls.
(non-diabetics). Lipid profile values of non-diabetics Vs diabetics are statistically highly significant with p values < 0.01 at two tail levels.

Hypercholesterolemia is typically due to a combination of environmental and genetic factors. Environmental factors include obesity and dietary choices. Genetic contributions are usually due to the additive effects of multiple genes, however occasionally may be due to a single gene defect such as in the case of familial hypercholesterolemia. A number of lifestyle changes are recommended in those with high cholesterol including smoking cessation, limiting alcohol consumption, physical activity, maintaining a healthy weight and a diet low in saturated fats. A statistically significant (p = < 0.01) high cholesterol levels are found in our diabetic subjects than their non-diabetic counterparts.

Inspite of all the diabetes related complications, hyperglycemia, high blood pressure and hypercholesterolemia are considered as the three most significant risk factors. It has been suggested that improvements in glycemic control, blood pressure and cholesterol level can reduce a person’s risk for complications.

**Ferritin – an inflammatory marker and diabetes**

Ferritin has been known as an index for body iron stores and also as an inflammatory marker. Epidemiological studies have reported a strong association between elevated serum ferritin (iron stores) concentrations and increased risk for diabetes. Ferritin is a ubiquitous intracellular protein that stores iron and releases it in a controlled fashion. It serves to store iron in a non-toxic form to deposit it in a safe form, and to transport it to
areas where it is required. The present study reveals elevated ferritin concentrations in diabetic patients compared to normal subjects \( (p = < 0.01) \), and the values are highly statistically significant. Therefore, excessive serum (fasting) ferritin concentration can be a marker of iron overload and subclinical haemochromatosis in diabetics.

**C-peptide and diabetes**

C-peptide levels are measured instead of insulin levels because, insulin concentration in the portal vein ranges from 2 – 10 times higher than in the peripheral circulation. Elevated C-peptide in plasma in diabetics is reported by many authors.\(^ {116, 117} \) Decreased level of C-peptide is associated with fasting or post-prandial glucose levels in Type-2 diabetes mellitus.\(^ {118} \) A drastic decline of C-peptide level is noticed in the serum (fasting) samples of our diabetic cases than the controls, and the values are statistically highly significant \( (p = < 0.01) \).

Diabetes mellitus is a group of metabolic disorder characterized by hyperglycemia due to absolute or relative deficiency of insulin, impaired action of insulin or both. T2DM is heterogenous, multifactorial resulting from relative insulin insufficiency/insulin resistance/insulin receptors abnormalities.\(^ {397, 398} \) A statistically highly significant \( (p = < 0.01) \) low insulin values are obtained in our diabetic subjects than their respective non-diabetic counterparts.

**Thyroid hormones and diabetes**

Hypothyroidism is the most common functional disorder of the thyroid gland. Thyroid disorders either hypothyroidism or
hyperthyroidism and diabetes mellitus are quite common endocrinopathies seen in general population. Thyroid disorder in general population is estimated to be 6.6%, while the prevalence in diabetic population has been estimated at 10.8%. Subclinical hypothyroidism is reported by many researchers. The present study reveals mild sub-clinical hypothyroidism in both male and female diabetics and a marginal increase of other thyroid hormones like fT3, fT4, TT3 and TT4 have been noticed in diabetics of both sexes and the values are highly statistically significant (p = < 0.01).

The co-existence of diabetes and thyroid disorders has been associated with long-term morbidity and mortality. Although the benefits of treating overt thyroid disease are clear the management of clinical or sub-clinical hypothyroidism is still obscure. If it is left unnoticed and untreated in Diabetes mellitus cases, an array of complications will be emerged and the consequences may be very cruel.

**Liver function abnormalities and diabetes**

Individuals with Type-2 diabetes have a higher incidence of liver function abnormalities than the normal subjects. Most common are elevated alanine aminotransferase (ALT). Elevated levels of serum aspartate transaminase (AST), alkaline phosphatase (ALP), gama glutamyl transferase (GGT), and lactate dehydrogenase (LDH) indicate about liver problems.

Previous studies indicated that, elevated serum GGT is associated with an increased risk of metabolic syndrome and Type-2 diabetes. Our results show that, the above mentioned
marker enzymes of the liver function are noticed in an enhanced level in diabetics than the respective non-diabetic subjects and the values are found as statistically significant. It is quite obvious from the study that, the elevated serum GGT is associated with an increased risk of metabolic syndrome and Type-2 diabetes.

Studies shown that, the elevation of liver enzymes could be expression of excess deposition of fat in liver, which is regarded as a feature of the insulin resistance syndrome. This hypothesis correlates with the increased serum GGT and the increased risk for the development of Type-2 diabetes. The increased levels of liver enzymes may reflect inflammation, which impairs insulin signaling both in the liver and systemically.

Measurement of serum albumin reveals how well the liver is making this protein, albumin-globulin ratio can give clues about problems in the body and protein electrophoretic pattern indicates any changes in protein bands owing to any pathological problems in the individuals. But, there is only a very narrow difference in total serum protein, albumin, and A/G ratio in our diabetic cases than the normal subjects. Protein electrophoretic study shows the normal electrophoretic pattern of serum protein.

Serum bilirubin level is considered as liver function, as it reflects the liver’s ability to take up, process and secrete bilirubin into the bile. Elevated level of bilirubin is detected in T2DM cases. A sharp increase of serum total bilirubin is detected in our diabetic subjects than the non-diabetics and the values showed a high statistical significance (p = < 0.01).
Biomarkers of kidney function

Studies shown that, microalbuminuria is a predictor of cardiovascular and renal death in patients with D. mellitus. Microalbuminuria can be a fore-runner of diabetic nephropathy and an early manifestation of generalised endothelial dysfunction. This urinary marker is closely associated with hyperglycemia, obesity and hypertension. Proteinuria may be a signal of renal damage and D. mellitus is one of the main causes for proteinuria.

Irrespective of age and sex, our diabetic subjects show increased urinary protein and albumin values than their respective non-diabetic groups with a high statistical significance (p=< 0.01). Recent study has shown that, a high serum uric acid concentration may be an etiological factor for diabetes, hypertension, metabolic syndrome and heart disease. It is true in our study too. Reports say about 90% diabetic patients have increased serum LDH levels with renal infarction. Both of our male and female diabetic cases show a high level of serum LDH with a highly significant p values < 0.01.

Blood urea nitrogen (BUN) is a marker of kidney function. Kidney failure is a complication of diabetes. A BUN of over 20 mg/dL is an indicator of decreased kidney function. Our results show that, eventhough the BUN values in the diabetics are within the range, there is a vast increase of these values in this group compared to the non-diabetic subjects (p = < 0.01). The age and sex specific increase of BUN values are reported in one study. Our study too supports this view.
Serum creatinine is the most commonly used indicator of renal function. One report says that, a higher serum creatinine level is associated with an increased risk for the development of T2DM. Our diabetic subjects also show a higher creatinine value than their respective non-diabetic counterparts.

**Cardiac biomarkers and diabetes**

Creatine kinase is a prominent risk factor for atherosclerosis, ischaemic heart disease and diabetes. Another very important cardiac marker is lactate dehydrogenase. Reports say about 90% diabetic patients have increased serum LDH levels with renal infarction. Elevated levels of pseudocholinesterase in acute myocardial infarction and serum cholinesterase activity in T2DM patients is reported by many workers. In the present study both male and female diabetics show a statistically highly significant (p=<0.01) increase of creatine kinase, LDH and ChE activities than their respective non-diabetic counterparts. Results further show that, the diabetic subjects are in line with the development of cardiac problems by and large and they are in need of better medical treatment to curb this diabetic menace.

Serum amylase, a pancreatic inflammatory marker is found in an elevated level in T2DM patients. The same elevated trend of this enzyme is found in our diabetic cases and the values are highly statistically significant (p < 0.01) against their respective non-diabetic subjects.

The elevated level of serum sodium in NIDDM patients are reported in a work. Another report says serum potassium level is an independent predictor of incident of T2DM. one report says
that insufficiency of calcium may negatively influence glycemia.\textsuperscript{143} An elevated serum chloride is a positive indication of kidney diseases.\textsuperscript{140} A slightly elevated levels of serum potassium, calcium, sodium and chloride is noticed in our diabetic subjects, which indicates that the quantitative expression of these chemical substances are in accordance with the pathological conditions of the patients.

**Blood components and diabetes**

Immune dysfunction is prominently present in Type-2 diabetes. A significant increase of WBC count,\textsuperscript{195, 415} erythrocyte sedimentation rate,\textsuperscript{192-194} prothrombin time,\textsuperscript{197, 416} and platelet count\textsuperscript{196} is noticed in diabetics. Anemia is common in diabetics, for whom it constitutes an additional burden.\textsuperscript{198}

Elevated levels of ESR, prothrombin time and platelet count and decrease of RBC and WBC count are noticed in our diabetic cases than their respective non-diabetic subjects. ESR, a measure of the tendency of red cells to aggregate is used to screen for the presence of hidden inflammation. It is also directly associated with diabetes can be considered as an independent marker of diabetes. Chronic inflammation may play a vital role in the pathogenesis of Type-2 diabetes. Thus the quantification of the cells of the blood system may play a crucial role in the diagnosis and progression of Type-2 diabetes mellitus.

The prime causes/factors/determinants of the surge of diabetes in the present physically active agrarian community is explained by a hypothetical model (i.e) tri-way hypothesis (Fig.15). (a) determinant-I (heredity): is a key player for the diabetic
complications. (b) determinant – II (individual): is the main player for the onset of metabolic syndrome and the related diabetes. By and large the individual (trouble maker) is inviting the trouble, owing to his uncontrolled way of life. (c) determinant – III (environment): is another key player in the modern days for the surge of diabetes and the related metabolic syndrome, but the role played by the habitat is only partial.

So, if you want to evade or avoid diabetes, you should completely block the above mentioned three ways of causation. Unless a complete block of the above mentioned three ways of causation, diabetes control will continue as a day dream.

Metabolic syndrome the prominent cause of diabetes has been mounted on the people by the following ways; (1) **invited** – adequate revenue/money flow increases the affordability of people which changed the lifestyle pattern of the individual is the main cause. (2) **inherited** – parental contribution is the second cause (3) **imposed** – metabolic syndrome is imposed from the habitat, so environment is the third cause.

Fast food culture and sedentarianism are thought to be the main driving forces for the diabetes epidemic in the present physically active agrarian group. Lifestyle modifications and proper medications are the urgent primary modalities for the management of diabetes. Efficient diabetes management can be achieved through proper education and better understanding of the disease and apt prophylactic measures.

In brief, the present study reveals: (1) The prevalence of diabetes is markedly higher in the middle age-group than the lower
age group. (2) A shift in the age of onset in the middle age-group (highly potential group) is an alarming signal to the nation and this could make serious effects on the health and wealth of future India. (3) Early detection of diabetic risk factors and proper guidance such as weight reduction, modifying dietary habits, promoting day-to-day physical activities could improve our physical fitness and thereby we can post-pone or prevent diabetic menace from the globe. For this we need health consciousness and awareness.

Do not forget that nothing is impossible under the sun and above the soil. It is not too late to curb this human menace.