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Study of biochemical parameters with insulin resistance type 2 diabetes mellitus subjects

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***Abstract*---**Introduction: Diabetes results from hyperglycemia and improper glucose, lipid, and protein metabolism. The elderly population will quadruple in 10 years. LMICs have the highest type 2 DM patients. Insulin resistance and beta cell abnormalities cause T2DM. This study compared HbA1c, FPG, and lipids to controls. Materials and methods: The study was carried out in the Department of Biochemistry L.LRM Medical College, Meerut. The study was done on 250 individuals, who included 100 uncontrolled type-2 diabetic (Group III), 100 controlled type-2 diabetic (Group II) and 50 healthy individuals (Group I). Blood biochemistry and immunology for various parameters such as Fasting Blood Sugar (FBS), Glycosylated haemoglobin (HbA1c), Total Cholesterol (TC), Triglyceride (TG), High density-lipoprotein cholesterol (HDL-c), Low density lipoprotein cholesterol (LDL-c), Very low density lipoprotein cholesterol (VLDL-c), Urea, Creatinine were carried out for all three groups. SPSS16.0 was used to analyse the results. Results: In

our study we found highly significant increase (P< 0.001) of fasting blood sugar and glycosylated hemoglobin levels in group II and group III as compared to group I. In the present study, the patterns of lipid profile parameters in type-2 diabetic subjects were also studied. We observed that mean values of TC, TG, HDL-c, and LDL-c were found significantly higher in group II and group III. The overall results revealed that the all lipid profile parameters were increase highly significantly (P< 0.001) in all study groups except HDL-c which was decreased significantly. The other study parameters in diabetic subjects of group II and group III showed same pattern of significant change in urea, creatinine and insulin resistance as compared to group I (P< 0.01) while highly significant (P< 0.001). Conclusions: Uncontrolled diabetes have significant role to play in multiple parameters of the body to become variable to cause disruption of the body function.

***Keywords*---**biochemical, insulin resistance, type 2 diabetes mellitus.

Introduction

Diabetes mellitus is a metabolic disorder characterized by hyperglycemia with disturbances of carbohydrate, fat and protein metabolism, resulting from defects in insulin action and secretion or both (Valder R, et al. 2007), it is fast becoming an epidemic in some countries including (INDIA) world with the number of people affected expected to double in the next decade due to increase in ageing population (Abdulfatai B, et al. 2012)[1], it is estimated that 366 million people had DM in 2011; by 2030 this would have risen to 552 million (International Federation Society Dec. 2011). The number of people with type 2 DM is increasing in every country with 80% of people with type 2 DM living in low and middle–income countries. Individuals with T2DM show both insulin resistance and beta cell defects (Base JB, 2008)[2].

The Chronic hyperglycemia of diabetes is associated with the long-term consequences of diabetes that include damage, dysfunction and failure of various organs, especially the eyes, kidneys, nerves, heart, and blood vessels. 50% of people with diabetes die of cardiovascular disease (primarily heart disease and stroke). T2DM is commonly linked to obesity, which can cause insulin resistance (Henegar JR, et al. 2001; Chagnac A, et al. 2003)[10]. Despite the different pathogenic mechanisms of T1DM and T2DM, they share common symptoms including glucose intolerance, hyperglycemia, hyperlipidemia and similar complications. A pivotal role for reactive oxygen species (ROS) has been proposed in both the development of insulin resistance and in the pathogenesis of both micro- and macro-vasculature complications (Sharma K, et al. 1999; Zanatta CM, et al. 2008; Brosius FC, et al. 2008)[17]. 5% of all deaths globally each year (Ram vinod M, et al. 2011)[]. A number of studies have revealed that the level of HgbA1C is directly proportional to FBG concentrations. The reaction between glucose and beta chain of haemoglobin (HB) is a slow, irreversible, non-enzymatic, is continuous over the life span of red blood cell (RBCs) and is proportional to the blood glucose concentration to which the red cell is exposed. (Davidson MB ,et al. 1986)[].

Type 2 DM has been traditional accepted as a risk factor for development of coronary heart disease (CHD) .It has been established that hyperglycemia will lead to alteration in lipid profile, increase in low density lipoprotein cholesterol (LDL-C) and decrease in high density lipoprotein cholesterol (HDL-C) (Mitchell BD. et al.1995). Oxidized LDL-C has been proved to be main triggering event in the atherogenes is process leading to microvascular obstruction and its related complication (Bloomgarden ZT . et al.2003). The current study has been undertaken to know the relation between HbA1c, fasting plasma glucose, lipid profile in type 2 DM patient in comparison to healthy controls in west UP.

Method and Material

The study was carried out in the Department of Biochemistry L.LRM Medical College, Meerut. The study was done on 250 individuals, who included 100 uncontrolled type-2 diabetic, 100 controlled type-2 diabetic and 50 healthy individuals. All diabetic patients were on medication with oral hypoglycemic drugs. Age matched healthy control subjects were selected from known families. The written consent of patients was also taken before starting the study. A record of clinical history and previous investigations of patients disorders were compiled in a proforma (Proforma enclosed). A proforma containing the relevant findings of clinical, biochemical and physiological investigations were recorded on preset questionnaire as base line record. All ethical measures were taken prior and during the study.

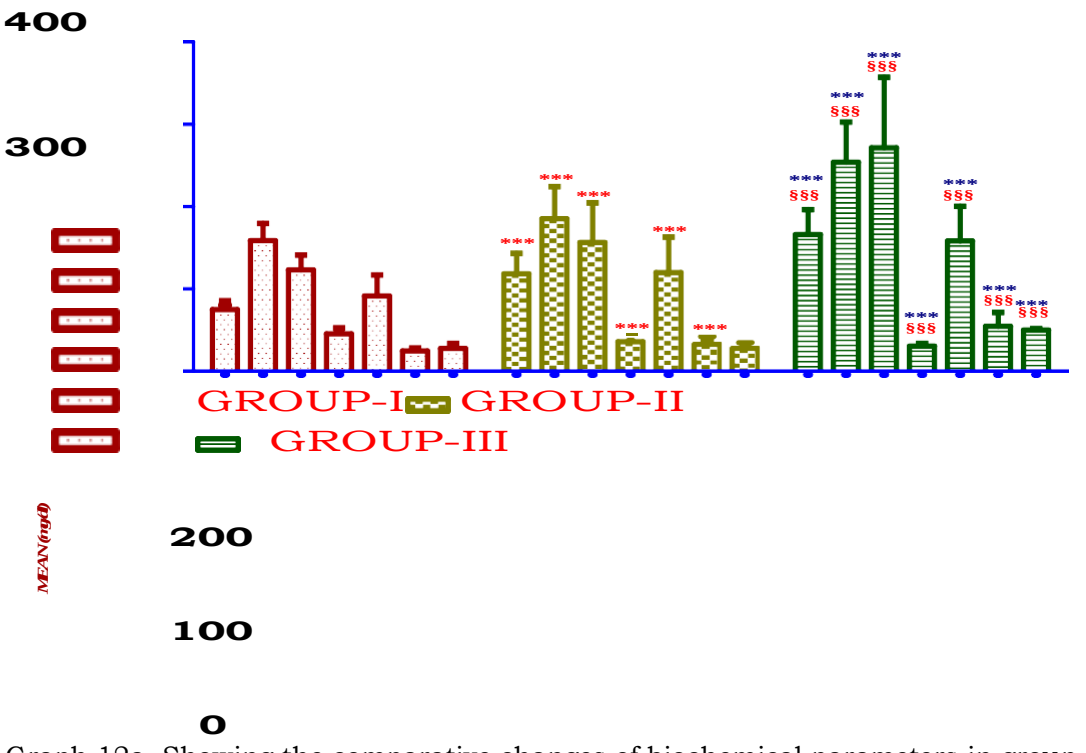
5 ml of blood sample was withdrawn from the anticubital vein following overnight fasting. The blood sample was collected in plain, fluoride and EDTA vacutainers. The blood sample was analyzed for biochemical and immunological investigations which include: The assay was performed exactly as recommended by the manufacturer. Data analysis was performed by using SPSS software version 16.0.

Biochemical Parameters

1. Fasting Blood Sugar (FBS)
2. Glycosylated haemoglobin (HbA1c)
3. Total Cholesterol (TC)
4. Triglyceride (TG)
5. High density-lipoprotein cholesterol (HDL-c)
6. Low density lipoprotein cholesterol (LDL-c)
7. Very low density lipoprotein cholesterol (VLDL-c)
8. Urea
9. Creatinine

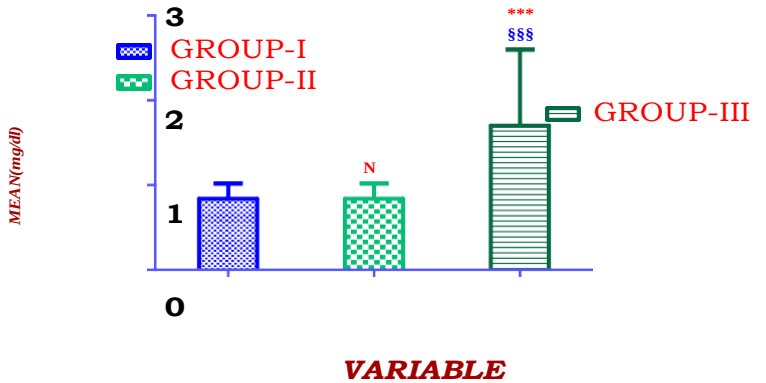
Result and observation

Table No. 1. Showing the comparative changes of biochemical in control group-I healthy control, group –II control diabetic subjects and group-III Uncontrolled Diabetic subjects. FBS, HbA1c, TC, LDL, TG and VLDL were significant at ($P<0.001$) with significant decrease ($P< 0.).0O1$) of HDL-c in group III subjects (N=100, 50 and 100 respectively.

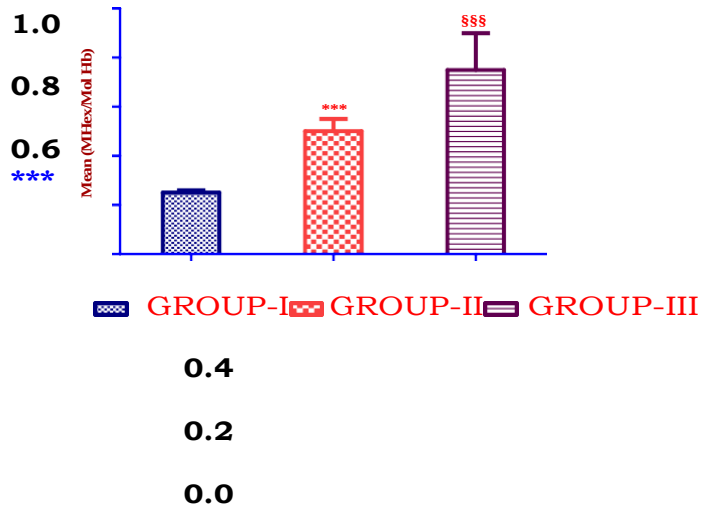


Graph 12a. Showing the comparative changes of biochemical parameters in group I, group II and group III subjects.

Variables



Graph 12b. showing the comparative changes of Creatinine in group I, group II and group III subjects



Graph 12c. showing the comparative changes of HbA1c in group I, group II and group III subjects

Table no. 1 showing the comparative changes of biochemical parameters inhealthy control Group I, control diabetic group II and uncontrolled diabetic group III subjects

GROUPS		FBS	HbA1C	TC	TG	HDL-C	LDL-C	VLDL-C	UREA	CREA.
GROUP I	*In*	60.00	00.21	107.00	70.00	34.00	33.77	14.00	17.00	00.50
	Max	99.00	00.28	210.00	156.00	59.00	189.00	31.00	40.00	01.20
	Mea.	74.95	00.25	158.72	123.04	45.37	91.31	24.62	27.55	00.84
	±*SD*	10.42	00.01	20.67	18.02	07.27	25.57	03.53	06.19	00.18
GROUP II	*Min*	69.00	00.32	137.00	82.00	30.00	62.50	16.40	17.00	00.50
	Max	170.00	00.60	290.00	290.00	52.00	227.00	58.00	40.00	01.20
	Mea.	118.38	00.50	185.12	156.34	35.75	119.86	31.26	27.30	00.84
	±*SD*	24.69***	00.05***	39.05***	48.18***	04.92***	42.96***	09.63***	07.17NS	00.18NS
	SE	03.49	00.00	05.52	06.81	00.69	06.07	01.36	01.01	00.02
GROUP III	*Min*	128.60	00.44	179.00	148.00	21.00	63.40	29.60	16.00	00.23
	Max	276.00	00.99	432.00	567.00	39.00	289.70	113.40	89.60	04.80
	Mea.	166.09	00.75	253.94	271.48	30.43	158.28	54.52	50.03	01.70
	±*SD*	30.30*** §§§	00.15*** §§§	48.64*** §§§	85.48*** §§§	03.44*** §§§	42.07*** §§§	16.93*** §§§	31.01*** §§§	00.90*** §§§
	SE	03.03	00.01	04.86	08.54	00.34	04.20	01.69	03.10	00.09

*** Highly Significant at 0.001 ($p<0.001$) between Group I, Group II and Group III.
§§§ Highly Significant at 0.001 ($p<0.001$) between Group II and Group III.

Discussion & Conclusion

Diabetes mellitus is a metabolic disorder of multiple etiology characterized by chronic hyperglycemia and glycosuria with disturbances in carbohydrate, fat and protein metabolism resulting from defects in insulin secretion, insulin action or both (Smith LL et al, 2003). Chronic hyperglycemia in diabetes is associated with specific micro and macro-vascular pathology affecting many tissue and organs, causing retinopathy, nephropathy, neuropathy, cardiovascular diseases, and peripheral vasculardiseases (Brownlee M, 2001; Crispin JC, et al, 2003).

The increasing prevalence of diabetes represents a significant burden to human health because of its numerous and often serious complications. Many factors are known to contribute to the development of diabetes and its complications. These include genetics, diet, sedentary life style, perinatal factors, age and obesity (Singh R, et al. 2004). Still relation and interaction of various risk factors with severity of disease is unsettled so in the proposed study, we intended to find out the possible relationship between biochemical markers glycosylated haemoglobin, lipid profile, urea, creatinine, , so that proper measure can be recommended to decrease the burden of diabetes in the country.

Type-2 diabetes is also characterized by an increase in insulin resistance in conjugation with the inability of pancreatic beta cells to secrete sufficient insulin to compensate (centre for disease control and prevention, 2005). The inhibition of signaling downstream of the insulin receptor is a primary mechanism through which inflammatory signaling leads to insulin resistance. Insulin resistance and insulin deficiency give rise to a hyperglycemic state that is a major risk factor for the development of diabetic complications (King GL, et al. 2008).

The study was conducted in 250 human subjects out of which 100 were normal healthy individual (group I), 150 were from type-2 DM subjects which further sub divided into two groups: 50 were type-2 DM without complications (group II) and 100 were type-2 DM with complications (group III). The blood samples were analyzed in fasting state of subjects for the biochemical and immunological parameters like FBS, HbA1c, lipid profile, urea, creatinine, , and compare them with healthy control . The mean and SD values were calculated for each parameter and P-value was calculated for the assessment of the clinical significant difference. Physical parameters of diabetic and non-diabetic subjects (number of subjects, sex, age and BMI) were measured.

In our study we found highly significant increase ($P< 0.001$) of fasting blood sugar and glycosylated hemoglobin levels in group II and group III as compared to group I . When we observed 't' values of HbA1c & FBS, we found that in group III with duration of diabetes 11-15 years, the results were statistically more highly significant. The results were consistent with the research work of Bastard JP, et al. 2006; Al-Dhar MHS, et al. 2010; Sheetz MJ, et al. 2002. The increase in HbA1c is due to high concentration of glucose present in both inside and outside the cells favoring the occurrence of spontaneous and non-enzymatic reactions between glucose and protein in intra and extracellular compartments resulting in advanced glycation end products (Suji G, et al. 2004). Furthermore AGEs bind to specific receptors on endothelial cells causing vascular permeability, procoagulant

activity, adhesion molecule expression and monocytes influx in the cell contributing vascular injury in type-2 DM. The continues mechanism of protein modification and vascular changes are due to high HbA1c formation which is magnified by ambient glucose concentration in type-2 DM subjects (Sheetz MJ, et al. 2002; Vlarsana H, et al. 2002; Creager MA, et al.2003; Mahato RU, et al 2011).

In the present study, the patterns of lipid profile parameters in type-2 diabetic subjects were also studied. We observed that mean values of TC, TG, HDL-c, and LDL-c were found significantly higher in group II and group III . Study reveals that high prevalence of dyslipidemia is a well known risk factor for cardiovascular diseases (Yach D, et al. 2004). Insulin affects the liver apolipoprotein production which regulates the enzymatic activity of lipoprotein lipase (LPL) and cholesterol ester transport protein which are the factors leading to dyslipidemia in diabetes mellitus. Insulin deficiency reduces the activity of hepatic lipase and several steps to produce altered LPL in diabetes mellitus (Samatha P, et al. 2012). The overall results revealed that the all lipid profile parameters were increase highly significantly ($P< 0.001$) in all study groups except HDL-c which was decreased significantly ($P< 0.01$). Lipid abnormalities are due to resistance to insulin and hyperglycemia which decreases high density lipoprotein (HDL-c) and increases low density lipoprotein and elevated triglycerides (Ronald M, et al. 2004)

The other study parameters in diabetic subjects of group II and group III showed same pattern of significant change in urea, creatinine and insulin resistance as compared to group I ($P< 0.01$) while highly significant ($P< 0.001$). These findings are consistent with the research work of Pick up JC, et al. 2000; Verma M, et al. 2006; Liu S,et al. 2007; Smith S, et al. 2008; and Al- dhar MHS, et al. 2010.

Insulin resistance is also a fundamental defect that precedes the development of the full insulin resistance syndrome as well as β cell failure and type-2 diabetes mellitus. Adipose tissue of obese humans subjects and are implicated in the induction of insulin resistance seen in obesity and type-2 diabetes (Cao YC, et al. 2008). Several studies have documented increased adipose expression of TNF-α mRNA in non-diabetic subjects with obesity dependent insulin resistance, in normoglycemic subjects with increased insulin resistance and in type-2 diabetic subjects (Al-Dhar MHS, et al. 2010). It is possible that in coming years the hope of new therapeutic strategies based on Biochemical properties with beneficial actions on diabetic complications can be translated in to real better clinical treatments in west UP.

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