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Cardiovascular Status in the Hypoglycemic Type II Diabetic Subjects

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Abstract:

Introduction: *Diabetes mellitus (DM) is a group of metabolic diseases which if not controlled can cause life threatening complications.*

Aim: *To evaluate Cardiovascular Status in the Hypoglycemic Type II Diabetic Subjects.*

Methodology: *Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), total cholesterol (TC), high density lipoprotein (HDL), low density lipoprotein (LDL), very low density lipoprotein (VLDL), triglyceride (TG) and Microalbumin levels were evaluated. Total sample size was 60, which was divided into 30 study group with type II DM having hypoglycemia (blood glucose level <70 mg/dl) who attended the Medicine OPD of AVBRH Hospital and 30 age, sex matched healthy controls included in the study.*

Results: *Results of serum lipid profile showed that the mean values for TC, TG, HDL, LDL and VLDL in study group were 228.50 ± 30.75, 152.10 ± 40.98, 40.73 ± 6.58, 153.13 ± 27.74 and 33.33 ± 9.93 mg/dL, respectively. TC, TG and LDL level were significantly higher in the cases as compared to controls ($p<0.0001$). Mean value for HbA1c in the study group was 6.94± 0.47, which was significantly higher in the cases as compared to the controls ($p<0.0001$) and the mean value for FBS in the study group was 61.43 ± 2.84, which was significantly lower in the cases as compared to the controls ($p<0.0001$). Mean value for Microalbumin levels in the study group were 70.71 ± 5.57 respectively, which were significantly higher in the cases as compared to the controls ($p<0.0001$). HbA1c has significant negative correlation with HDL ($p<0.01$).*

Conclusion: *Early detection of lipid profile abnormalities along with microalbuminuria can minimize the risk for development of cardiovascular complications in the hypoglycemic type II diabetic patients.*

Keywords: ***Diabetes mellitus, Hypoglycemia, Glycated hemoglobin, Lipid Profile panel, Microalbuminuria.***

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defect in insulin secretion, insulin action, or both.[1] Type II DM is caused by a combination of resistance to insulin action and an inadequate compensatory insulin secretary response. This form of DM, accounts for approximately 90 - 95%. According to the International Diabetic Foundation, currently the disease affects >62 million Indians, which is >7.1% of India's adult population. According to Wild et al.[2] the prevalence of diabetes is predicted to double globally from 171 million in 2000 to 366 million in 2030, with maximum increase in India. Due to the alarming increase in the incidence and prevalence of diabetics in India, WHO has declared India as the - Diabetic Capital of the World (Gupta, 2002).[3] Chronic hyperglycemia is associated with significant long-term complications like damage to the nerves, heart, blood vessels, eyes and kidneys (Yki-Yarvinen1998).[4] Hypoglycemia, also called low blood glucose or low blood sugar, occurs when the level of glucose in the blood drops below normal. According to National Institute of Diabetes and Digestive and Kidney Diseases for diabetics hypoglycemia means blood glucose level is 70 mg/dL or less. Hypoglycemia is a medical emergency, where there is reduction in plasma glucose concentration causing signs and symptoms of altered mental status, sympathetic nervous system stimulation due to abnormalities in the mechanisms of glucose homeostasis.[5] Incidence of hypoglycemia with diabetes varies in compared to people without diabetes.[6] Hypoglycemia is the commonest side effect of treatment of diabetes and is associated with adverse health outcomes like dementia, falls, fall-related fractures, cardiovascular events, poor quality of life, and increased mortality. Diabetes mellitus increases the risk of dyslipidemia, there is an elevated triglyceride level and a decreased HDL cholesterol level is seen commonly.[7] Diabetes is associated with a greater risk of morbidity and

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mortality from cardiovascular disease (CVD). An early intervention to normalize circulating lipid levels has been shown to reduce cardiovascular complications and mortality (Windler, 2005).[8] Serum lipids are frequently abnormal and are likely to contribute to the risk of coronary artery disease.[9] Atherosclerosis is characterised by the deposition of cholesterol into the artery wall. Atherosclerosis accounts for around 80% of all deaths among diabetic patients. Prolonged exposure to hyperglycaemia is now recognized a major risk factor in the pathogenesis of atherosclerosis in diabetes. Hyperglycaemia induces a large number of alterations at the cellular level of vascular tissue that potentially accelerate the atherosclerotic process. There are three major mechanisms that encompass most of the pathological alterations observed in the diabetic vasculature- 1) Nonenzymatic glycosylation of proteins and lipids, which can interfere with their normal function by disrupting molecular conformation, alter enzymatic activity, reduce degradative capacity and interfere with receptor recognition; 2) Oxidative stress; and 3) Protein Kinase C (PKC) activation with subsequent alteration in growth factor expression. Worsening of glycemic control deteriorates lipid abnormalities in diabetes mellitus.[10] According to the American Diabetes Association (ADA) HbA1c level of <7% is the goal of optimal blood glucose control[11] and the American Association of Clinical Endocrinologist has further recommended HbA1c level of <6.5% is the target goal.[12] Criteria for abnormal lipid profiles were based on the ADA criteria, Hypercholesterolemia refers to a total cholesterol level ≥ 200 mg/dl, Hypertriglyceridemia refers to a level is ≥ 150 mg/dl, HDL was considered low when the level is < 40 mg/dl in males and < 50 mg/dl in females, LDL was considered high when the level is ≥100 mg/dl. The glycated hemoglobin (HbA1c) provides an index of average blood glucose level during the past 2–3 months and considered to be the most reliable measure of long-term metabolic control of blood glucose level in type II diabetes mellitus (Nathan 1984).[13] HbA1c is formed by the condensation of glucose with the N-terminal Valine residue of each β-chain of HbA to form an unstable Schiff-base, which is the most widely used as the long-term glycemic control, as well as an independent risk factor for cardiovascular diseases (stroke).[14] American Diabetes Association (ADA) proposed the use of HbA1c in the definition of diabetes and the category of increased diabetes risk (which also includes impaired fasting glucose and impaired glucose tolerance) in 2010 (American Diabetes Association Diabetes Care2010).[15] Estimated risk of CVD has shown to be increased by 18% for each 1% increase in absolute HbA1c value in diabetic population (Selvin,2004).[16] Lower HbA1c values, has been shown to delay the onset and slow the progression of diabetic retinopathy, nephropathy, and neuropathy in Diabetes.[17]

Microalbuminuria is a term to describe a moderate increase in the level of urine albumin. It occurs when the kidney leaks small amounts of albumin into the urine, in other words, when there is an abnormally high permeability for albumin in the glomerulus of the kidney. People with type II diabetes develop severe renal and cardiovascular complications early, especially those with high urinary albumin excretion.[18] Microalbuminuria can be diagnosed from a 24-hour urine collection (between 30–300 mg/24 hours) or, more commonly, from elevated concentration in a spot sample (20 to 200 mg/L).

Even though Diabetes is prevalent in India, studies are lacking to find out the risk of developing hypoglycemia and its associated complications like cardiomyopathy with HbA1c, Lipid Profile and Microalbumin levels in type II Diabetics.

Our study is a rural hospital based study and it will provide the necessary insight into the situation. Our aim is to evaluate the cardiovascular status in the Hypoglycemic Type II Diabetic Subjects. We hypothesize with hypoglycemia in type II Diabetics may lead to various cardiovascular complications.

The study was carried out in the Department of Biochemistry in association with Department of Medicine, Jawaharlal Nehru Medical College and Acharya Vinoba Bhave Rural Hospital, Sawangi (Meghe), Wardha, Maharashtra, India.

MATERIALS & METHODS

A comparative and cross-sectional study was conducted. Institutional Ethical Committee approved the study. The study was done from August 2016 to February 2017, total sample size 60 including males and females and divided into two groups. Informed written consent was taken for the study purpose. 30 study group with type II DM with hypoglycemia (blood glucose level <70 mg/dl) who attended the outpatient clinic of the Medicine Department of AVBRH Hospital, Sawangi (Meghe), Wardha, India and 30 age, sex matched healthy controls. All patients with known history of type II DM within the age group of 35-75 years included in the study. Information about subject's age, sex, lifestyle, family history of diabetes and other chronic diseases/disorders were written in pre-design format. HbA1c assay was done by immunoassay method, fasting blood glucose by GOD/POD method[19], total cholesterol by enzymatic endpoint method[20], triglycerides liquid stable GPO-POD method[21], HDL direct enzyme method, LDL using Friedewald formula, VLDL by appropriate formula and Microalbumin by Immunoturbidimetric method - all measured by Randox auto-analyzer on the same day of collection.

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Sample Collection

3ml blood sample was collected from each subject. Fasting blood sample in sterile fluoride bulb for FBS, plain bulb for lipid profile and EDTA bulb for HbA1c under all the aseptic conditions with consent of the patient. Spot morning urine sample – collected for urinary micro albuminuria in urine jar. Blood Sample was allowed to stand for clotting for 25 to 30 minutes. Serum was separated by centrifuging blood at 3000 rpm for 10 minutes.

Inclusion Criteria

All patient with known history of type II DM, age group between 35-75 years blood glucose level <70 mg/dl and diabetic patients, those who gave the consent for the study were included in the study.

Exclusion Criteria

Patient with major illness like liver disease, renal failure, cardiovascular disease, which can directly or indirectly affect the result, previous or current treatment with drugs known to interfere with glucose and lipid metabolism were excluded from the study.

Statistical Analysis

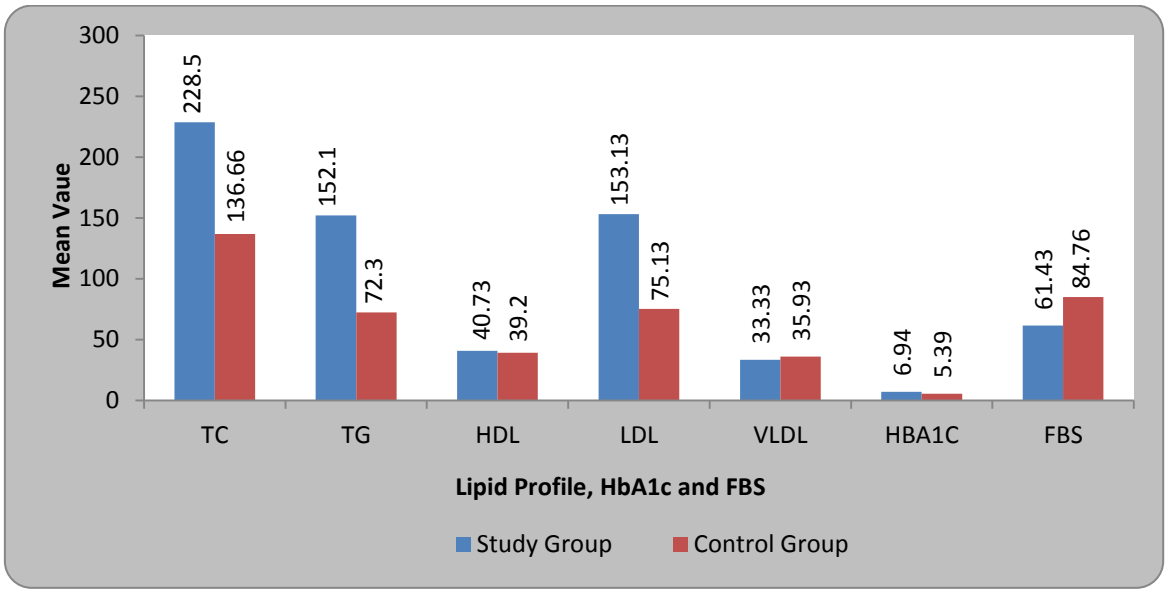
Statistical analysis was done by using descriptive and inferential statistics using Student's unpaired t test and Pearson's Correlation Coefficient and software used in the analysis were SPSS 17.0 version and EPI-INFO 6.0 version and $p<0.05$ is considered as level of significance.

RESULTS

Table 1: Comparison of biochemical parameters in two groups

	Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
TC	Study	30	228.50	30.75	5.61	16.05	0.0001,**S**
	Control	30	136.66	5.964	1.08		
TG	Study	30	152.10	40.98	7.48	10.62	0.0001,**S**
	Control	30	72.30	3.56	0.65		
HDL	Study	30	40.73	6.58	1.20	1.06	0.29,**NS**
	Control	30	39.20	4.37	0.79		
LDL	Study	30	153.13	27.74	5.06	15.11	0.0001,**S**
	Control	30	75.13	5.36	0.97		
VLDL	Study	30	33.33	9.93	1.81	1.14	0.25,**NS**
	Control	30	35.93	7.57	1.38		
HbA1c	Study	30	6.94	0.47	0.08	16.26	0.0001,**S**
	Control	30	5.39	0.23	0.04		
FBS	Study	30	61.43	2.84	0.52	29.43	0.0001,**S**
	Control	30	84.76	36.27	0.59		
	Control	30	0.89	0.20	0.03		
Microalbumin	Study	30	70.71	5.57	1.01	48.34	0.0001,**S**
	Control	30	15.25	2.89	0.52		

Graph 1.1: Comparison of Lipid Profile, HbA1c and FBS in two groups



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Graph 1.2: Comparison of Microalbumin levels in two groups

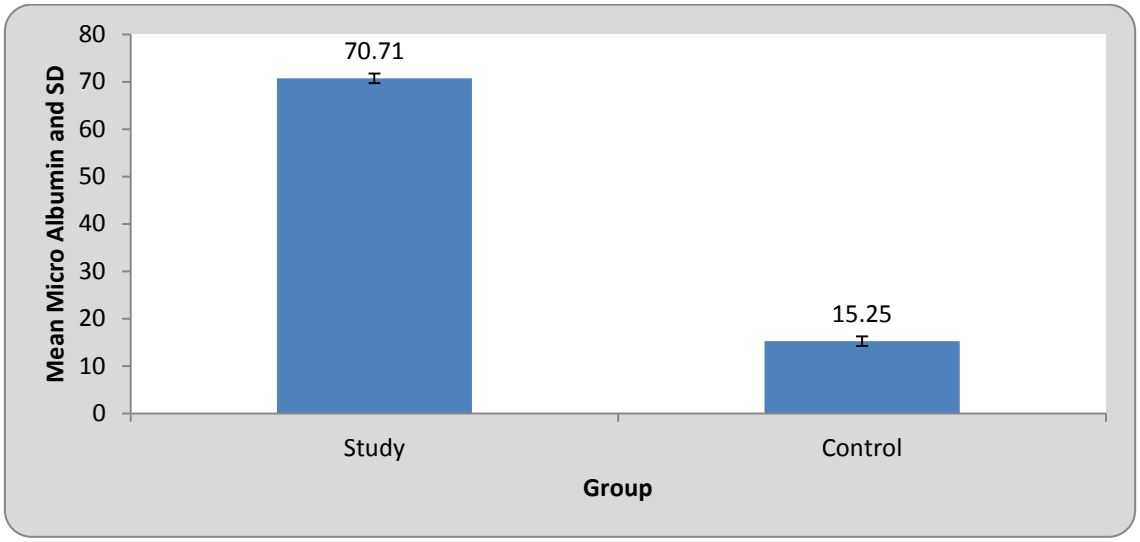

Table 2: Correlation of HbA1c with other parameters in study group

	Mean	Std. Deviation	N	Correlation 'r'	p-value
HbA1c	6.94	0.47	30	-	-
TC	228.50	30.75	30	0.08	0.65,NS
TG	152.10	40.98	30	0.16	0.39,NS
HDL	40.73	6.58	30	-0.45	0.01,S
LDL	153.13	27.74	30	0.14	0.44,NS
VLDL	33.33	9.93	30	0.10	0.59,NS
FBS	228.50	30.751	30	0.08	0.65,NS
Micro Albumin	70.71	5.57	30	0.12	0.51,NS

Graph 2.1: Correlation of HbA1c with HDL in study group

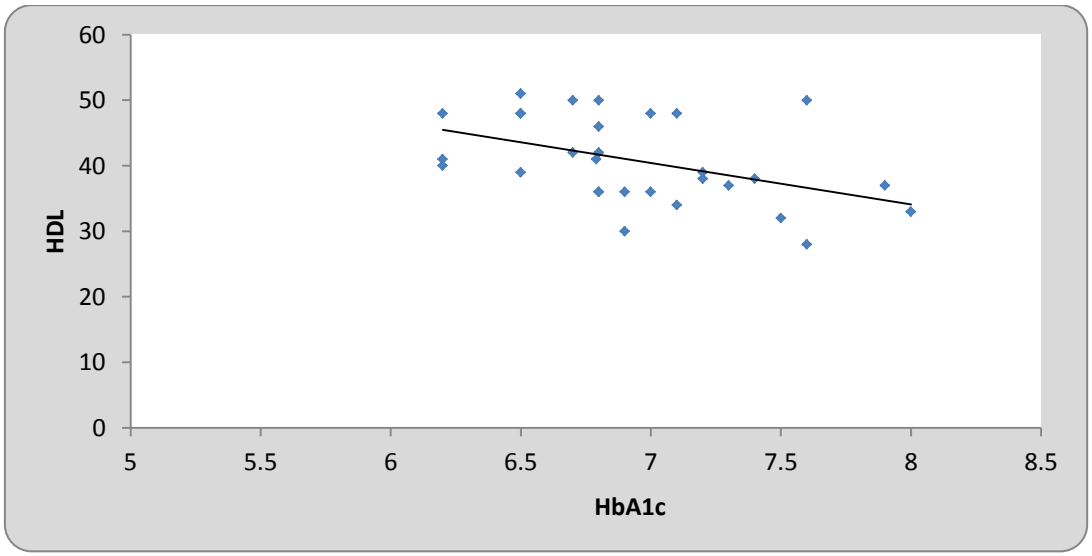

Table 1 shows results of serum lipid profile showed that the mean values for TC, TG, HDL, LDL and VLDL in study group were 228.50 ± 30.75, 152.10 ± 40.98, 40.73 ± 6.58, 153.13 ± 27.74 and 33.33 ± 9.93 mg/dL, respectively. TC, TG and LDL level were significantly higher in the cases as compared to controls (p<0.0001). Mean value for HbA1c in the study group was 6.94± 0.47, which was significantly higher in the cases as compared to the controls (p<0.0001) and the mean value for FBS in the study group was 61.43 ± 2.84, which was significantly lower in the cases as compared to the controls (p<0.0001). Mean value for Microalbumin levels in the study group were 70.71 ± 5.57 respectively, which were significantly higher in the cases as compared to the controls (p<0.0001). Table 2 shows HbA1c has significant negative correlation with HDL (p<0.01).

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DISCUSSION

In the present study, we have evaluated the Cardiovascular Status in the Hypoglycemic Type II Diabetic Subjects. The present study was carried out at AVBRH and JNMC, Sawangi (Meghe), Wardha, India. The findings are as follows-

HbA1c, TC, TG, HDL and LDL levels were found higher in the cases as compared to controls, which is in accordance with the study of Wexler et al.[22]

In our study, positive correlations were observed between serum levels of TC, TG, LDL,VLDL with HbA1c, which is in accordance with the study of Erciyas et al, (2004).[23] HbA1c shows significant negative correlation with HDL ($p<0.01$).

Diabetic patients with elevated HbA1c and altered lipid profile considered as a very high risk group for severe complications. Improving glycaemic control can reduce the risk of various complications in diabetic subjects.[24]

According to the Diabetes Complications and Control Trial (DCCT) HbA1c is the gold standard of glycaemic control and the level of HbA1c value ≤7.0% was said to be appropriate for reducing the risk of cardiovascular complications.[25]

It has also been showed in previous study conducted by Khaw et al that by reducing the level of glycated hemoglobin (HbA1c) by 0.2% could lower the mortality rate by 10%.[26]

Goldberg in their study showed that the cause of altered lipid profile in type II diabetes maybe due to the insulin is not working properly or secreted in a proper manner, which can affect the production of liver apolipoprotein.[27]

HbA1c reflects average blood glucose concentration over the course of the RBC lifespan in normal individuals. Action to Control Cardiovascular Risk in Diabetes (ACCORD) trial indicated an increased hypoglycemia risk in type II diabetic participants with poorer glycemic control compared with subjects with desirable HbA1c levels.[28] HbA1c is the most widely used biomarker for long-term glycemic status, as well as an independent risk factor for coronary heart disease (CHD) and stroke.[29]

Defective insulin secretion leads to various metabolic diseases in Type II diabetes, spanning from hyperglycemia due to defective insulin-stimulated glucose uptake and up regulated hepatic glucose production, along with dyslipidemia, which includes impaired homeostasis of fatty acids, triglycerides, and lipoproteins.[30]

Microalbuminuria is a marker of greatly increased cardiovascular morbidity and mortality for patients with type II diabetes. Thus, the finding of microalbuminuria is an indication for screening for possible vascular disease and aggressive intervention to reduce the cardiovascular risk factors.

In our study there is significant increase in urinary Microalbumin levels in the cases as compared to the controls ($p<0.0001$). The causal risk factors for microalbuminuria are raised blood pressure and poor glycaemic control. Some studies have revealed duration of diabetes, male sex, and pre-existing retinopathy as major risk factors for microalbuminuria.[31] In our study, multiple logistic regression analysis revealed age, duration of diabetes, HbA1c, and fasting plasma glucose as the risk factors for microalbuminuria. Gupta et al reported HbA1c to be associated with microalbuminuria.[32] The association of glycaemic control with microalbuminuria has been well established by various studies.[31,33] According to a study by Tobe et al, reduction of HbA1c level by 1% (7.5 to 6.5%) also significantly decreases microalbumin levels, even to normal.[34]

In our studies we have also seen that increase the duration of diabetics, prolonged use and improper dosing of insulin leads to hypoglycemia in the type II diabetic patients. Hypoglycemia along with lipid profile abnormalities and microalbuminuria in the type II diabetics may lead to various cardiovascular complications in them.

Conclusion

The prevalence of Type II diabetes mellitus is increasing day by day and is associated with a very high mortality rate, reduced quality of life and high costs of treatment, despite intensive insulin treatment. HbA1c can be use as a predictor of dyslipidemia and early detector of diabetic complications and hypoglycemia in addition to glycemic control. Lipid profile estimation and screening for microalbuminuria will allow the identification of patients with cardiovascular complications at very early course of the disease. Risk factor modification, HbA1c levels, lipid profile monitoring and combined therapies are the current integrated approaches to predict the diabetic complications- like cardiomyopathy in patients with type II diabetes mellitus.

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Conflict of interest: None declared

References

[1] Diagnosis and Classification of Diabetes Mellitus, American Diabetes Association, Diabetes Care 2009 Jan; 32(Supplement 1): S62-S67, http://dx.doi.org/10.2337/dc09-S062.
[2] Wild S, Roglic G, Green A, Sicree R, King H. Global prevalence of diabetes-estimates for the year 2000 and projections for 2030. Diabetes Care. 2004; 27(3):1047–53. [PubMed].
[3] Gupta, V 2002. Diabetes in Elderly Patients. JK Practitioner, 91(4): 258-259.
[4] Yki-Yarvinen, H. 1998. Toxicity of hyperglycaemia in type 2 diabetes. Diabetes Metab Rev. 14(Suppl 1): S45-S50.
[5] Stedman, Thomas Lathrop (December 2005) [1911]. "Stedman's Medical Dictionary" (28th ed.).Baltimore: Lippincott Williams & Wilkins. p. 2100.
[6] Turnbull FM, Abraira C, Anderson RJ, et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. Diabetologia. Aug 5 2009.
[7] Mooradian, AD (2009) Dyslipidemia in type 2 diabetes mellitus. Nat Clin Pract Endocrinol Metab. 5:150-159.
[8] Windler, E. 2005. What is the consequence of an abnormal lipid profile in patients with type 2 diabetes or the metabolic syndrome. Atheroscler. Suppl 6: 11-14.
[9] Jamshaid T, Qureshi A. Hyperlipidemia in Diabetics. Pac Postgrad Med J 2002; 13: 159-60.
[10] Grundy SM. Hypertriglyceridemia, insulin resistance, and the metabolic syndrome. Am J Cardiol 2006; 83: 25-29.
[11] American Diabetes Association. (2003). Implications of the United Kingdom Prospective Diabetes study. Diabetes Care, 26, 28-32.
[12] The American Association of Clinical Endocrinologists medical guidelines for the management of diabetes mellitus 2002. The AACE system of intensive diabetes self-management-2002 update. Endocrine Pracice, 8, 40-82.
[13] Nathan, D.M., Singer, D.E., Hurxthal, K., and Goodson, J.D. 1984. The clinical information value of the Glycosylated hemoglobin assay. N. Engl. J. Med. 310:341–346.
[14] Selvin E, Coresh J, Shahar E et al (2005) Glycaemia (hemoglobin A1c) and incident of ischemic stroke: the Atherosclerosis Risk in Communties (ARIC) Study. Lancet Neurol 4:821-826.
[15] American Diabetes Association. 2010. Diagnosis and classification of Diabetes Mellitus. Diabetes Care 33: s6 2-s69.
[16] Selvin, E., Marinopoulos, S., Berkenblit, G., Rami, T., Brancati, F.L., Powe, N.R., 2004. Meta-analysis: glycosy-lated hemoglobin and cardiovascular disease in diabetes mellitus. Ann. Intern. Med. 14: 421-431.
[17] Kadiyala R, Peter R, Okosieme OE. Thyroid dysfunction in patients with diabetes: clinical implications and screening strategies. Int J Clin Pract. 2010, 64(8):1130-1139.
[18] Michel Marre, Michel Lievre, Gilles Chattellier. Effects of low dose ramipril on cardiovascular and renal outcomes in patients with type 2 diabetes and raised excretion of urinary albumin randomized, double blind, placebo control trial (theDIABHYCAAR study) BMJ 2004; 328: 495.
[19] Maughan RJ. A simple, rapid method for the determination of glucose, lactate, pyruvate, alanine, 3- hydroxybutyrate and acetoacetate on a single 20-mul blood sample. Clinica Chim Acta 1982; 122(2):231-240.
[20] Sullivan DR, KrulJswljk Z, West CV, et al. Determination of serum triglycerides by an accurate enzymatic method not affected by free glycerol. Clin Chem 1985; 31(7):1227-1228.
[21] Buccolo G, David H. Quantitative determination of serum triglycerides by the use of enzymes. Clin Chem 1973; 19(5):476-482.
[22] Wexler DJ, Grant RW, Meigs JB, et al. Sex disparities in treatment of cardiac risk factors in patients with type 2 diabetes. Diabetes Care 2005; 28(3):514-520.
[23] Erciyas F, Taneli F, Arslan B, et al. Glycemic control oxidative stress and lipid profile in children with type 1 diabetes mellitus. Arch Med Res 2004; 35(2):134-140.
[24] Selvin E, Wattanakit K, Steffes MW, et al. HbA1c and peripheral arterial disease in diabetes: the atherosclerosis risk in communities study. Diabetes Care 2006; 29(4):877-882.
[25] Rohlfing CL, Wiedmeyer HM, Little RR, et al. Defining the relationship between plasma glucose and HbA1c: analysis of glucose profiles and HbA1c in the diabetes control and complications trial. Diabetes Care 2002; 25(2):275-278.
[26] Khaw KT, Wareham N, Luben R, et al. Glycated hemoglobin, diabetes and mortality in men in Norfolk cohort of European prospective investigation of cancer and nutrition (EPIC Norfolk). BMJ 2001; 322(7277):15- 18.

DOI: 10.23958/ijirms/vol02-i05/08

[27] Goldberg IJ. Lipoprotein lipase and lipolysis: central roles in lipoprotein metabolism and atherogenesis. J Lipid Res 1996; 37(4):693-707.
[28] Miller ME, Bonds DE, Gerstein HC, et al.; ACCORD Investigators. The effects of baseline characteristics, glycaemia treatment approach, and glycated haemoglobin concentration on the risk of severe hypoglycaemia: post hoc epidemiological analysis of the ACCORD study. BMJ. 2010, 340:b5444.
[29] Selvin E, Coresh J, Shahar E et al (2005) Glycaemia (HbA1c) and incident of ischemic stroke: the Atherosclerosis Risk in Communties (ARIC) Study. Lancet Neurol 4:821-826.
[30] J.D. Baxter and P.Webb, "Thyroid hormone mimetics: potential applications in atherosclerosis, obesity and type 2 diabetes,"Nature Reviews Drug Discovery, 2009; 8(4):308–320.
[31] Klein R, Klein BEK, Moss SE (1993) Prevalence of microalbuminuria in older-onset-diabetes. Diabetes Care 16:1325-1329.
[32] Gupta DK, Verma LK, Khosla PK, et al. (1991) the prevalence of microalbuminuria in diabetes: a study from north India.Diabetes Res Clin Pract 12:125–128.
[33] Haffner SM, Morales PA, Gruber MK, et al. (1993) Cardiovascular risk factors in non-insulin dependent diabetic subjects with microalbuminuria. Arterioscler Thromb 13:205–210.
[34] Tobe SW, McFarlane PA, Naimark DM. Microalbuminuria in diabetes mellitus.CMAJ 2002; 167:499‑503.

DOI: 10.23958/ijirms/vol02-i05/08