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RESEARCH ARTICLE

SERUM LIPID PROFILE AND MAGNESIUM LEVEL 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 study serum Lipid Profile and Magnesium level 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 Magnesium (Mg) 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: 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 ($p<0.0001$). Mean value for Magnesium level in the study group was 1.06 ± 0.25, which was significantly lower in the cases as compared to the controls ($p<0.0001$). HbA1c has significant negative correlation with HDL ($p<0.01$) and also negative correlation with magnesium.
Conclusion: Early detection of serum magnesium and lipid profile abnormalities can minimize the risk for development of diabetic complications in the hypoglycemic type II diabetic patients.

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

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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 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].

Magnesium is involved on multiple levels in insulin secretion, binding and its activity and Magnesium deficiency has been found to be associated with diabetic micro vascular disease.

Hypomagnesemia has been demonstrated in patients with diabetic retinopathy, with lower magnesium levels predicting a greater risk of severe diabetic retinopathy.[18] Magnesium depletion has been associated with multiple cardiovascular implications: arrythmogenesis, vasospasm, and hypertension and platelet activity.[19]

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 Magnesium 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 study serum Lipid Profile and Magnesium level in the hypoglycemic Type II Diabetic subjects.

We hypothesize with hypoglycemia in type II Diabetics may lead to the Cardiovascular complications in them.

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 and 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[20], total cholesterol by enzymatic endpoint method[21], triglycerides liquid stable GPO-POD method[22], HDL direct enzyme method, LDL using Friedewald formula, VLDL by appropriate formula and Magnesium by Xylidyl Blue colorimetric method - all measured by Randox auto-analyzer on the same day of collection.

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 magnesium and EDTA bulb for HbA1c under all the aseptic conditions with consent of the patient. Blood Sample was allowed to stand for clotting for 25 to 30 minutes. Serum was separated by centrifuging blood at 3000rpm for 10 mins.

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.

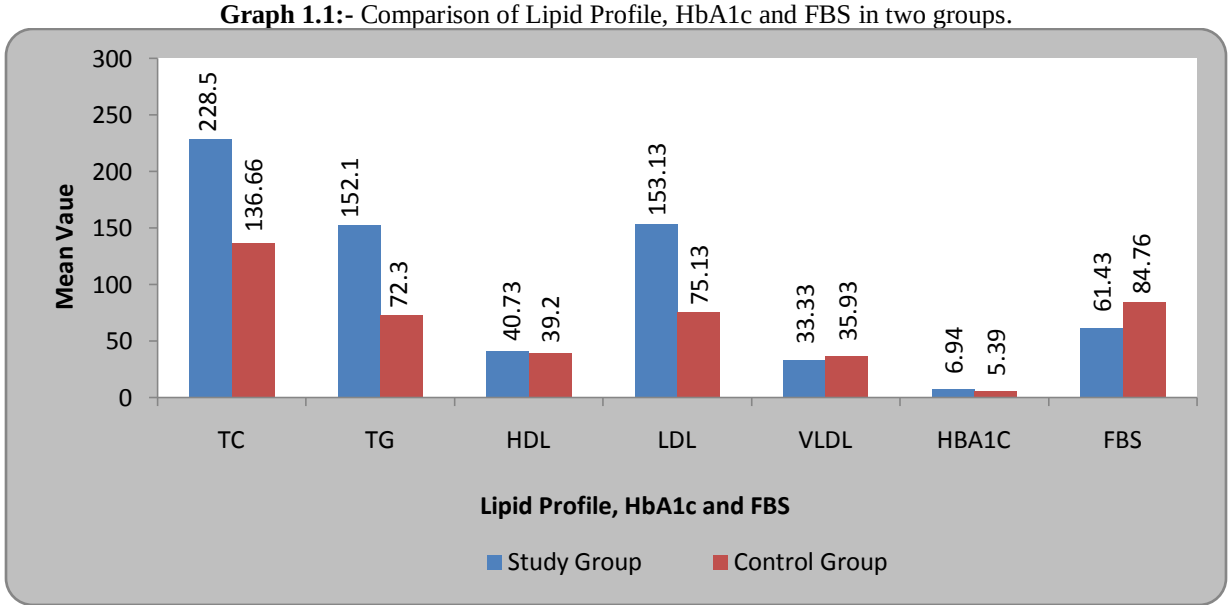
Results:-

Table 1 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 Magnesium levels in the study group was 1.06 ± 0.25 respectively, which was significantly lower in the cases as compared to the controls ($p<0.0001$). Table 2 shows HbA1c has significant negative correlation with HDL ($p<0.01$) and HbA1c also has negative correlation with Magnesium.

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		
Magnesium	Study	30	1.06	0.25	0.04	16.08	0.0001**,S**
	Control	30	1.94	0.16	0.02		

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



Graph 1.2:- Comparison of Magnesium levels in two groups.

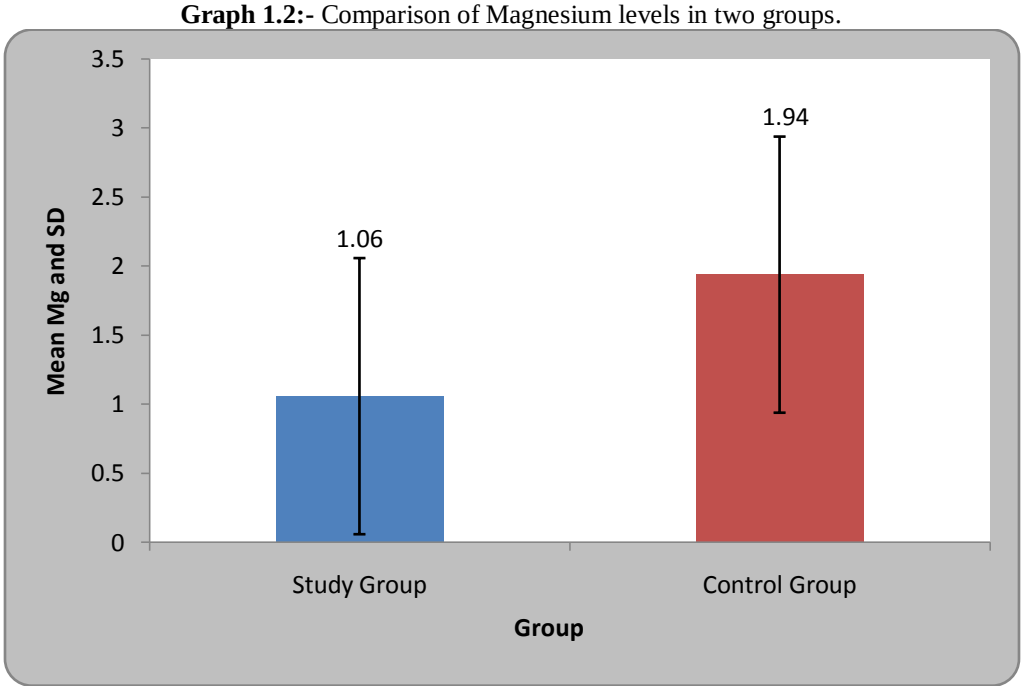
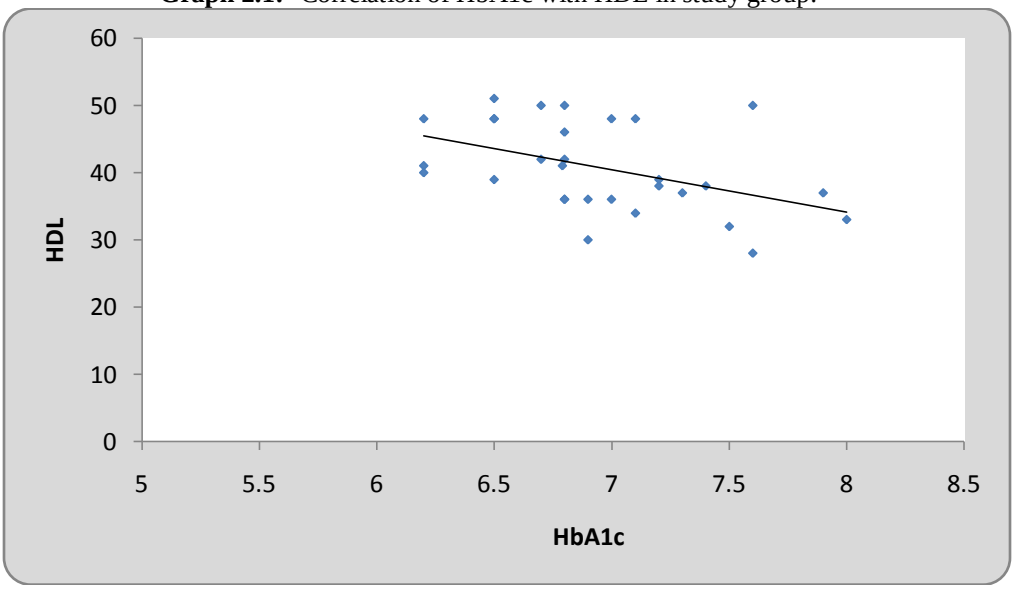


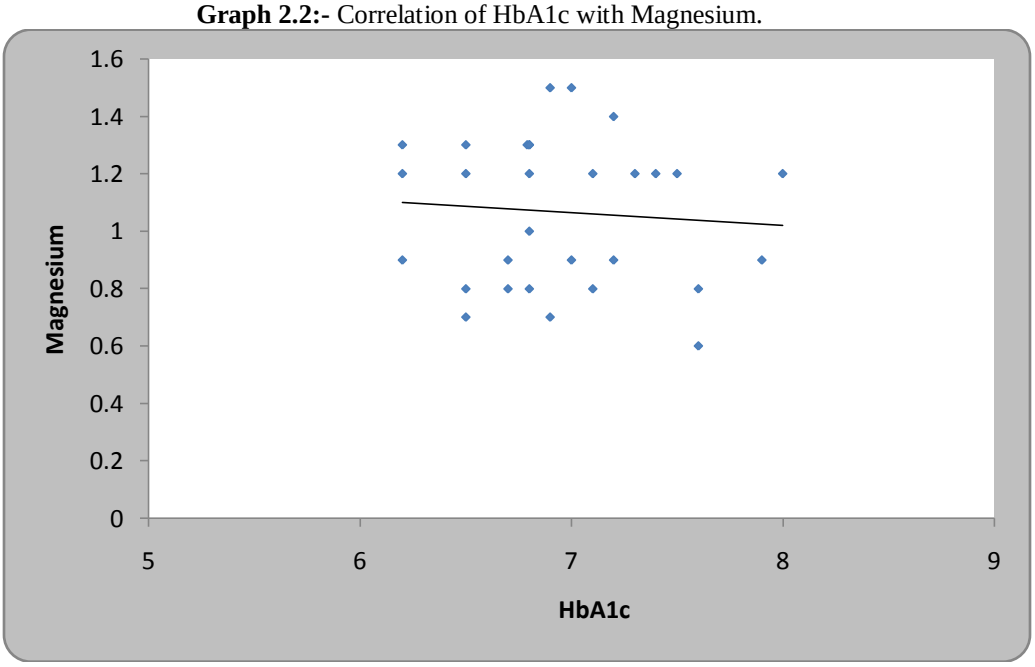
Table 2:- Correlation of HbA1c with other parameters in study group.

	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
Mg	1.06	0.25	30	-0.081	0.67,NS

Graph 2.1:- Correlation of HbA1c with HDL in study group.



Graph 2.2:- Correlation of HbA1c with Magnesium.



Discussion:-

In the present study, we have evaluated serum Lipid Profile and Magnesium level 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. [23]

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).[24]

HbA1c shows significant negative correlation with HDL ($p<0.01$). HbA1c also has negative correlation with magnesium.

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.[25]

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.[26]

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%.[27]
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.[28]

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. [29] 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.[30]

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.[31]

In our study there is significant lower serum magnesium levels found in the cases as compared to controls, which is in accordance with the study of Nadler et al.[32]

Marked magnesium deficiency has been reported in the previous studies in patients with type II diabetes.[33] Prevalence of hypomagnesemia in type II diabetics was reported by Nadler et al. in type II diabetics attending outpatient clinics in the US.[34] The reasons for the high prevalence of magnesium deficiency in diabetes are not clear, but may include increased urinary loss, lower dietary intake, or impaired absorption of magnesium compared to healthy individuals. Several studies have reported increased urinary magnesium excretion in type I and type II diabetes.[33,34]

In our studies we have also seen that increase the duration of diabetes, prolonged use and the improper dosing of insulin leads to hypoglycemia in the type II diabetic patients.

Conclusion:-

The prevalence of Type II diabetes 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 and magnesium level estimation will allow the identification of patients with diabetic complications at very early course of the disease. Risk factor modification, HbA1c levels, lipid profile and magnesium level monitoring and combined therapies are the current integrated approaches for early diagnosis of diabetic complications- like cardiomyopathy in the hypoglycemic type II diabetics.

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