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Magnesium And Electrolyte Profile In The Hypoglycemic Type II Diabetic Subjects.

Biochemistry

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ABSTRACT

Introduction: Diabetes mellitus (DM) is a group of metabolic diseases which if not controlled can cause serious complications.
Aim: Magnesium and Electrolyte Profile Evaluation In The Hypoglycemic Type II Diabetic Subjects.
Methodology: Fasting blood glucose (FBG), glycated hemoglobin (HbA1c), serum sodium (Na+), potassium (K+) and Magnesium 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: Serum Sodium and Magnesium levels were significantly lower and the level of serum Potassium were significantly higher in the cases as compared to controls ($p<0.0001$).
Conclusion: Early detection of Magnesium and Electrolyte abnormalities can minimize the risk for development of various diabetic complications in the hypoglycemic type II diabetic subjects.

KEYWORDS:

Diabetes mellitus, Hyponatremia, Hyperkalemia, Magnesium.

INTRODUCTION

Diabetes mellitus (DM) is a group of metabolic diseases characterized by hyperglycemia resulting from defects 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 homeostasis5. Incidence of hypoglycemia with diabetes varies in compared to people without diabetes6.

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.

According to the American Diabetes Association (ADA) HbA1c level of <7% is the goal of optimal blood glucose control 7 and the American Association of Clinical Endocrinologist has further recommended HbA1c level of <6.5% is the target goal 8. 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)9. 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.10 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).11 Lower HbA1c values, has been shown to delay the onset and slow the progression of diabetic complications like- retinopathy, nephropathy, and neuropathy in Diabetes 12.

Diabetic patients frequently develop electrolyte disorders. These disturbances are particularly common in decompensated diabetics, especially in- diabetic ketoacidosis or nonketotic hyperglycemic hyperosmolar syndrome. These patients have markedly potassium, depleted.

The most important causal factor of chronic hyperkalemia in diabetic individuals is the syndrome of hypoaldosteronism. Other factors are impaired renal function, potassium sparing drugs and insulin deficiency also involved in the development of hyperkalemia. Diabetes mellitus (DM) is linked to both hypo- and hyper-natremia and have the coexisting mechanism of hyperglycemia. Hyperglycemia increases serum osmolality, resulting in movement of water out of the cells and subsequently in a reduction of serum sodium levels [Na+] by dilution.

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.13 Magnesium depletion has been associated with multiple cardiovascular implications: arrythmogenesis, vasospasm, and hypertension, retinopathy,nephropathy and platelet activity.14

Even though Diabetes is prevalent in India, studies are lacking to find out the risk of developing diabetic complications with HbA1c, electrolyte profile and magnesium levels in the hypoglycemic 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 Magnesium and Electrolyte Profile in the Hypoglycemic Type II Diabetic Subjects. We hypothesize with hypoglycemia in type II Diabetics may lead to various diabetic 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 June

2016 to January 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 35-70 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 method15, Sodium by Sodium Calib. Set Barcode Levels, Potassium by Potassium Calib. Set Barcode Levels 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 sodium, potassium, magnesium and in 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 35-70 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

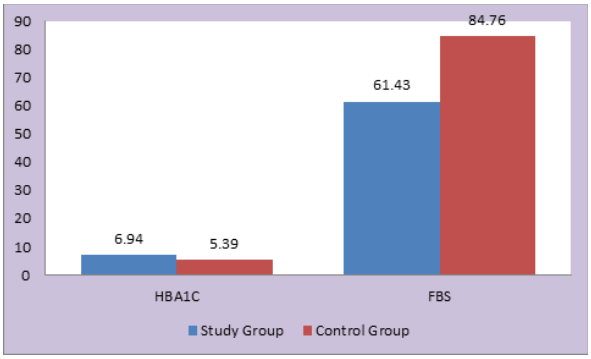
Table 1 shows mean value for HbA1c in the study group was 6.94± 0.47, which was significantly higher in the cases as compared to the controls ($p<0.0001$) and the mean value for FBS in the study group was 61.43 ± 2.84, which was significantly lower in the cases as compared to the controls ($p<0.0001$). Serum Sodium level in the cases were 128.26 ± 2.46 which was significantly lower in the cases as compared to controls ($p<0.0001$). Level of serum Potassium level in the cases were 6.09 ± 0.23 which was significantly higher in the cases as compared to controls ($p<0.0001$). Mean value for Magnesium levels in the study group was 1.06 ± 0.25, which was significantly lower in the cases as compared to the controls ($p<0.0001$). Table 2 shows HbA1c has negative correlation with Magnesium.

Figures and Tables:

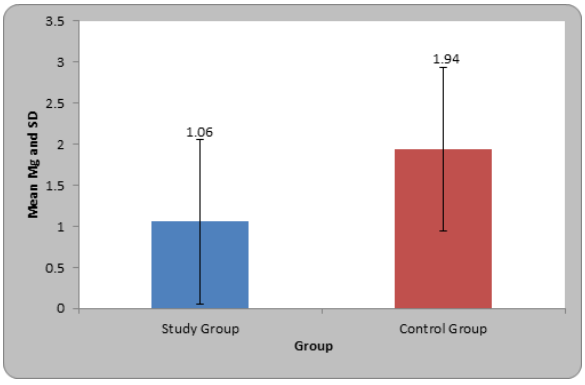
Table 1: Comparison of biochemical parameters in two groups

	Group	N	Mean	Std. Deviation	Std. Error Mean	t-value	p-value
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		
Magnesium	Study	30	1.06	0.25	0.04	16.08	0.0001, S
	Control	30	1.94	0.16	0.02		
Na+	Study	30	128.26	2.46	0.44	13.73	0.0001, S
	Control	30	138.30	3.15	0.57		
K+	Study	30	6.09	0.23	0.04	24.22	0.0001, S
	Control	30	4.03	0.40	0.07		

Graph 1.1: Comparison of HbA1c and FBS in two groups



Graph 1.2: Comparison of Magnesium levels in two groups



Graph 1.3: Comparison of Na+, K+ in two groups

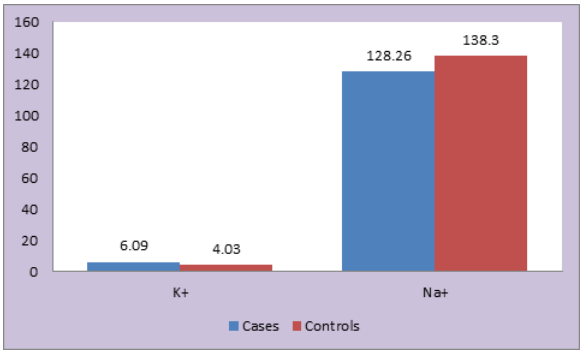
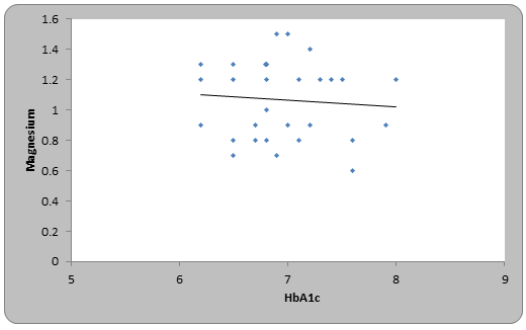


Table 2: Correlation of HbA1c with other parameters in study group

	Mean	Std. Deviation	N	Correlation 'r'	p-value
HbA1c	6.94	0.47	30	-	-
FBS	228.50	30.751	30	0.08	0.65,NS
Na+	153.13	27.74	30	0.14	0.44,NS
K+	33.33	9.93	30	0.10	0.59,NS
Mg	1.06	0.25	30	-0.081	0.67,NS

Graph 2.1: Correlation of HbA1c with Magnesium



DISCUSSION

In the present study, we have evaluated the Risk Factors of Hypoglycemia in Type II Diabetic Subjects. The present study was carried out at AVBRH and JNMC, Sawangi (Meghe), Wardha, India. The findings are as follows- In our study, HbA1c in the study group was significantly higher in the cases as compared to the controls ($p<0.0001$). Diabetic patients with elevated HbA1c considered as a very high risk group for severe complications. Improving glycaemic control can reduce the risk of various complications in diabetic subjects.16

According to the Diabetes Complications and Control Trial (DCCT) HbA1c is the gold standard of glycaemic control and the level of HbA1c value $\leq$7.0% is the level of significance for reducing diabetic complications.17

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%.18

HbA1c reflects average blood glucose concentration over the course of the RBC lifespan in normal individuals. HbA1c is the most widely used biomarker for long-term glycemic status. 19

In our study there is significant lower sodium values are seen in the cases ($p<0.0001$). This is due to Hyperglycemia increases serum osmolality, resulting in movement of water out of the cells and subsequently in a reduction of serum sodium levels [Na+] by dilution. Moreover, in diabetic ketoacidosis ketone bodies (b-hydroxybutyrate and acetoacetate) obligate urinary electrolyte losses and aggravate the renal sodium wasting.20,21

Drug-induced hyponatremia due to hypoglycemic agents (chlorpropamide, tolbutamide, insulin) or other medications (e.g., diuretics, amitriptyline for the treatment of diabetic neuropathy) should be considered in every diabetic patient with low [Na+].22,23 In our study there is also significantly higher potassium levels are also seen ($p<0.0001$). Causes of Hyperkalemia may be due to redistribution of potassium from the intracellular to the extracellular compartment (shift hyperkalemia), reduced glomerular filtration of K+ (due to acute kidney injury and chronic kidney disease), many drugs that interfere with K+ excretion are associated with hyperkalemia. In the typical healthy diabetic diet is often rich in K+ and low in sodium contributing to the occurrence of hyperkalemia in susceptible individuals24,25 and the most common cause of chronic hyperkalemia in diabetics is the reduced tubular secretion of K+ due to the syndrome of hyporeninemic hypoaldosteronism. 26

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.27

Marked magnesium deficiency has been reported in the previous studies in patients with type II diabetes.28 Prevalence of hypomagnesemia in type II diabetics was reported by Nadler et al. in type II diabetics attending outpatient clinics in the USA29 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.28,29

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 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 early detector of diabetic complications and hypoglycemia in addition to glycemic control. Electrolyte 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, magnesium levels and electrolyte profile monitoring and combined therapies are the current integrated approaches to manage the diabetic complications like electrolyte imbalance, hypomagnesaemia, nephropathy in patients with hypoglycemic type II diabetes.

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