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SERUM ELECTROLYTES CHANGES WITH ATHEROGENIC INDEX OF PLASMA IN HYPOTHYROID DIABETIC (TYPE-2) YOUNG MALES

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ABSTRACT:

Background: Atherogenic index of plasma, a newly emerging lipid parameter, has been employed only in a few studies of diabetics and not at all in hypothyroid type -2 diabetic young males with electrolytes imbalance.

Methods: Association between diabetic hypothyroid and electrolytes with atherogenic index of plasma in 50 subjects and aged (25-45 years) matched healthy controlled were studied retrospectively. Glucose and lipid parameters were measured on fully automated analyzer using standard reagent kits. Serum TSH and serum Electrolytes were measured by TOSOH-AIA-360, immunoassay method and Easylyte Na/K analyzer, respectively.

Results: On comparing the different parameters, a significant correlation (r=-0.38, p=0.005) between serum sodium and AIP was seen.

Conclusions: Decrease sodium values and increased AIP values indicated the higher risk of CVD, in the type -2 diabetic hypothyroid young males, while there were no changed in serum potassium values.

INTRODUCTION: Electrolytes play an important role in many body processes, such as controlling fluid levels, acid-base balance (pH), nerve conduction, blood clotting and muscle contraction [1].

Thyroid disease is common in the general population, and the prevalence increases with age. The assessment of thyroid function by modern assays is both reliable and inexpensive. In India, 42 million people are suffering from thyroid diseases; hypothyroidism being the commonest thyroid disorder [2].

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Hypothyroidism is a clinical entity resulting from the deficiency of thyroid hormones or from their impaired activity [3]. Thyroid hormones perform a wide array of metabolic functions including regulation of lipid, carbohydrate, protein and electrolyte and mineral metabolisms [4].

Thyroid hormones regulate the activity of sodium potassium pumps in most of the tissues. Sodium and potassium are important components of the enzyme Na-K ATPase, which is an enzyme on the cell membrane that helps in the transport of water and nutrients across the cell membrane [5]. In hypothyroidism, because of low potassium levels, and because of deficiency of thyroid hormones, this enzyme (Na-K ATPase) is affected, resulting in accumulation of water inside the cells and causing edema. This is said to be one of the mechanisms responsible for weight gain seen in hypothyroid patients with the diabetes mellitus type-2 [6].

Even subclinical hypothyroidism can exacerbate the coexisting dyslipidemia commonly found in type-2 diabetes and further increase the risk of cardiovascular diseases [7]. It has been suggested that diabetic patients has 2-4 times higher risk of cardiovascular disease compared to their non-diabetic counterpart [8]. The signs and symptoms of diabetes are related to hyperglycemia and other complications relating to lipid production, vascular and micro vascular damage, organ damage and slower healing as men are more prone to CVD than women [9].

It is well recognized that the major cause of CVD is atherosclerosis, the build-up of plaque in the inner lining of an artery and the major preventable risk factors for CVDs are tobacco smoking, high blood pressure, high blood cholesterol, insufficient physical activity, overweight and obesity, poor nutrition and diabetes [10, 11]. AIP (Atherogenic Index of Plasma), a relatively new lipid parameter, has been studied in diabetics (mostly to determine the role of various drugs). AIP can be easily calculated from standard lipid profile as log (TG/HDL-C), with TG and HDL-C expressed in molar concentrations [12, 13, 14].

As a marker of lipoprotein particle size it adds predictive value beyond that of the individual lipids, and/or TC/HDL-C ratio [15]. AIP which is inversely correlated with LDL particle size has become popular as a marker of plasma atherogenicity and has been shown to be increased in people at higher risk for coronary heart disease [13].

In view of the aforementioned controversial literature, it was decided to evaluate the relationship between serum electrolyte level and AIP level in young hypothyroid type -2 diabetic males and to find out the correlation between these biochemical parameters along with the changes in serum lipid profile.

MATERIALS AND METHODS: This study was conducted at Shri Ram Murti Smarak Institute of Medical Sciences, Bareilly (north Indian city), on subjects, under which they were tested for various biochemical parameters, including fasting blood glucose and serum lipid profile, serum thyroid hormone profile (T_3, T_4, TSH) and serum electrolytes in the hospital's clinical biochemistry laboratory. Fifty such male attendees between March 2011 and August 2011 who were diabetic hypothyroid and aged between 25 and 45 years were included in this retrospective study.

Inclusion criteria were diabetic type- 2, young male and hypothyroid or exclusion criteria were renal disorder and hepatic disorder male used. The lipid profile and blood glucose levels of these 50 subjects obtained from our clinical biochemistry laboratory were used for the study and compare them with fifty healthy ages matched non diabetic normo thyroid male subjects. As per our clinical laboratory procedure, serum was separated from venous blood of fasting subjects and analysed within two hours of collection.

Serum glucose, serum TG and serum TC were was analysed spectrophotometrically by GOD-PAP, GPO-PAP and CHOD-PAP methods respectively by employing reagent kits (Dialab, Austria) on a fully automated analyser of the XL series (Vital Scientific, the Netherlands). Serum HDL-C was measured using reagent kit (Accurex, Mumbai) on semiautoanalyser- BTR-830 (Biosystems SA, Spain). This uses the supernatant for HDL-C assay by the same enzymatic method used for TC analysis, after the other lipoproteins are precipitated by phosphotungstate and Mg^{2+}. VLDL-C and LDL-C was calculated by Friedewald's formula;

(Friedewald *et al*., 1972) as TG was <400 mg/dl in all the subjects.

Lipid ratios (TC/HDL-C and LDL-C/HDL-C, TG/HDL) were calculated by simple division, non-HDL-C was determined by subtracting HDL-C from TC, AIP was calculated as log (TG/HDL-C) with TG and HDL-C expressed in molar concentrations (Dobiasova & Frohlich, 2001). It has been suggested that AIP value of −0.3 to 0.1 is associated with low CAD risk, 0.1 to 0.24 medium and above 0.24 high risks [16].

Serum Thyroid stimulating hormone (TSH) was measured by TOSOH-AIA-360, Immunoassay method supplied by TOSOH Biosciences, Inc. 6000 Shoreline Ct, Suite 10, Southsan Franciscoc A94080, USA. Serum electrolytes were estimated by Easylyte (ISE electrode) Na/K analyzer.

All results were expressed in mean±S.D. Difference between mean were calculated by Student't' test. The level of significance was set as p< 0.05. Statistical analysis was performed using Graph Pad Prism version 5.00 for Windows, Graph Pad software, San Diego California USA, www. graphpad.com.

RESULTS: The fasting serum glucose, lipid profile and other calculated lipid parameters viz. TC/HDL-C, LDL-C/HDL-C, non-HDL-C and AIP levels of 50 male. Subjects and 50 age matched healthy control were obtained after calculation from data in our clinical laboratory records over 5 months period.

Table 1 compares the blood glucose and serum electrolytes with serum thyroid stimulating hormone and atherogenic index of plasma in diabetic hypothyroid male with non-diabetic normo-thyroid male subjects between age group 25-42 years. Blood glucose (194.04±50.09 vs. 99.88±17.01, p=0.0001), serum sodium (135.14±7.27 vs 138.02±5.74, p=0.0303) and Serum TSH (19.47±20.03vs 2.85±1.22, p= 0.0001) and AIP (0.26±0.13 vs 0.16±0.12, p=0.0002) had a significant difference, whereas serum potassium (4.02±3.93 vs 3.98±0.53, p=0.9320) was not statically significant.

Table 2 showed serum lipid profile in cases and control group, there were present a significant difference serum total cholesterol (187.52±44.69 vs 133.32±14.46, p=0.0001), serum triglyceride (140.20±28.10 vs 124.94 ± 29.68, p= 0.0096) serum high density lipoprotein(35.90±3.00 vs 32.88±7.60, p= 0.0104), serum low density lipoprotein(182.68± 47.59 vs. 123.62±14.96, p=0.0001) and serum very low density lipoprotein (28.04±5.61vs 24.98±5.93, p=0.0096), respectively in cases and control group.

Table 3 showed a significant difference between cases and control group, TG/HDL,(4.48±1.28 vs 3.50±0.91, p= 0.0001) TC/HDL(6.03±2.08 vs 3.73±0.48 p=0.0001), LDL/HDL (5.92±2.26 vs 3.46±0.48 p=0.0001) and non HDL cholesterol (154.64±46.15 vs 97.42±14.61 p=0.0001), respectively.

Graph A represent a significant negative correlation (r=-0.38, p=0.005) between serum sodium and AIP. It showed that decreased the level of serum sodium in diabetic hypothyroid male increased the risk of cardiovascular disease, while serum potassium level remained normal in these controls.

TABLE 1: DIFFERENT LAB PARAMETERS IN CONTROL AND CASES

Subjects (25-45 year)	MEAN ± S.D. Blood Glucose	MEAN ± S.D. Serum Na+	MEAN ± S.D. Serum K+	MEAN ± S.D. Serum TSH	MEAN ± S.D. AIP
All Diabetic hypothyroid male (n=50)	194.04 ± 50.09	135.14 ±7.27	4.02 ± 3.93	19.47 ±20.03	0.26 ± 0.13
All Non- Diabetic normal thyroid male (n=50)	99.88 ± 17.01	138.02 ± 5.74	3.98 ±0.53	2.85 ± 1.22	0.16 ± 0.12
P-value	0.0001*	0.0303**	0.9320***	0.0001*	0.0002*

***** Extremely statistically significant, ****** statistically significant, *******Not statistically significant, Na+= sodium, K+=potassium, TSH= thyroid stimulating hormone, AIP= atherogenic index of plasma.

TABLE 2: DIFFERENT LIPID PROFILE PARAMETERS IN CONTROL AND CASES

Subjects (25-45 year)	MEAN ± S.D. Serum TC	MEAN ± S.D. Serum TG	MEAN ± S.D. Serum HDL	MEAN ± S.D. Serum LDL	MEAN ± S.D. Serum VLDL
All Diabetic hypothyroid male (n=50)	187.52 ± 44.69	140.20 ± 28.10	35.90 ± 3.00	182.68 ± 47.59	28.04 ± 5.06
All Non- Diabetic normal thyroid male (n=50)	133.32 ± 14.46	124.94 ± 29.68	32.88 ± 7.60	123.62 ± 14.96	24.98 ± 5.93
P-value	0.0001*	0.0096*	0.0104**	0.0001*	0.0096*

***** Extremely statistically significant, ****** statistically significant, TC=total cholesterol, TG= triglyceride, HDL =high density lipoprotein, LDL= low density lipoprotein, VLDL= very low density lipoprotein.

TABLE 3: SOME OTHER LAB PARAMETER DERIVED FROM LIPID PROFILE IN CONTROL AND CASES

Subjects (25-45 year)	MEAN ± S.D. Serum TG/HDL	MEAN ± S.D. Serum TC/HDL	MEAN ± S.D. Serum HDL/LDL	MEAN ± S.D. Serum NON HDL-C
All Diabetic hypothyroid male (n=50)	4.48 ± 1.28	6.03 ± 2.08	5.92 ± 2.26	154.64 ± 46.15
All Non- Diabetic normal thyroid male (n=50)	3 .51 ± 0.91	3.73 ± 0.48	3.46 ± 0.48	97.42 ± 14.61
P-value	0.0001*	0.0001*	0.0001*	0.0001*

* Extremely statistically significant

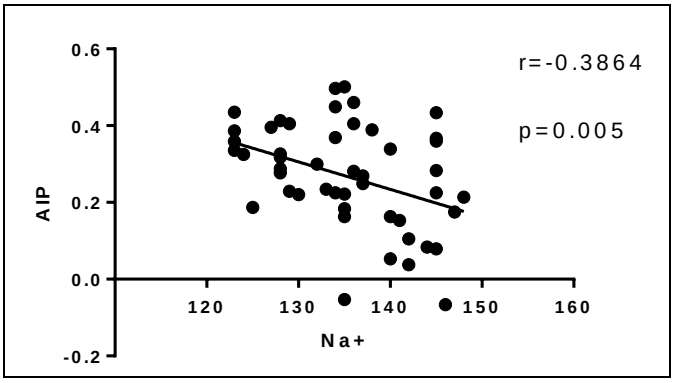

FIGURE (A): CORRELATION BETWEEN SERUM SODIUM (Na^+) AND ATHEROGENIC INDEX OF PLASMA (AIP) IN HYPOTHYROID DIABETIC TYPE-2 YOUNG MALES. CORRELATIONS WERE EVALUATED USING PEARSON'S METHOD.

DISCUSSION: Hyponatremia is the most common electrolyte abnormality encountered in clinical practice [17]. Sodium and potassium depletion is a common feature of essential hypertension and type II diabetes [18]. Reduction in serum Na^+ and K^+ in diabetic subjects might be a result of electrolyte loss which arises due to dehydration or a result of kidney dysfunction caused by diabetes [1]. But in our study, there were hyponatremia in hypothyroidism and diabetic male patients while these subjects had no renal disorder.

According to Roopa Murgod, Serum potassium levels were found to be decreased in hypothyroid patients when compared to controls, though it was statistically significant. But when potassium values were studied in relation to serum TSH values, a significant negative correlation was found (p= -0.002). Higher the value of TSH, lower was the level of serum [6]. In our study, serum potassium values were not statistically significant (p=0.9320) in hypothyroid diabetic type-2 males, or there were no correlation between TSH and serum potassium values. The presence of hypoglycemia is uncommon in isolated thyroid hormone deficiency and should raise the possibility of hypopituitarism in a hypothyroid patient. More importantly, hypothyroidism is accompanied by a variety of abnormalities in plasma lipid metabolism, including elevated triglyceride and low-density lipoprotein (LDL) cholesterol concentrations. Even subclinical hypothyroidism can exacerbate the coexisting dyslipidemia commonly found in type-2 diabetes and further increase the risk of cardiovascular diseases. Adequate thyroxin replacement will reverse the lipid abnormalities [7].

The most important effect on lipid metabolism includes mobilization of triglycerides from the adipose tissue causing increased. HDL level was found to be increased in hypothyroid cases when compared to controls. The cause of normal or elevated levels of HDL in hypothyroid cases is due to reduced activities of Cholesterol Ester Transfer protein (CETP) and hepatic lipase concentration of free fatty acids in plasma [19], in our study instead of increase the serum HDL values, decreased the level of serum HDL in diabetic type-2 hypothyroid males. In patients with overt hypothyroidism, there is an increase in serum total cholesterol (TC), Low Density Lipoproptein cholesterol (LDL-C), Apolipoprotein B, Lipoprotein (a) levels and possibly triglyceride (TG) levels 4. Abnormal lipid profile in diabetics might have resulted from insulin deficiency which plays major roles in intermediary metabolism [20, 21].

The observed increase in total cholesterol, LDL-cholesterol, triglycerides and CHD risk ratio accompanied with reduced HDL-cholesterol in diabetics shows lipid abnormalities and is synonymous with increased risk of atherosclerosis [22, 23]. AIP reflects the delicate metabolic interactions within the whole lipoprotein complex [15]. Universally, AIP has been used by some practitioners as a significant predictor of atherosclerosis. Researchers have also shown that AIP is a better predictor of cardiovascular risk than

other previously used lipid parameters [24]. Furthermore, in situations where other atherogenic risk parameters appear normal, AIP may be the diagnostic alternative [25].

In our study, a significant correlation occurred between serum sodium and AIP, when increased the AIP at the same time decreased the serum sodium concentration in these patients. While there were no changed in the serum potassium level or it could be slightly decrease, but no correlation between AIP and serum potassium. Our study has some limitations. It is a retrospective study which is inferior to prospective studies when the associations between different variables are to be ascertained. Our study is limited only to men between 25 and 45 years of age. A wider range of age and sex would have been more useful in gauging the distribution of the studied parameters in the population.

CONCLUSION: We are able to conclude that there were a significant negative correlation between serum sodium and AIP level in hypothyroid type-2 diabetic males while at the same there were no changes in the serum potassium level. According this study will further assist physicians in the use of only serum sodium and AIP for the diagnosis of cardiovascular disease risk, while need not to be assessed serum potassium level in type-2 diabetic hypothyroid males.

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DECLARATION OF INTEREST: None.

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