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TYPE 2 DIABETICS;
EVALUATING SERUM COBALAMIN WITH SPECIAL REFERENCE TO DYSLIPIDEMIA

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ABSTRACT…Objectives: To evaluate serum cobalamin with special reference to dyslipidemia in type 2 Diabetic subjects. **Study Design:** Observational study **Place and Duration:** Department of Medicine, Isra University Hyderabad, Sindh from January 2014 to July 2014. **Methodology:** A sample of 107 type 2 diabetic subjects was selected according to inclusion and exclusion criteria. Cobalamin was measured on Roche Cobas e411 chemistry analyzer and blood lipoproteins by standard laboratory methods. Data was analyzed by SPSS 21.0 (IBM, Incorporation, USA) using student t and Chi square tests for continuous and categorical variables respectively. P-value of ≤ 0.05 was taken significant. **Results:** Cobalamin deficiency was noted in 51 (47.6%) of diabetics and cobalamin deficiency was associated with dyslipidemia. Mean ± SD of cobalamin in normal and reduced cobalamin groups were noted as 355±29.5 and 183±17.5 pg/ml respectively (p=0.0001). Triglycerides, total cholesterol, HDLc, LDLc and VLDLc differed significantly in the normal and reduced cobalamin subjects (p<0.001). Lipoprotein sub fractions showed a negative correlation with serum cobalamin (p≤0.02). **Conclusion:** Cobalamin deficiency is common in type 2 diabetics and is associated with dyslipidemia.

Key words: Cobalamin Dyslipidemia Type 2 diabetics

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INTRODUCTION

Cobalamin (vitamin B_{12}) is a key micronutrient essential for DNA methylation and plays role in metabolic reactions of lipids. Cobalamin deficiency has been suggested as a cause of endothelial dysfunction.[1,2] Exclusive source of cobalamin is the food of animal origin. Daily gut absorption is approximately 5 μg and daily body requirement is 3 μg /day. Cobalamin remains stored in liver for as long as 3-5 years before manifest deficiency. Liver stores are approximately 2000-5000 μg in normal nons-vegans.[3]

Dietary deficiency is one of commonest cause, followed by intrinsic factor (IF) deficiency, a lack of IF receptor, disease of terminal part of ileum, gut surgery, chronic pancreatitis, congenital transcobalamin deficiency, and Diphyllobothrium latum infestation.[3]

Cobalamin functions as co-enzyme for various cellular enzymes to catalyze biochemical reactions.[3] Cobalamin, as co-enzyme, exists as methyl-cobalamin and S-adenosyl-cobalamin. S-adenosyl-cobalamin is co-enzyme for L-methylmalonyl-CoA–coenzyme A mutase which catalyzes the reaction of conversion of methylmalonyl-CoA to succinyl-CoA, while methyl-cobalamin is co-enzyme for methionine synthetase, which catalyzes conversion of homocysteine to methionine.[3,4]

A recent study has reported adverse effects of cobalamin defienciency on blood lipids in type 2 diabetics.[1] Previous study has shown association of low vitamin B12 with macro-vascular diseases such as myocardial infarction[5] and cerebral ischemia[6] as well as coronary artery disease (CAD).[7] However, a systematic review of published cohort studies was inconclusive.[8] Cobalamin deficiency causes microvascular complications such as diabetic neuropathy[9] and may worsen the existing neuropathy due to other conditions.[10] The present study was conducted to

evaluate serum cobalamin with special reference to dyslipidemia in type 2 diabetic subjects.

SUBJECTS AND METHODS

A prospective case control study was conducted at the Department of Medicine, Isra University Hyderabad, and Sindh from January 2014 to July 2014. A sample of 107 subjects was selected through non-probability purposive sampling according to inclusion and exclusion criteria. Volunteer diagnosed type 2 diabetics of 20-50 years were included. Diabetics with chronic liver disease, renal failure, taking lipid lowering agents, multivitamins and any major systemic illness were excluded. Patients taking metformin were strictly excluded from study protocol.

Dyslipidemia was defined (ATP III) as one or more of the following: total cholesterol more than 200mg/dL, low density lipoprotein-cholesterol (LDL-C) more than 130mg/dL, high-density lipoprotein-cholesterol (HDL-C) below 40mg/dL, very low density lipoprotein-cholesterol (VLDL-C) more than 30mg/dL, and triglycerides more than 150mg/dL.

Lipids determination

Obtained serum was pipetted into a clean blood sample bottle and analyzed on the day of collection after a 12 hour fasting. Serum total cholesterol was determined by an enzymatic (CHOD-PAP) colorimetric method and triglycerides were determined by an enzymatic (GPO-PAP) method. HDL-Cholesterol was estimated by a precipitant method and LDL-Cholesterol by was estimated by using Friedewald's formula as; LDL-C = TC - HDL-C – (TG/5).[11]

Glucose determination

Serum glucose was determined by the glucose oxidase method.

Cobalamin detection

Cobalamin was detected on a Cobas e411 analyzer; Roche Diagnosis GmbH, Mannheim, Germany. Cobalamin levels were defined as; normal ≥240pg/ml, and reduced cobalamin <240 pg/ml.[3]

DATA ANALYSIS

Data was analyzed on SPSS version 21.0. (IBM Corporation, USA) Normality of data was checked by Shapiro Wilk testing. Continuous and categorical variables were analyzed by student's t test and chi square test respectively. Significant p-value was taken at ≤ 0.05.

RESULTS

Of total 107, 78 (72.1%) were male and 29 (27.1%) female (p=0.0001). Male population predominated in present study. Mean±SD age was 48±7.7 years. BMI, obesity, hypertension, smoking habits, blood glucose, urea and serum creatinine are shown in table-I.

Normal (≥240pg/ml) and reduced cobalamin (<240 pg/ml) were noted in 56 (52.3%) and 51 (47.6%) of diabetics respectively. Mean± SD in normal and reduced cobalamin subjects was noted as 355±29.5 and 183±17.5 pg/ml respectively (table-II) (p=0.0001). Triglycerides, total cholesterol, HDLc, LDLc and VLDLc differed significantly in the normal (≥240pg/ml) and reduced cobalamin (<240 pg/ml) groups. Statistically significant differences were noted as shown in table-III. Various lipoprotein fractions showed a negative correlation with cobalamin levels as shown in table-IV. Negative r-value with significant p-values was noted for all lipoprotein fractions (p≤0.02).

Age	48±7.7 years
Male	78 (72.8%)
Female	29 (27.10%)
BMI (kg/m^2)	25±6.79
Obesity	41 (38.3%)
Hypertesion	56 (52.3%)
Smokers	27 (25.2%)
Blood glucose (mg/dl)	253±61.5
BUN (mg/dl)	13±4.5
Serum creatinine(mg/dl)	0.9±0.5

Table-I. Characteristics of type 2 diabetic subjects (n=107)

	Cobalamin ≥240pg/ml	Cobalamin <240 pg/ml
No. of Pt. (%)	56 (52.3%)	51 (47.6%)
Mean±SD (pg/ml)	355±29.5	183±17.5

Table-II. Cobalamin levels in type 2 diabetics (n=107)

	Cobalamin ≥240pg/ml	Cobalamin <240 pg/ml	p-value
Triglycerides (mg/dl)	132.9±45.7	231.1±110.7	0.001
Cholesterol-Total (mg/dl)	158.3±25.9	211.1±44.9	0.0001
HDLc (mg/dl)	39.9±8.5	32.5±7.3	0.02
LDLc (mg/dl)	96.3±19.6	126.6±17.3	0.001
VLDL (mg/dl)	41 ± 14	29.3 ± 8.1	0.00

Table-III. Lipid profile of type 2 diabetic subjects (n=107)

	r-value	p-value
Triglycerides (mg/dl)	-0.29	0.02
Cholesterol - total (mg/dl)	-0.39	0.04
HDLc (mg/dl)	-0.38	0.0001
LDLc (mg/dl)	-0.32	0.03
VLDL (mg/dl)	-0.22	0.001

Table-IV. Correlation of serum cobalamin with lipoprotein fractions (n=107)

DISCUSSION

The present study is an original research work conducted at Isra University Hospital Hyderabad, Sindh. Our study is the first one to evaluate the frequency of cobalamin deficiency in the Sindhi population with special reference to dyslipidemia in type 2 diabetics. Two important findings were observed in type 2 diabetics; First, cobalamin deficiency was noted in 51 (47.6%) of diabetics and second, cobalamin deficiency was associated with dyslipidemia. Normal and reduced cobalamin were noted as 355±29.5 and 183±17.5 pg/ml respectively (p=0.0001). The findings are consistent with previous studies which had reported a prevalence of cobalamin deficiency of 5.8% to 33%.[12,13] On the contrary, other studies had reported very high frequency referenced as.[14,15] Adaikalakoteswari[1] has reported a prevalence of 27% in type 2 diabetics and 32.1% in type 2 diabetics on metformin therapy. Previous studies from India had reported prevalence of 67% in middle-aged men[14] and 54% in diabetes patients.[15] The findings of above studies contradict with present and previous studies.[1,12,13] Reason might be different study population, cobalamin detection methods, and dietary habits of indigenous population.

Triglycerides, total cholesterol, HDLc, LDLc and VLDLc differed significantly in the normal (≥240pg/ml) and reduced cobalamin (<240 pg/ml) groups. Statistically significant differences were noted as shown in table III. Various lipoprotein fractions showed a negative correlation with cobalamin levels, shown in table IV. Negative r-value with significant p-values was noted for all lipoprotein fractions. In this study, cobalamin deficiency was independently associated with triglycerides, cholesterol, VLDL, LDL, HDL ratio in type 2 diabetics. Findings are in keeping to previous studies.[1,16,17]

Cobalamin functions as a co-enzyme in the conversion of methyl-malonyl-CoA) to succinyl-CoA.[3] Cobalamin deficiency blocks the above biochemical reaction, and result is accumulation of methyl-malonic acid. Methylmalonyl acid inhibits carnitine palmitoyl transferase, this results in accelerated lipogenesis.[16,19] Accelerated lipogenesis is one of the postulated mechanisms of dyslipidemia in diabetics. A previous study reported an independent association of cobalamin deficiency to cardiovascular disease.[18] Similar results had been reported by previous studies.[19,20] However, few of previous randomized clinical trials had reported negative results.[21,23] Previous studies had established the association of cobalamin and folate deficiency with dyslipidemia in type 2 diabetics.[24,26]

Based on findings of present study and review of available literature, it may be claimed that cobalamin deficiency contributes to dyslipidemia in type 2 diabetics. Present study has some limitations like; first: other risk factors were not studied which might have affected results by confounding effects, and second any effect of diet

on cobalamin deficiency was not analyzed. The cause effect relationship cannot be ascertained due to cross sectional design of study. The cobalamin deficiency and its association with dyslipidemia is a worth finding of present study.

CONCLUSIONS

Cobalamin deficiency is common in type 2 diabetics and is associated with dyslipidemia. Further studies are recommended to evaluate cobalamin deficiency as cause of dyslipidemia in large study population to confirm the observations of present study.

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PREVIOUS RELATED STUDY

Mohammad Mohsin Rana, Muhammad Saeed Akhtar, Badar Bashir, Abaid-ur-Rehman. TYPE 2 DIABETICS; THE RELATIONSHIP BETWEEN THE SERUM CHOLESTEROL AND TRIGLYCEROIDS (Original) Prof Med Jour 14(2) 337-343 Apr, May, Jun, 2007.

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