# POTENTIAL EFFECTS OF OMEGA-3 FATTY ACIDS ON HIGH DENSITY LIPOPROTEIN CHOLESTEROL AND LOW DENSITY LIPOPROTEIN CHOLESTEROL IN MIDDLE AGED PATIENTS WITH DIABETES MELLITUS

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**Abstract**

***Background:*** *The one of the most common metabolic disorder that remains worldwide is Diabetes mellitus. Dietary intake of omega-3 fatty acid may confer a protective effect against diabetes, improves high density lipoprotein (HDL-C) and reduce low density lipoprotein cholesterol (LDL-C) levels.*

***Objective:*** *To observe the effect of supplementation of omega-3 fatty acid on HDL and LDL levels in type 2 DM.*

***Methods:*** *A prospective interventional study was conducted from January 2017 to December 2017. A total numbers of 52 diagnosed type 2 diabetic patients of both sexes were selected with age ranging from 40 to 50 years. Among them, 27 type 2 diabetic patients with supplementation of omega 3 fatty acid (2g/day) for 12 weeks was considered as study group. Another 25 type 2 diabetic patients without supplementation of omega 3 fatty acid were considered as control group for comparison. The study subjects were selected from Outpatient Department of Endocrinology, Dhaka Medical College Hospital, Dhaka and personal contact from Dhaka city on the basis of inclusion and exclusion criteria. The research work was carried out after obtaining ethical clearance from concerned departments, Research Review Committee and Ethical Review Committee of Dhaka medical college, Dhaka. The study parameters serum HDL was estimated by enzymatic colorimetric method in auto-analyzer and serum low density lipoprotein was calculated by using Friedwald formula in Department of Laboratory Medicine, Dhaka Medical College Hospital, Dhaka. The parameters were studied 2 times in study and control groups i.e. at the beginning of study (base line) and after 12 weeks of study period. Data were collected in pre-designed structured questionnaire from the researcher by herself. For statistical analysis, Paired Student's 't' test and Unpaired Student's 't' test were performed as applicable using SPSS for windows version 16.0.*

***Results****: In this study High density lipoprotein cholesterol that is good cholesterol increased and low density lipoprotein cholesterol was decreased in diabetic patients after supplementation with omega-3 fatty acid in comparison to that of their baseline value. Again, after 12 weeks, high density lipoprotein was higher and low density lipoprotein cholesterol was lower in diabetic patients after supplementation with omega-3 fatty acid in comparison to control group.*

***Conclusion:*** *After analyzing the results of the study, it can be concluded that omega-3 fatty acid can improve HDL and lowers LDL levels in diabetic patients may be helpful to minimize the complications of type-2 diabetes mellitus.*

***Key words****: Diabetes mellitus, glycemic status, lipid-profile, high density lipoprotein, Low density lipoprotein, Omega-3 fatty acid.*

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## Introduction

Diabetes mellitus (DM) is a group of metabolic disease characterized by hyperglycemia resulting from defect in insulin secretion or insulin action or both. The chronic hyperglycemia of diabetes is associated with long term damage dysfunction and failure of various organs especially the eyes, kidneys, nerve, heart and blood vessel[1].Diagnostic criteria of diabetes mellitus are fasting plasma glucose level e"7.0mmol/l (126mg/dl) or plasma glucose 2 hours after an oral glucose e" 11.1 mmol /L (200mg/dl) and HbA1ce" 6.5%[2].The prevalence of T2DM is expected to rise from 285 million in 2010 to 438 million by the year of 2030 [3].Within 2030, the prevalence of diabetes mellitus will be 11.1 million in Bangladesh[4].

Insulin is the potent anabolic hormone which is essential for appropriate tissue development, growth and maintenance of whole body glucose homeostasis. Insulin regulates glucose homeostasis by increasing the rate of glucose uptake into striated muscle and adipose tissue. In the skeletal muscle, insulin prompts glucose uptake by stimulating translocation of GLUT-4 to plasma membrane[5]. Insulin resistance occurs when the insulin sensitive tissue loses response to insulin. The basic effect of insulin resistance on glucose metabolism is to prevent the uptake and utilization of glucose by most cells of the body. As a result blood glucose concentration increases, cell utilization of glucose falls, utilization of fat increases and free fatty acid level increases in blood [6].

Omega-3 Fatty acids are a group of polyunsaturated fatty acids consists of alpha-linolenic acid (ALA), eicosapentaenoic acid (EPA) and docosahexanoic acid (DHA). They are found in seafood including fatty fish (e.g. salmon, tuna and trout) and shellfish (e.g. crab, mussels and oysters).The omega 3 fatty acid; increases insulin sensitivity, helps in blood clotting, promote fat digestion, improve fertility, acts as a mood elevator and helps in brain development [7].

Consumption of fish oil can decreases free fatty acid level, improve insulin sensitivity as well as reduce the incidence of type 2 DM [8]. Poly unsaturated fatty acid act directly on insulin sensitive tissues, increases number of insulin receptors thus reducing insulin resistance[9].Intake of diet rich in polyun-saturated fatty acid, particularly n-3 and n-6, facilitate the action of insulin through various metabolic pathways, which are suppression of hepatic lipogenesis, reduction of the release of triglycerols from liver, improvement in ketogenesis, and oxidation of fatty acids in liver [10]. Moreover, intake of polyunsaturated fatty acid improve lipid metabolism and decreases triglyceride and total cholesterol level.

Omega- 3 fatty acid prevents this change by increasing peroxisome proliferator receptor gamma, increasing hepatic uptake and oxidation of free fatty acid in skeletal muscle [11].Some author found significant reduction in serum total cholesterol and triglyceride [12].Therefore the present study is intended to assess the effect of supplementation of omega-3 fatty acid in Bangladeshi diabetic patient to improve the lipid profile.

## Methods

This prospective, interventional study was done from Department of Physiology, Dhaka Medical College, Dhaka from January 2017 to December 2017.The research work was carried out after obtaining ethical clearance from concerned departments, Research Review Committee and Ethical Review Committee of Dhaka medical college, Dhaka. The patients were selected from outpatient department of Endocrinology, Dhaka medical college and personal contact from Dhaka city. At the Beginning of study 60 diagnosed type-2 diabetic patients were randomly selected on the basis of exclusion and inclusion criteria. There were 30 patients of control group and 30 patients of study groups recruited for completion of study, After 6 weeks of study period, 3 patients were dropped out from study group and 5 patients were dropped out from control group. Finally, total 52 type diabetic patient of both sexes with the age ranging from 40-50 years with FBG 7.0 mmol/l or 126 mg/dl, HbA1c 6.5%, serum total cholesterol >200 mg/dl, serum triglyceride >150 mg/dl, LDL>130 mg/dl, BMId"30 Kg/$m^2$ and patients with oral hypoglycemic drug were included in this study. Subjects having history

of heart, liver, endocrine disorder, insulin therapy, pregnant and lactating women were excluded from this study. For this study 27 diagnosed type-2 diabetic patients with omega-3 fatty acid supplementation were selected as study group and 25 type-2 diabetic patients without oral omega-3 fatty supplementation were selected as control group. The study group again sub-divided into pre-supplementation group and after 12 weeks of supplementation as post supplementation group. The control group was sub-divided as pre and post follow-up group. After selection, the nature, purpose and benefits of the study were explained to each subject and informed written consent was taken from participants. Before taking blood detailed family and medical history were taken. Anthropometric measurement of the subjects was recorded and blood pressure was measured. All the information were recorded in a prefixed questionnaire. With aseptic precaution, 5 ml of venous blood was collected from ante-cubital vein by a disposable plastic syringe from each subject after overnight fasting for biochemical tests. Serum high density lipoprotein cholesterol was estimated by enzymatic colorimetric method in auto-analyzer and low density lipoprotein was calculated by using Friedwald formula in department of Laboratory Medicine Dhaka Medical College Hospital, Dhaka. Omega-3 fatty acid (2gm) was supplied to study group then they were asked to intake twice daily for 12 weeks with proper instructions. Subjects were instructed not to change their diet and physical activities during the course of the study. A regular telephonic contact and periodic visit was made to participants because most of them are employee of Dhaka medical college. For statistical analysis, Paired Student's't' test and Unpaired Student's 't' test were performed as applicable using SPSS for windows version 16.0**.**Data were expressed as mean ± SE. The *p* value of < 0.05 was accepted as level of significance.

**Results**

In this study no significant difference were observed in age, sex, BMI, systolic and diastolic blood pressure between study and control group (Table 1).In this study, the mean serum high density lipoprotein cholesterol and low density lipoprotein cholesterol levels were almost similar and there is no statistical difference were observed at the beginning of the study. In study group, the mean serum high density lipoprotein ($p$<.0.001) was found higher and mean serum low density lipoprotein cholesterol ($p$<.0001) level were found significantly lower in post supplementation group, than pre-supplementation group. Again the mean serum high density lipoprotein ($p$<.0001) levels were found significantly higher and mean serum low density lipoprotein ($p$<.0001) levels were found significantly lower and in study group compared to control group. In control group, there was no statistical difference were observed in mean serum HDL –C and LDL-C between pre-follow-up and post follow-up group.

**Table-I**

*General characteristics of the patients in both groups (N=52)*

Parameters

| | Study group (n=27) | Control group (n=25) |
|---|---|---|
| Age (years)[a] | 45.90±3.80 [ns] | 44.92±3.75 |
| Sex (%)[b] | | |
| Male | 18 (66.7%) [ns] | 11 (44 %) |
| Female | 9 (33.3%) [ns] | 14 (56%) |
| BMI (kg/m$^2$)[a] | 25.03±2.27 [ns] | 25.87±1.75 |
| Systolic BP[a] (mmHg) | 119.07±7.08 [ns] | 121.79±4.47 |
| Diastolic BP[a] (mmHg) | 79.63±6.26 [ns] | 80.00 ± 0.00 |
| Duration of disease[a] (years) | 5.43 ± 1.50 [ns] | 5.35 ± 1.57 |

Results were expressed as mean ± SD. a=Unpaired Student's't' test was performed to compare between the groups. b= Chi Square test was performed to compare male and female between the groups. The test of significance was calculated and *p* value < 0.05 was accepted as level of significance. N= total number of subjects, n = number of subjects in each group ns= non-significant */**/***= significant. T2DMS=Type 2 diabetes mellitus with supplementation T2DM=Type 2 diabetes mellitus without supplementation

**Table II**

*Serum total cholesterol and serum triglyceride levels in different groups (N=52)*

| Parameters | Study group(n=27) | | Control group (n=25) | |
|---|---|---|---|---|
| | Pre-supplemenation group | Post supplementation group | Pre-follow-up group | Post follow-up group |
| HDL (mg/dl) | 29.95 ± 7.34 | 38.48 ± 3.67** | 29.20 ± 4.20 | 29.96 ± 4.43## |
| LDL (mg/dl) | 157.41 ± 40.00 | 128.75± 18.02* | 157.68 ± 14.68 | 156.88 ± 15.20## |

Results are expressed a s mean ± SD. a= Paired student's t test was performed for comparison within groups and b=unpaired t test was performed to compare between groups. *p* value < 0.05 was accepted as level of significance. N= total number of subjects, n = number of subjects in each group, HDL=High density lipoprotein ,LDL=triglyceride (*= study group baseline vs study group after 12 weeks of supplementation; # = study group after 12 weeks vs control group after 12 weeks); (* *p*<.01, **p<.001;# *p*<.01,## *p*<.001).

## Discussion

In the present study, the mean serum high density lipoprotein was significantly higher and low density lipoprotein levels were lower in patients of T2DM after supplementation with omega-3 fatty acid in comparison to that of their baseline value. Again, after 12 weeks, mean high density lipoprotein (.001) level was significantly higher in type-2 diabetic patients supplemented with omega-3 fatty acid in comparison to that of diabetic control group without omega-3 fatty acid. N-3 fatty acids are considered as well tolerated drug in treatment of cardiovascular risk factors. The Poly unsaturated fatty acid increases Scavenger Receptor Class B Type-1 receptor (SR-B1) which helps in increasing plasma HDL level by increasing expression of main hepatic genes which helps in reverse cholesterol transport[13]. Almost similar type of result were observed by different researchers of different countries [14,15,16,17]. On the contrary, found no significant difference in lipid profile in patients after supplementation of omega-3 fatty acid in comparison to that of their baseline values and diabetic control group who were not supplemented with omega-3 fatty acid. There were a history of less physical activity in the study subjects that might be contributed the result of those study. Literature review suggested that, Omega-3 fatty acid has a role on reducing serum low density lipoprotein level. Diet rich in polyunsaturated fatty acid decreases LDL to binding with its receptor as a result in change of membrane fluidity. Thus, omega-3 fatty acid reduces serum low density lipoprotein level that facilitates the binding of insulin to its receptor and improves insulin sensitivity [18].

In the present study serum-high density lipoprotein level rises and serum low density lipoprotein levels decreases in patients with T2DM after supplementation of omega-3 fatty acid in comparison to their baseline value and control group. Omega-3 fatty acid supplementation increases serum HDL level and it also decreases LDL by altering membrane fluidity. This facilates the binding of insulin to its receptor and improves insulin sensitivity.

## Conclusions

After analyzing the results of the study, it can be concluded that supplementation of omega-3 fatty acid can improve serum HDL-C and serum LDL-C levels in patients with type-2 diabetes mellitus. Therefore, omega-3 fatty acid containing food may be helpful to minimize the complications in type-2 diabetes mellitus.

**Conflict of Interest:** None

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