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**Original Article**

# Effects of Omega-3 Fatty Acid Supplementation on Serum Alanine Transferase and Aspartate Transferase Levels in Middle Aged Patients with Type 2 Diabetes Mellitus

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**Abstract**

**Background:** People with type2 diabetes mellitus (DM) are at amplified chance of non-alcoholic fatty liver disease. **Objective:** The purpose of the present study was to observe the effects of omega-3 fatty acid supplementation alanine transferase (ALT) and aspartate transferase (AST) in middle age patients with type 2 DM**. Methodology:** A prospective interventional study in 2017 had been recruited 52 type 2 diabetic patients of both sexes aged 40 to 50 years. Among them, 27 patients were given fish oil capsule orally ( omega 3 fatty acid 2g/day) for consecutive 12 weeks and r 25 patients without supplementation w and ere selected as control also studied after 12 weeks serum serum ALT and AST of all patients was estimated by enzymatic colorimetric method at baseline and after 12 weeks For statistical analysis, **Results**: In this study ALT and AST significantly decreased in patients supplemented with omega-3 fatty acid after 12 weeks, ALT (alanine aminotransferase) and AST (aspartate transaminase) were decreased in diabetic patients after supplementation with omega-3 fatty acid in comparison to control group. **Conclusion:** It can be concluded that omega-3 fatty acid supplementation was effective to reduce ALT and AST levels in diabetic patients and it may be helpful to minimize the risk of fatty liver in type-2 DM. [*Journal of Science Foundation, July 2020;18(2):62-66*]

**Keywords**: Diabetes mellitus; fatty liver; ALT; AST; Omega-3 fatty acid

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## Introduction

Type 2 diabetes mellitus is a hormonal disorder characterized by hyperglycemia and hyperlipidemia and the chronic hyperglycemia of type 2 diabetes is associated with long term damage of liver causing fatty liver disease (Jun et al., 2011). Insulin is the hormone which is necessary for appropriate tissue development, growth and maintenance of whole body glucose homeostasis (Pessin and Saltiel 2000). Insulin resistance happens 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 (Delarue and Magnan 2007). Omega-3 (ω-3) Fatty acids are a group of polyunsaturated fatty acids consists of alpha- linolenic acid, eicosapentaenoic acid and docosahexanoic acid found in sea fish (salmon, tuna and trout) and shellfish (crab, mussels and oysters) stimulates insulin sensitivity (Baynest et al., 2015).

Consumption of fish oil can decrease free fatty acid level, promotes insulin sensitivity as well as reduce the incidence of type 2 DM (Albert et al., 2016). Omega-3 capsule act directly on insulin sensitive tissues, rises number of insulin receptors thus inhibits insulin resistance (Laila and Lanza 2016). Intake of food rich in omega-3 fatty acid, particularly n-3 and n-6, facilitate the action of insulin through various metabolic pathways, including suppression of hepatic lipogenesis, decreased release of triglycerols from liver, improvement in ketogenesis, and oxidation of fatty acids in hepatic cells (Portillo-Sanchez et al., 2015).

Non alcoholic fatty liver diseases are very common in type 2 diabetic patients (Han et al., 2012). Nonalcoholic fatty liver diseases is the main cause of chronic liver diseases associated with diabetes mellitus. Liver plays an important role in the regulation of carbohydrate homeostasis, hepatocellular accumulation of glycogen causes abnormal elevation of alkaline phosphatase and Aspartate aminotransferase (Mandal et al., 2018). Moreover, intake of polyunsaturated fatty acid decreases serum ALT and AST level (Parker et al., 2012). Fish oil consumption reduces liver fat and ALT and AST by reducing circulating FGF21 levels in T2DM patients. Fibroblast related growth factor is an inflammatory markers that is related to NAFLD and T2DM, so when it reduces serum biomarker of liver also reduces and improvement occurs in T2DM patient (Qin et al., 2015).

Omega- 3 fatty acid prevents this change by increasing peroxisome proliferator receptor gamma, increasing hepatic uptake and oxidation of free fatty acid in striated muscle. Therefore the present study was intended to assess the effect of supplementation of omega-3 fatty acid in Bangladeshi diabetic patient on ALT and AST to observe the liver function.

## Methodology

This prospective, interventional study was carried out in the Department of Physiology at Dhaka Medical College, Dhaka, Bangladesh from January 2017 to December 2017 after approval from Research Review and Ethical Review Committee of Dhaka Medical College, Dhaka, Bangladesh. The patients were selected from outdoor of Endocrinology, Dhaka medical college and personal contact from Dhaka city by purposive sampling. At the beginning 60 diagnosed type-2 diabetic patients of both sexes with the age ranging from 40 to 50 years with FBG 7.0 mmol/L or 126 mg/dl, HbA1c 6.5%, serum total cholesterol more than 200 mg/dl, serum triglyceride more than 150 mg/dL, LDL more than 130 mg/dl, BMI $\leq$30 Kg/m$^2$ and patients with oral hypoglycemic drug and fatty liver were enrolled. 30 patients were given supplementation with Omega-3 fatty acid for 12 consecutive weeks and 30 patients were without supplementation and uses as control. Serum ALT and AST of all patients are assessed at baseline and after 12 weeks. The control subjects studied at before and after 12 weeks of follow-up. After selection, the nature, purpose and benefits of the study were explained to each subject and informed written consent was taken from participants. 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 after overnight fasting was obtained from ante-cubital vein by a disposable plastic syringe from each subject for biochemical tests. Serum ALT and AST was estimated by enzymatic colorimetric method in auto-analyzer. Omega-3 fatty acid (2gm) in the form of fish oil capsule was supplied to patients free of cost and they were asked to take orally twice daily for 12 weeks with proper directions. Fish oil capsule were purchased from the local market.

Patients were instructed not to change their diet and physical activities during the course of the study. A regular telephonic communication and periodic visit was made to participants to ensure the intake of capsule.

For statistical analysis, Paired 't' test and Unpaired 't' test were performed as applicable using SPSS for windows version 16.0**.** Data were expressed as mean±SE. The *p* value of less than 0.05 was accepted as level of significance.

**Results**

After 6 weeks of study period, 3 patients were relinquished from study group and 5 patients were dropped out from control group. Finally, data of 27 patients under supplementation and 25 type diabetic patients without supplementation were used for analysis. Fattty liver was diagnosed by abdominal ultrasonography. Subjects having history of heart disease, endocrine disorder, insulin therapy, viral hepatitis, acute or chronic infections, pregnant and lactating women were excluded from this study.

**Table 1: General Characteristics of the Patients in Both Groups (n=52)**

| **Parameters** | **Supplemented T2DM (n=27)** | **Control group (n=25)** |
|---|---|---|
| Mean Age (Years)[a] | 45.90±3.80 | 44.92±3.75 |
| Male[b] | 18(66.7%) | 11 (44 %) |
| Female[b] | 9 (33.3%) | 14 (56%) |
| BMI (kg/m$^2$) | 25.03 ± 2.27 | 25.87 ± 1.75 |
| SBP (mmHg) | 119.07 ± 7.08 | 121.79 ± 4.47 |
| DBP(mmHg) | 79.63 ± 6.26 | 80.00 ± 0.00? |
| Duration of DM [a] (Years) | 5.43 ± 1.50 | 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 2: Serum alanine transaminase and serum aspartate transaminase levels in different groups (n=52)**

| **Parameters** | **Supplemented** (n=27) | | **Control Group** (n=25) | |
|---|---|---|---|---|
| | Pre- | Post- | Pre follow-up | Post follow-up |
| ALT(IU/L) | 34.6±2.71 | 28.5±1.67** | 39.2±4.20 | 39.96 ± 4.43## |
| AST(IU/L) | 41.3±4.03 | 38..5±1.02* | 47.68±2.68 | 46.8± 2.20## |

Results are expressed as 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, ALT=Alanine transaminase, AST=aspartate transaminase (*= 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).

In this study no significant difference were seen in age, sex, BMI, systolic and diastolic blood pressure between study and control group (Table I).In this study, the mean serum ALT and AST levels were almost similar and there is no statistical difference were observed at baseline after 12 weeks of supplementation of fish oil serum ALT (p<0.0.01) and mean serum AST ($p$<.01) level significantly decreased. Again the mean serum ALT levels and mean serum AST levels were not significantly different in post follow up compared to baseline value in patients without supplementation. More over, serum ALT (p<0.01) levels and mean serum AST (p<0.01) levels were significantly lower and in post supplemented group compared to post follow up control group.

## Discussion

In the present study, the mean serum ALT and AST levels reduced and high density lipoprotein increased in patients of T2DM after supplementation with omega-3 fatty acid. Insulin resistance in T2DM cause impaired fatty acid oxidation in liver and subsequent accumulation of fat in liver (Lopez et al., 2014). When diabetic patient suffers from nonalcoholic fatty liver diseases ALT and AST rises (Bhat and Smith 2015).

Almost similar type of result were observed by other previous studies (Shresta et al., 2017; Jameil et al., 2014). On the contrary, supplementation of omega-3 fatty acid could not bring significant change in lipid profile in T2 DM (Lopez et al., 2014). Literature review suggested that, fat accumulation in liver leads to rise of serum triglyceride level which in turn cause rise serum ALT and AST levels due to impaired liver function (Ni et al., 2012). The binding of insulin with its receptor through releasing some inflammatory mediator from liver that decreases insulin receptor signaling activity, this facts are influenced by rising serum TG level.

Omega-3 fatty acid has a role on reducing serum triglyceride level. Peroxisome proliferator receptor–α exists in the liver which increase in number in presence of omega-3 fatty acid. An increase in PPAR–α leads to increased hepatic uptake of free fatty acid. It also increases the free fatty acids oxidation in skeletal muscle (Shidfar et al., 2018). As a result, free fatty acid level is reduced in blood. The consequence of free fatty acid reduction helps to decrease triglyceride synthesis. Thus, fish oil capsules reduces serum triglyceride level that promotes the binding of insulin to its receptor and improves insulin sensitivity (Fernandez and West 2005).

Fish oil activate PPAR-α (peroxisome proliferator activated receptor alpha) and down regulate sterol regulatory element binding protein-1c (SREBP-1) that improve fatty acid oxidation and reduces liver enzyme (ALT and AST) (Jameil et al., 2014).

## Conclusions

After analyzing the results of the study, it can be concluded that supplementation of omega-3 fatty acid can reduces serum ALT and AST levels in patients with type-2 diabetes mellitus. Therefore, omega-3 fatty acid containing diet may be useful to keep down the complications in type-2 diabetes mellitus.

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