Original Article

Lipid Profile Changes in Type 2 Diabetes Mellitus after Treatment with Metformin

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Abstract:

Background:
Insulin resistance and type 2 Diabetes Mellitus (T2DM) are associated with a clustering of interrelated plasma lipid and lipoprotein abnormalities. Treating uncontrolled glucose levels can indirectly improve lipids. Evidence suggest that, Metformin can decrease the TG's by 10% and LDL-C by 10 to 15% and increase the HDL-C by up to 7% beyond its glucose lowering properties. Considering very limited studies focusing this issue, the study was planned to assess the changes in lipid profile following metformin therapy.

Methods:
This hospital based prospective and longitudinal study was conducted in outpatient Department of Medicine in Rangpur Medical college Hospital (RpMCH), for six months period from 4th November 2018 to 3rd May of 2019 following approval of this protocol. People with T2DM having dyslipidemia attending in OPD of Medicine department were approached for inclusion of the study. All patients were followed up by two times: at day 0, and day 60. Relevant investigation were performed to achieve the objective of the study.

Results:
Among 300 patients, 52% were males and 48% were females. Mean age was 45.65±11.51 years, ranging from 25 to 71 years. Majority patients (39%) were aged >50 years. Among all, 60% patients came from urban area and 40% came from rural area. Base line (day 0) TC, LDL, HDL and TG level were 192.55±52.21 mg/dl, 110.99±28. 11mg/dl, 43.16±9.64 mg/dl and 192.01±100.46 mg/dl. At day 60, the level of TC, LDL, HDL and TG level has changed into 182.50±51.84 mg/dl, 100.93±28. 09mg/dl, 45.17±9.66 mg/dl and 171.65±72.08 mg/dl, respectively. Further analysis showed that this changes were statistically significant ($p<0.05$ in all cases).

Conclusion:
Metformin has a beneficial role in lipid profile in newly detected type 2 DM patients.

Key words: Lipid profile, Type 2 Diabetes Mellitus, Metformin

Introduction:

Diabetes is a serious, chronic disease that occurs either when the pancreas does not produce enough insulin (a hormone that regulates blood sugar, or glucose) , or when the body cannot effectively use the insulin it produces.[1] The International Diabetes Federation (IDF) estimated that 1 in 11 adults aged 20–79 years had diabetes mellitus globally in 2015, 90% of whom have type 2 diabetes mellitus (T2DM).[2,3] Asia is a major area of the rapidly emerging T2DM global epidemic, with China and India the top two epicentres.[3] In Bangladesh, the overall prevalence of type 2 diabetes ranged between 4.5% and 35.0% with male predominance in urban areas and vice-versa in rural areas.[4]

Several studies supported that the onset of both micro and macrovascular complications is more than those with poor glycemic control.[5,6] Dyslipidemia is a well-recognized and modifiable cardiovascular disease risk factors and plays an important role in the progress of atherosclerosis,

the underlying pathology of CVD.[7] The prevalence of dyslipidemia in type 2 diabetes is double with respect to the general population.[8] The characteristic features of diabetic dyslipidemia are a high plasma triglyceride concentration, low HDL cholesterol concentration and increased concentration of small dense LDL-cholesterol particles. Strategies aimed at primary prevention dyslipidemia along with glycemic control provide an outstanding opportunity for reducing the onset and burden of cardiovascular (CV) disease.[9] The American Diabetes Association (ADA) and the European Association for the Study of Diabetes (EASD) recommend lifestyle modifications and initiation of metformin therapy in newly diagnosed patients with T2DM.[11] Besides this, it is the most commonly prescribed anti-diabetic drugs in the world.[12,13] It inhibits hepatic glucose production, increases glucose uptake, and serves as an insulin sensitizer.[10] Therefore, it has been believed that can be useful in management of dyslipidemia in diabetic individuals and few studies showed positive result. However, still there is no consensus regarding this issue. For that reason, the study was designed to see the pattern of changes in lipid profile after initiation of metformin in Type 2 DM.

Materials and Methods:

This prospective longitudinal study was planned to evaluate the role of metformin on lipid profile in Type 2 DM patients attending the outpatients department of Medicine of Rangpur Medical college Hospital from 01 november 2018 to 01 may 2019 over a period of six months after approval of protocol by ethical committee. We used purposive convenient sampling for patient selection. During the study period, 300 newly diagnosed Type2 DM patients of more than 18 years with dyslipidemia attending at OPD were included in this study. Patients having any kind of microvascular and macrovascular complications, type I DM, severely ill patient, patients already receiving treatment for dyslipidemia, known case of chronic kidney disease, hepatic disease, pregnancy or patients having contraindication of metformin use were excluded from the study. Prior interview of the patients, written informed consent were obtained from the patients and or guardian. Face to face interview were conducted by using a semi-structured questionnaire containing socio-demographic parameters and relevant information of DM measuring of fasting and two hours after blood sugar and measuring of fasting lipid profile by formula LDL-C (mg/dl) = total cholesterol-HDL-C-(TRIGLYCERIDES/5) (Friedewald calculation). In this study, all patients received tab metformin 500 mg to 2500 mg(as per need) daily along with standard diet and exercise schedule. During inclusion of the study, 5 ml blood were collected with maintaining proper aseptic precautions for lipid level estimation. Similarly, at day 60 all of the study participants were requested to perform another lipid profile in same lab and sample procedure of estimation. Both report were analyzed further. After collection of all the required data, these were checked, verified for consistency and tabulated using the SPSS (v. 20) software. Statistical significance is set as 95% confidence level at 5% acceptable error level. Data were presented as the proportion of valid cases for discrete variables and as means ± standard deviations and/or medians with interquartile ranges for continuous variables. Differences and/or relation in baseline characteristics were compared using unpaired t test and the Pearson chi square test. Results were presented with a 95% confidence interval (95% CI). A p value of <0.05 was considered significant.

Result:

Total 300 patients of diabetes mellitus type 2 were included in this study. Mean age was 45.65±11.51 years, ranging from 25 to 71 years. Majority patients (39%) were aged >50 years. (Figure-1)

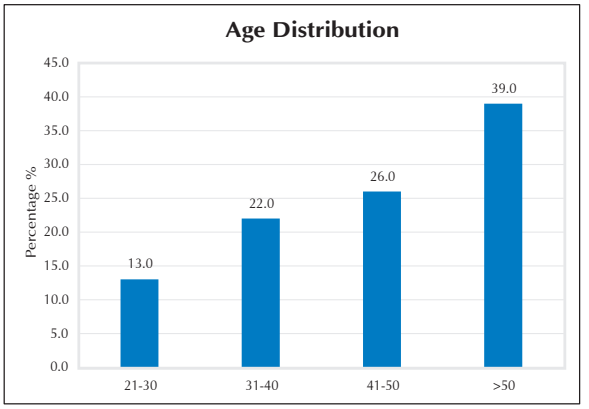


Figure-1: Distribution of age among patients (n=300)

Of 300 patients, 52% were male and 48% were female. (Figure-2)

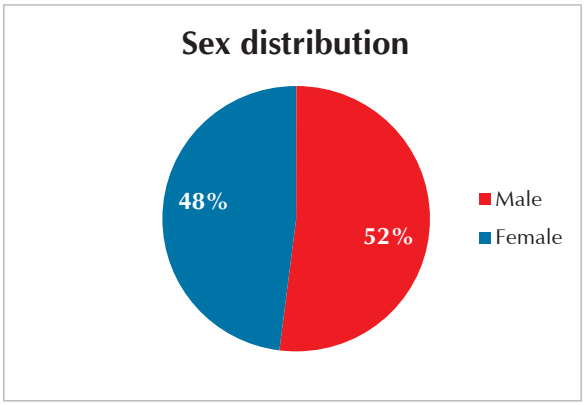


Figure-2: Distribution of sex of patients (n=300)

Among all majority patients were housewives (27%), 25% were doing non government job, 22% were businessman, 10% were government employee and 4% were unemployed. Twelve percent patients were involved in other occupation.

Mean fasting blood sugar was 8.69±0.22 mmol/l, mean 2HABF was 11.97±0.34 mmol/l and mean HbA1c was 8.08±1.77% at admission (Table-I).

Table-I: Glycemic profile of patients at admission (n=300)

Glycemic profile	Mean±SD
FBS (mmol/l)	8.69±0.22
2 hour ABF (mmol/l)	11.97±0.34
HbA1c %	8.08±1.77

TC, LDL and TG decreased significantly after 60 days of metformin therapy. HDL increased significantly after metformin therapy in diabetic patients (Table-II).

Table-II: Serum lipid profile at admission and 60 days after metformin therapy

Serum lipid profile (mg/dl)	At admission Mean±SD	60 days after metformin therapy Mean±SD	P value
Total Cholesterol (TC)	192.55±52.21	182.50±51.84	<0.001
Low density lipoprotein (LDL)	110.99±28.11	100.93±28.09	<0.001
High density lipoprotein (HDL)	43.16±9.64	45.17±9.66	<0.001
Triglyceride (TG)	192.01±100.46	171.65±72.08	<0.001

Serum lipid level was classified using ATP III targets of serum lipid level in diabetes patients. Serum total cholesterol level at admission was desirable in 69%, borderline high in 14% and high in 17%. Sixty days after metformin therapy it was desirable in 77%, borderline high in 9% and high in 14% patients (Table-III).

Table-III: Serum total cholesterol level at admission and 60 days after metformin therapy

Total Cholesterol Level	At admission N (%)	60 days after metformin therapy N (%)
Desirable (<200 mg/dl)	207(69)	231 (77)
Borderline High (200–239 mg/dl)	42 (14)	27 (9)
High(≥240 mg/dl)	51 (17)	42 (14)

Serum LDL cholesterol level at admission was optimal in 51%, near optimal in 30%, borderline high in 8% and high in 11%. Sixty days after metformin therapy it was desirable in 57%, near optimal in 28.3%, borderline high in 11.3% and high in 3.3% patients (Table-IV).

Table-IV: Serum LDL cholesterol level at admission and 60 days after metformin therapy

LDL cholesterol Level	At admission N (%)	60 days after metformin therapy N (%)
Optimal (<100 mg/dl)	153 (51)	171 (57)
Near optimal/ above optimal (100–129 mg/dl)	90 (30)	85 (28.3)
Borderline high (130–159 mg/dl)	24 (8)	34 (11.3)
High (160–189)	33 (11)	10 (3.3)

Serum HDL level at admission was low in 53%, normal in 39% and high in 8%. Sixty days after metformin therapy it was low in 42%, normal in 47.7% and high in 10.3% patients (Table-V).

Table-V: Serum HDL cholesterol level at admission and 60 days after metformin therapy

HDL cholesterol Level	At admission N(%)	60 days after metformin therapy N(%)
Low (<40 mg/dl)	159(53)	126(42)
Normal (40 - 59 mg/dl)	117(39)	143(47.7)
High (≥60 mg/dl)	24(8)	31(10.3)

Serum TG level at admission was normal in 44%, borderline high in 35%, high in 16% and very high in 5% patients. Sixty days after metformin therapy it was normal in 52.3%, borderline high in 27.7% and high in 20% patients (Table-VI).

Table-VI: Serum TG level at admission and 60 days after metformin therapy

TG Level	At admission N(%)	60 days after metformin therapy N(%)
Normal (<150 mg/dl)	132 (44)	157 (52.3)
Borderline High (150–199 mg/dl)	105 (35)	83 (27.7)
High(200-499 mg/dl)	48 (16)	60 (20.0)
Very high (≥500 mg/dl)	15 (5)	0

Discussion:

Total 300 patients of type 2 diabetes mellitus were studied. Mean age of the study population was 45.65±11.51 years. Majority patients were aged more than 50 years (39%). Previous studies have shown that diabetes mellitus is more common among older patients. Islam[14] found a mean age of 46.81±9.98 years among 112 patients of type II diabetes mellitus. Imam[15] found that diabetic prevalence is higher in the age group >= 40 years which is more than twice as compared to age group < 40 years. Akter et al[16] recorded a mean age of 53.01±0.54 years among diabetes patients. Haque et al.[17] studied complications among diabetic patients. In their study the mean age of 400 patients was 55.18±11.24 years. Rana et al[18] found 51% patients aged more than 50 years in their study conducted in India.

Sex distribution of diabetes patients were nearly equal in this study. Among all, 52% patients were male and 48% patients were female. Akhter et al[19] found studied the prevalence of diabetes in a rural population of Bangladesh and found 468 male (55.9%) and 368 female (44.1%) female patients with diabetes, which roughly corresponds roughly with the findings of this study. But, in contrast to this study Chowdhury et al[20] and Bhowmik et al[21] found higher female prevalence of diabetes. Chowdhury et al[20] found 52.1% male diabetic patients and 47.9% female diabetic patients. Bhowmik et al[21] found 44.2% male and 55.8% female diabetic patients.

In this study majority patients were housewives (27%), followed by 25% doing non-government jobs and 22% businessman in second and third. Overall occupational status shows that most of the patients were doing activity requiring less physical work. Sitting idle decreases the work performance of large skeletal muscles in legs and back. Over the time course of a single day, physical inactivity may induce negative effects on relatively fast acting cellular processes in the skeletal muscles or other tissues. This may have chronic effects on the propensity to become overweight leading to diabetes.[22]

Majority patients came from higher income category and had a monthly income of 40000 BDT (30%). This corresponds with the findings of Chowdhury et al[20], Akter et al[16] and Islam[14]. Educated and wealthy individuals may be used to living in urban areas, consuming more fast food, and fatty foods, as well as participating less in physical exercise, which may be the important causes of being overweight and obese, prolonging the correlate of diabetes[23].

On admission mean fasting blood sugar was 8.69±0.22 mmol/l, mean 2HABF was 11.97±0.34 mmol/l and mean HbA1c was 8.08±1.77%. In comparison Bhowmik et al[21] found mean FBS of 9.5 mmol/l and mean 2HABF of 13.9 mmo/l among diabetic patients which is nearly similar to the findings of this study. Mean HbA1c was at admission was 8.00±1.83 among diabetic patients in the study by Lin et al[24] which concordant with the findings of this study.

Mean TC at admission was 192.55±52.21 mg/dl, mean LDL was 110.99±28.11 mg/dl, mean HDL was 43.16±9.64 mg/dl and mean TG was 192.01±100.46 mg/dl. In the study conducted by Bhowmik et al mean TC, LDL, HDL and TG was respectively 4.9mmol/l, 2.84mmol/l, 0.81mmo/l and 1.9 mmol/l which translates to respectively 189.48 mg/dl, 109.82mg/dl, 31.3mg/dl and 168.282 mg/dl. Which nearly-corresponds to the findings of this study.

All the patients were given metformin for 60 days. Sixty days after treatment with metformin significant improvement was noted across all categories of serum lipid profile in this study. TC, LDL and TG decreased significantly after 60 days of metformin therapy. HDL increased significantly after metformin therapy in diabetic patients. This findings is consistent with the findings of Lin et al[24] who gave three categories of treatment among diabetic patients with metformin (1000 mg/day to one group, 1500mg/day to another and 2000mg/day to the last group). They noted followed up patients at 6 months and 12 months after therapy. They noted improvement in lipid profile of all patients in all categories. They also concluded that metformin modifies serum lipid in a dosage- independent manner. Which implies that lower dose is adequate to achieve the lipid lowering effect of metformin in type 2 diabetes patients thus avoiding the side effect associated with higher dose.

Conclusion:

In this study people of fourth or fifth decade of age were frequently seek medical advice for diabetes mellitus. There is no male or female preponderance as both sex are almost equally in risk of DM. Educated populations and people from urban area were more concern about their follow up visits for DM. Incidence of DM didn't vary significantly with the economical status as poor, middle class and solvent are equally affected by DM . They commonly present with classical symptoms of diabetes mellitus. At the same time some are incidentally diagnosed as a case of DM during routine checkup on outdoor visit. Metformin has been introduced in all patients of newly detected diabetes mellitus apart from those who are not ideal candidate for metformin. Their base line lipid profile was significantly improved with metformin after a certain period . Metformin has a beneficial role in lipid profile in newly detected type 2 DM patients. However , further larger cohort study is needed to finalize the findings.

Limitation of the study:

This is a single center based study, sample size was not so big and long term follows up was not possible.

Recommendations:

Depending upon the study findings, following recommendations are suggested:

1. This findings could be used to design further randomized controlled trial
2. Type 2 DM patients should be prescribed metformin along with other drugs if not contraindicated

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