Original Article

Effect of Metformin on Lipid Level in Patients Presenting with Metabolic Syndrome

Qaisar Farooq[1], Muhammad Uthman[2], Amna Malik[3] and Farhan Fateh Jang[4]

ABSTRACT

Objective: To compare the mean lipid level with metformin versus control in patients presenting with metabolic syndrome.

Study Design: Randomized Control Trial Study

Place and Duration of Study: This study was conducted at the Department of Medicine, Shaikh Zayed Hospital, Lahore, from July, 2019 to January, 2020.

Methodology: After meeting the inclusion criteria 110 patients were enrolled. Informed consent and demographic information was taken. Then blood sample were sent to the laboratory of the hospital for assessment of lipid level including total cholesterol and triglycerides. Patients were randomly divided in 02 groups by using lottery method. In group A, patients were advised to take 1000 mg metformin twice daily for 3 months. In group B, patients were advised diet plan and patients were followed-up in out-patient department for 3 months. After 3 months, blood sample reports were assessed and levels were noted.

Results: The average age of the patients was 49.35±11.44 years, 69(62.73%). On post evaluation, in metformin group the average HDL of the patients was 43.26±6.64mg/dl while in control group the average HDL of the patients was 36.70±3.78mg/dl (p=<0.001) and decrease triglyceride level in metformin groups was noted on follow up.

Conclusion: Metformin is very useful and tolerable drug for the management of patients presenting with metabolic syndrome.

Keywords: Metformin, Metabolic Syndrome, Lipid Profile, HDL, Triglyceride

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INTRODUCTION

Metabolic syndrome is a medical condition that is a group of the following five conditions, at least presence of three: central obesity, hypertension or high blood pressure, diabetes or hyperglycemic level, dyslipidemia or high tri-glycerides but low high-density lipoprotein concentration in blood. It is a severe risk factor for macrovascular events and for the onset of diabetes too.[1,2] In Pakistan, Metabolic Syndrome was present in 83% of the study population, 43% were male and 57% were female.[3] Metformin is preferred as first-line treatment protocol and is usually prescribed by practitioners for oral treatment for type 2 diabetes mellitus.

[1.] Department of Medicine, Shaikh Zayed Hospital, Lahore.
[2.] Department of Medicine, Shaikh Zayed Federal Post Graduate Medical Institute, Lahore.
[3.] Department of Neurology / Neurosurgery[4], Sharif Medical and Dental College, Lahore.

Correspondence: Dr. Qaisar Farooq, Trainee Registrar, Shaikh Zayed Hospital, Lahore.
Contact No: 0302-8429970
Email: qaisarfarooqs@gmail.com

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But, the primary action and mechanism of metformin is not completely understood.[4] Regardless of use of metformin, as an anti-hyperglycemic agent for >50 years, the main key role of mechanism of metformin action is incompletely studied.[5] Clinical trials have pointed out that metformin might lower total lipids. Also it augments the lipid lowering effects of HMG-Co A inhibitors if prescribed to new onset type 2 diabetic patients.[6] Another lipid lowering effect of metformin is via activation of protein kinase pathway.[4,7]

One randomized trial found that the mean HDL and triglycerides were significantly lowered in the metformin than control group i.e. triglycerides 210.74±19.77mg/dl in metformin and 219.27±9.52 mg/dl with control (p=0.036) and HDL 45.65±6.14 mg/dl with metformin and 38.56±10.42mg/ dl with control (p=0.007).[8]

MATERIALS AND METHODS

This randomized controlled trial study was done in the Department of Medicine, Shaikh Zayed Hospital Lahore from 30-7-2019 to 30-1-2020. 110 cases; 55 cases in each group is calculated with 95% confidence interval, 80% power of study and taking magnitude of mean triglycerides level i.e. 210.74±19.77mg/dl with metformin and 219.27±9.52mg/dl without metformin. Patients of age 30-70years of either gender presenting

with metabolic syndrome for >1 year were included. Diabetic patients taking anti-glycemic other than metformin (on medical record), hyperprolactinemia (prolactin >30ng/ml) and thyroid dysfunction (TSH>5IU/mL), chronic or uncontrolled diabetes (HbA1c>8%), crushing syndrome, congenital adrenal hyperplasia and already taking statins for dyslipidemia were excluded.

110 patients (55 in each group), fulfilled selection criteria were included from the OPD, Department of Medicine. After taking informed consent, demographic data (name, age, sex, BMI and duration of symptoms) was recorded. Then blood sample was obtained in a 5cc BD syringe and stored in sterile vials. All samples were sent to laboratory for lipid level including HDL cholesterol and triglycerides and test done on machine, Beckman coulter it has chemiluminescence in it and for calibration spectrophotometry is used. Reports were assessed and levels were noted. Then patients were randomized in two groups. In group A, patients were advised to take 1000 mg metformin twice daily for 3 months. In group B, patients were advised diet plan and patients were followed-up in OPD for 3 months. After 3 months, blood sample was again obtained in a 5cc BD syringe and stored in sterile vials. All samples were sent to the laboratory for assessment of lipid level including HDL cholesterol and triglycerides. Reports were assessed and levels were noted.

RESULTS

The average age of the patients was 49.35±11.44 years with minimum and maximum ages of 30 & 70 years respectively. In metformin group the average age of the patients was 49.87±11.36 years whereas in control group the average age of the patients was 48.84±11.59 years (Table 1). Among 110 patients 69(62.73%) patients were male while 41(37.27%) patients were females**.** Among metformin group the 40(58%) patients were male and 15(36.6%) patients were females, similarly in control group 29(42%) patients were male and 26(63.4%) patients were females (Table 2). The mean duration of symptoms was 3.09±1.55 years with minimum and maximum duration of 1 & 5 years respectively.

Among metformin group the average duration of symptoms of the patients was 3.07±1.61 years while in control group the average duration of symptoms of the patients was 3.11±1.51 years**.** The mean BSR level of the patients was 158.94±10.85mg/dl with minimum and maximum values of 134.86 & 185.33mg/dl respectively. In metformin group the average BSR level of the patients was 159.01±10.06mg/dl and in control group the average BSR level of the patients was 158.86±11.67mg/dl. Statistically insignificant difference found between the BSR level and the study groups. i.e. p=0.941 (Table 3). On pre evaluation the average HDL level of the patients was 35.75±4.94mg/dl while on post follow up the average HDL level of the patients was 39.98±6.31mg/dl. Statistically significant difference was found between the pre and post evaluation of the HDL. i.e. p=<0.001 (Table 4).

Similarly, on post evaluation, in metformin group the average HDL of the patients was 43.26±6.64mg/dl while in control group the average HDL of the patients was 36.70±3.78mg/dl (p=<0.001) (Table 5). On pre evaluation the average triglyceride of the patients was 221.00±10.51mg/dl while on follow up the average triglyceride level of the patients was 216.32±12.67 mg/dl. On pre evaluation, in metformin group the average triglyceride of the patients was 219.52±10.44mg/dl while in control group the average triglyceride of the patients was 222.48±10.45mg/dl (p=0.141).

There is statistically significant difference was found in post evaluation of HDL & triglyceride of the patients between study groups stratified by age i.e. p=<0.05 (Table 6).There is statistically significant difference was found in post evaluation of HDL & triglyceride of the patients between study groups stratified by gender i.e. p=<0.05 (Table 7).There is statistically significant difference was found in post evaluation of HDL & triglyceride of the patients between study groups stratified by duration of symptoms i.e. p=<0.05 (Table8)**.**There is statistically significant difference was found in post evaluation of HDL & triglyceride of the patients between study groups stratified by BSR level i.e. p=<0.05 (Table 9).

Table No.1: Summary statistics of age (years) between study groups

		Study Groups	
		Metformin	Control
Age (years)	N	55	55
	Mean	49.87	48.84
	SD	11.36	11.59

Table No.2: Frequency distribution of gender between study groups

Gender	Study Groups		Total
	Metformin	Control	
Male	40	29	69
	58.0%	42.0%	100.0%
Female	15	26	41
	36.6%	63.4%	100.0%

Table No.3: Comparison of BSR (mg/dl) between study groups

		Study Groups		P value
		Metformin	Control	
BSR (mg/dl)	N	55	55	0.941
	Mean	159.01	158.86	
	SD	10.06	11.67	

Table 4: Pre and post follow up comparison of HDL (mg/dl)

		n	Mean	SD	P value
HDL (mg/dl)	Pre	110	35.75	4.94	<0.001
	Post	110	39.98	6.31	

Table No.5: Pre and post follow up comparison of HDL (mg/dl) between study groups

HDL	Study Groups	n	Mean	SD	P value
Pre	Metformin	55	35.80	5.95	0.921
	Control	55	35.71	3.73	
Post	Metformin	55	43.26	6.64	<0.001
	Control	55	36.70	3.78	

Table No.6: Pre and post follow up comparison of HDL (mg/dl) & triglyceride (mg/dl) between study groups stratified by age

Age (years)		Study Groups	Mean	SD	P value
≤ 50	Pre HDL	Metformin	36.33	5.77	0.599
		Control	35.73	3.02	
	Post HDL	Metformin	44.26	6.29	<0.001
		Control	35.92	3.64	
>50	Pre HDL	Metformin	35.28	6.19	0.813
		Control	35.67	4.73	
	Post HDL	Metformin	42.27	6.93	0.008
		Control	37.97	3.74	
≤ 50	Pre TG	Metformin	218.39	10.75	0.093
		Control	222.77	9.29	
	Post TG	Metformin	210.78	7.53	<0.001
		Control	222.79	11.42	
>50	Pre TG	Metformin	220.61	10.21	0.67
		Control	222.01	12.33	
	Post TG	Metformin	207.82	10.93	<0.001
		Control	224.29	11.97	

Table No.7: Pre and post follow up comparison of HDL (mg/dl) & triglyceride (mg/dl) between study groups stratified by gender

Gender		Study Groups	Mean	SD	P value
Male	Pre HDL	Metformin	35.98	6.36	0.615
		Control	35.35	2.79	
	Post HDL	Metformin	43.21	6.40	<0.001
		Control	36.03	3.70	
Female	Pre HDL	Metformin	35.32	4.86	0.604
		Control	36.11	4.57	
	Post HDL	Metformin	43.38	7.47	0.010
		Control	37.46	3.79	
Male	Pre TG	Metformin	219.42	11.15	0.685
		Control	220.54	11.32	
	Post TG	Metformin	209.28	9.62	<0.001
		Control	222.21	10.79	
Female	Pre TG	Metformin	219.77	8.60	0.101
		Control	224.64	9.12	
	Post TG	Metformin	209.25	9.29	<0.001
		Control	224.66	12.42	

Table No.8: Pre and post follow up comparison of HDL (mg/dl) & triglyceride (mg/dl) between study groups stratified by duration of symptoms

Duration of symptoms		Study Groups	Mean	SD	P value
≤ 3	Pre HDL	Metformin	36.02	5.75	0.771
		Control	35.68	2.66	
	Post HDL	Metformin	43.81	5.43	<0.001
		Control	35.95	3.70	
>3	Pre HDL	Metformin	35.55	6.28	0.908
		Control	35.73	4.76	
	Post HDL	Metformin	42.64	7.84	0.006
		Control	37.60	3.75	
≤ 3	Pre TG	Metformin	221.18	9.57	0.749
		Control	220.29	11.58	
	Post TG	Metformin	209.77	9.08	<0.001
		Control	221.62	11.43	
>3	Pre TG	Metformin	217.67	11.23	0.010
		Control	225.11	8.40	
	Post TG	Metformin	208.72	9.99	<0.001
		Control	225.47	11.57	

Table No.9: Pre and post follow up comparison of HDL (mg/dl) & triglyceride (mg/dl) between study groups stratified by BSR level

BSR (mg/dl)		Study Groups	Mean	SD	P value
≤ 150	Pre HDL	Metformin	39.08	4.39	0.058
		Control	35.98	3.20	
	Post HDL	Metformin	47.07	4.68	<0.001
		Control	36.48	3.33	
>150	Pre HDL	Metformin	34.98	6.05	0.563
		Control	35.62	3.90	
	Post HDL	Metformin	42.30	6.75	<0.001
		Control	36.77	3.95	
≤ 150	Pre TG	Metformin	222.81	8.80	0.768
		Control	224.05	11.06	
	Post TG	Metformin	208.54	7.00	0.001
		Control	227.19	14.55	
>150	Pre TG	Metformin	218.69	10.74	0.151
		Control	221.99	10.35	
	Post TG	Metformin	209.46	10.03	<0.001
		Control	222.18	10.37	

DISCUSSION

Metabolic syndrome is a worldwide health problem affecting both developed and under developed societies. It's a syndrome with increased risk of diabetes and cardiovascular disease. Studies report varied gender based effects on metabolic syndrome. In USA, metabolic syndrome is more prevalent in white males. In Korea, Iran, India, Oman, the syndrome is more prevalent in women than their sexual counterparts. The reason may be sedentary lifestyle of women residing theres.[9] The pharmacological key to the treatment of this entity along with non-pharmacological measures, is Metformin that owing toits insulin-sensitizer effect decreases serum leptin levels and thus reduces body weight and waist circumference.[9]

In this study serum triglyceride level was significantly decreased after the treatment with metformin while HDL of the patients significantly increased as compared to control. MourAo et al[10] studied metformin in metabolic syndrome .They documented a significant reduction (P <0.05)in cholesterol (229.0±29.5 to 214.2±25.0mg/dL),BMI (30.7±5.4 to 29.0±4.0kg/m2), waist circumference (124.6±11.7 to 117.3 ± 9.3cm), and decreased daily dose of insulin. Some authors proved reduction of total cholesterol and TG with an increase of HD with the use of metformin[11] even in non-diabetic patients[13] while others differ.[12]

One randomized trial found that the mean HDL and triglycerides were significantly lowered in the metformin than control group i.e. triglycerides 210.74±19.77mg/dl in metformin and 219.27±9.52mg/dl with control (p=0.036) and HDL 45.65±6.14mg/dl with metformin and 38.56±10.42mg/dl with control (p=0.007).[8]One study documented that the Metformin therapy significantly lowered; blood glucose levels ±SD) 227.2±37.5 to 168.6±20.5mg/dl (p<0.001) and triglycerides ±SI) 195.9±31.9 to 174.2±26.6mg/dl, P<0.01),while HDL increased ±SD) 37.7±5.1 to 39.5±4.9mg/dl, (P < 0.01) but conflictingly there was no change in BMI.[14]

Studies demonstrated that metformin was found to have pronounced beneficial effects in type 2 obese diabetic patients. Serum lipoproteins, body mass index,fasting blood sugar,triglycerides and HDL as compared to SU therapy.[15,16]

Shirin et al[9] also wrote that anthropometric measurements, fasting blood sugar, HbA1C, serum lipid profiles and lipoprotein ratio (LDL/HDL) showed a significant decrease after treatment with metformin (P <0.05).Contrary with ours, some authors reported reduction only in total cholesterol levels.[17,18]

CONCLUSION

Metformin is very useful and tolerable drug for the management of patients presenting with metabolic syndrome, it significantly decrease the serum triglyceride level of the patients and increase the HDL level of the patients on follow up.

Author's Contribution:

Concept & Design of Study:	Qaisar Farooq
Drafting:	Muhammad Uthman
Data Analysis:	Amna Malik and Farhan Fateh Jang
Revisiting Critically:	Qaisar Farooq, Muhammad Uthman
Final Approval of version:	Qaisar Farooq

Conflict of Interest: The study has no conflict of interest to declare by any author.

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