Synchronizing positive effect of vitamin C and chromium on hyper lipidemia, hyperglycemia, liver enzymes and BMI of diabetes mellitus type 2 patients

Neelam Sabar[1], Muhammad Imran Hussain[1], Hajra Saleem[2], Moha Akram Khan[3] Huba Khalid[1], Zartashia Kanwal[1] and Amber Yaseen[1]

[1]Riphah International University, Lahore, Pakistan
[2]Iqra Medical Complex, Lahore, Pakistan
[3]Rashid Latif Medical College, Lahore, Pakistan

Abstract: This study investigates the combined effect of vitamin C and chromium on BMI, lipid profile, LFTs and HbA1c of Diabetes Mellitus type 2 patients. This is randomized controlled trial study. For this study a total of 60 patients (n=28 female, n=32 male) Diabetes Mellitus type 2 patients were selected. They were divided into treatment group (vitamin C (500mg) Chromium (200µg) and control group (placebo) comprising thirty patients per group. Mean age in control group and treatment group is 33± 5.729 and 33±7.017 respectively. Statistical analysis showed significant results of lipid profile; total cholesterol (mg/dl) 198±66.1 P=0.008, High-Density Lipoprotein 38±7.5, P<0.001, Low Density Lipoprotein (LDL) (mg/dl) 105.1±22.4, P=0.002 and Triglycerides 191±64.3, P=0.02 are respectively. Levels of serum ALT (u/l) (34.7±9.1, P<0.001) and AST (u/l) (31.6 ±8.6, P<0.001) were significantly lower as compared to control group. HbA1c percentages were also normalized (5.45±0.2, P<.001) as compared to group 2. BMI values were also improved (P=0.01) after treatment. Combined supplementation of vitamin C and chromium reduce the plasma lipid percentage, blood glucose levels and also improve the ALT and AST functions.

Keywords: Vitamin C, chromium picolinate, lipid profile, diabetes mellitus type 2, HbA1c, AST, ALT.

INTRODUCTION

Diabetes mellitus is a prolonged health problem of all age groups, both genders, involves villages and town areas and emerging and industrialized republics worldwide (Al-Salameh *et al.* 2019). According to survey percentage of diabetes mellitus type two in Pakistan noted as eleven percent. Ratio in Punjab was noted as twelve percent in males and nine percent in females (Aamir *et al.*, 2019). International researches concluded that diet can change the risk factors of diabetes such as higher level of cholesterol and sugar in blood stream (Kebbe *et al.*, 2021). Physiological stress that exerts by free radicals of oxygen species, show main role in the commencement of diabetes mellitus plus arterial and brain diseases (El Sheikh *et al.* 2019). Many studies proved that taking antioxidants reduce the risk of chronic illnesses such as type two diabetes mellitus. Jiang *et al.* 2021). According to a study, vitamin C showed remarkable results (P<0.05) by lowering serum glucose levels, lower ranges of BMI as compared to control. In this study vitamin C group showed reduction in damage of pancreatic beta cell, also minimize the fasting sugar levels (P<0.05) and reduce complications related to DMT2 (Namkhah *et al.*, 2021). Ascorbic acid also known as well-known protector from various risk factors of diabetes such as vision problems (retinopathy), higher concentration of LDL and cholesterol and endothelial malfunctions (Dludla *et al.*,

2022). A study that conducted to check vitamin C effect on blood glucose level, revealed reduction in glucose concentration (P=0.02) in diabetic patients. Furthermore, vitamin C supplementation induced a greater reduction (P =0.02) of glucose levels (Ashor *et al.*, 2017).

Chromium picolinate is a supplemental form of chromium that gave to diabetes patient because it shows extra ordinary effects in glucose metabolism (Vincent *et al.*, 2017). Major role of Chromium is to increase binding capacity of insulin to the cell, enhance receptor number of insulin and speedup the activity of insulin receptor kinase that rise the sensitivity level of insulin receptor (Król *et al.*, 2020). Mechanism behind chromium control on insulin receptors is totally around about tyrosine kinase activity which is regulated by chromium binding protein (Chromodulin) (Vincent *et al.*, 2019). Lack of chromium leads to enhance plasma sugar, LDL, TC (total cholesterol) and triglycerides and reduced the amount of good cholesterol (HDL) and functions of insulin receptors either person is on normal diet (Sundaram *et al.*, 2012). A scientific study reported positive effect of chromium experimented on rats. After giving chromium, blood sugar levels of diabetic rats reduced (P=0.05) significantly. Oral antidiabetic drugs rate in treatment group was lesser (p< 0.05) as compared to control group (Ngala *et al.*, 2018). Another study that was conducted on DMT2 patients by giving chromium to check effect on lower density lipoprotein and high-density lipoprotein showed

Corresponding author: neelamsabar066@gmail.com

significantly reduction p<0.05 in triglycerides and total cholesterol plus LDL as compared to placebo group. Serum HbA1c percentages also reduced (P<0.001) by administering chromium (Rafighi Z *et al*., 2021).

With the best of the researcher's knowledge, various studies have been conducted on effect of vitamin C on diabetes as hypoglycemic and lowering blood cholesterol level. Many studies have been done to check out the effect of chromium on hyperglycemia and lipid profile in diabetes mellitus type 2. This study aims to find the more effective results of combine supplementation of Vitamin C and chromium given to the diabetes mellitus type 2 patients. As it is a clinical trial that will clearly show the better effects of both interventions.

MATERIALS AND METHODS

This study was performed in District Head Quarter Hospital Sheikhupura from February 2023 to May 2023. The sample size was calculated from the online calculator Raosoft. (Raosoft 2020) The study sample size was 60. Selected subjects for this study were divided into two groups i.e., 1) *Treatment group:* This group received metformin (Glucophage-500mg) BID as well as Vitamin C (500mg) and Chromium (200µg) QD. 2) *Control group:* This group received metformin (Glucophage-500mg) BID as well as placebo capsules STARCH QD.

Inclusion criteria
- Newly diagnosed patients suffering with diabetes mellitus type 2
- Age group will be 25-50
- Who were willing to be a part of this research
- Either consuming antidiabetic and antihyperlipidemic drugs

Exclusion criteria
- Having disease other than diabetes with hyperlipidemia (renal issues, hepatic disorder)
- Having history of any physical injury
- Having history of any psychological disorder
- Having addiction of smoking and alcohol abusing

Data collection procedure
1. Verbal and written consent was obtained from each participant.
2. The laboratory findings of the study participant were communicated with the responsible clinician assigned.
3. The parameters of anthropometric measurements which were used include weight in (kg) and height in (feet). Further lipid profile, HbA1c and LFTs tests performed.
4. For blood collection to perform HbA1c, LFT'S and lipid profile, blood was collected with care and adequate safety precautions to ensure test results will reliable, contamination of the sample was avoided and

infection from blood transmissible pathogens was prevented. Protective gloves were worn when collecting and handling of blood samples had done. Lancets, needles and syringes were sterilized (Cheesbrough *et al*., 2018).

Ethical approval
The study was approved by Research and Ethics committee of Riphah International University, Lahore. (No. REC/RCR & AHS/22/0806)

STATISTICAL ANALYSIS

The data was analyzed through different statistical tests by using SPSS 26.0 statistical software. A paired t-test was used to compare the mean of quantitative variables with normal distribution in each group between the beginning and the end of the study. The t-test was used to compare the mean between the two groups at the beginning and end of the study. A repeated ANOVA test was used for the variables measured two times during the study. Data were presented as mean±SD and p<0.05 was considered as level of significance.

RESULTS

This study is conducted with the aim to compare pre and post lipid profile (LP) (HDL+ LDL+ Triglycerides+ Total Cholesterol+ Total Fats), Liver Functions Test (LFT's) and HbA1c of Diabetes Mellitus Type 2 patients by giving Chromium Picolinate (200µg) and Vitamin C (500mg).

Baseline values of selected subjects
Number of samples in both groups is N=60, participants including 30 (50%) control group (Group 2) and remaining 30 (50%) were in treatment group (Group 1). Results revealed that mean age in control group and treatment group is 33± 5.729 and 33±7.017 respectively. Mean difference of age is 0.566±1.653. Serum samples were collected of 60 subjects that were enrolled in this study for 45 days. This serum collection further used for laboratory testing including LP, LFT's and HbA1c. Average values of lipid profile including TC, HDL, LDL, TGL for treatment and control groups were 221, 33, 116, 202 and 221, 31, 120 and 224 (mg/dl) respectively (table 1). Values for Alt and AST for treatment and control group were 40, 36.4, 44 and 40.3 (u/l) respectively.

Effect of vitamin C and Chromium on lipid profile
Post values of each group shown significant results. Group 1 indicates treatment group and group 2 indicates control group. Follow-up results for lipid profile are: TC 1(198±66.1)], [group 2 (238.3±46.3)] -p =0.008; HDL [group 1 (38±7.5)], [group 2(30.5±7.9)]-p<0.001; LDL [group 1 (105±22.4)], [group 2 (122.1 ±18.3)] -p =0.002 and TGL [group 1(191± 64.3)], [group 2 (231.7± 68.8)] -p =0.02 (table 2).

Table 1: Baseline features for biochemical parameters

Parameters	Groups (n=60)	
	Control	Treatment
	Mean ± SD	Mean ± SD
TC (mg/dl)	221.4±48.0	221.4±64.0
HDL (mg/dl)	31.8±8.2	33.3±8.3
LDL (mg/dl)	120.5±19.1	116.5±21.5
TGL (mg/dl)	224.1±66.8	202.1±63.8
ALT (u/l)	44±7.5	40±9.2
AST(u/l)	40.3±8.0	36.4±9.3
HbA1c (%)	9.5±2.7	10.05±2.6
BMI (kg/m^2)	28.7±4.8	29±4.8

TC: Total cholesterol, HDL: High-Density Lipoprotein, LDL: Low-Density Lipoprotein, TGL: Triglycerides, HbA1c: glycated hemoglobin, BMI: Body Mass Index

Table 2: Therapeutic effect of vitamin C and Chromium on Lipid profile, Liver enzymes, HbA1c and BMI of DMT2 patients.

Biochemical parameter	Groups	Before treatment	After treatment
		Mean ± SD	Mean ± SD
TC (mg/dl)	Control	221.4±48.0	238.3±46.3
	Treatment	221.4±64.0	198±66.1
HDL (mg/dl)	Control	31.8±8.2	30.5±7.9
	Treatment	33.3±8.3	38±7.5
LDL (mg/dl)	Control	120.5±19.1	122.1±18.3
	Treatment	116.5±21.5	105.1±22.4
TGL (mg/dl)	Control	224.1±66.8	231.7±68.8
	Treatment	202.1±63.8	191±64.3
ALT (u/l)	Control	44±7.5	46.9±6.9
	Treatment	40±9.2	34.7±9.1
AST(u/l)	Control	40.3±8.0	42.2±7.3
	Treatment	36.4±9.3	31.6±8.6
HbA1c (%)	Control	9.5±2.7	9.9±2.2
	Treatment	10.05±2.6	5.45±1.2
BMI (kg/m^2)	Control	28.7±4.8	29±4.4

*Post TC $p=0.008 < 0.05$, post HDL $p=0.03 < 0.05$, post LDL $p=0.002 < 0.05$, post TGL $p=0.02 < 0.05$

Therapeutic effect of vitamin C and Chromium on LFTs
After duration of therapeutic period of vitamin C and chromium showed remarkable results on liver enzymes ALT and AST (table 2). Treatment group showed significant reduction in values of AST from 36 to 31 (P<0.001) and ALT from 40 to 34.7 (P<0.001) u/l respectively.

Positive effect of vitamin C and Chromium on HbA1c
Combination of vitamin C and chromium supplementation significantly reduced values of glycated sugar percentages of diabetes mellitus type 2 patients (table 2). Post treatment HbA1C (%) result for treatment group was from 10% to 5.45% (P<0.001) as compared to control group from 9.5 to 9.9.

Effect of vitamin C and Chromium on BMI
The BMI of participants was significantly reduced (P=0.002) through combined supplementation of vitamin C and Chromium (table 2). In the control group, BMI was not significantly reduced whereas the highest reduction was observed in the treatment group from 29 to 26 kg/m ^{2}.

DISCUSSION

In the present study, combined effect of vitamin C and chromium on HbA1c, lipid profile (LP) and LFT's were analyzed for forty-five days. This study concluded that 500mg of vitamin C and 200 microgram chromium supplementation significantly reduced the values for LP, HbA1c, Liver enzymes and BMI in treatment group as compared to control. International researches concluded that diet can change the risk factors of diabetes such as higher level of cholesterol and sugar in blood stream (Kebbe *et al.*, 2021).

In current study Vitamin C reduced percentages of HbA1c from 10% to 5.45% that similar to a study of 12-weeks on 70 diabetic patients who were divided randomly into placebo and vitamin C (500mg) group. According to

intervention there was significant output by lowering HbA1c levels after 12 weeks of treatment with vitamin C (Dakhale, *et al.*, 2011). Chromium shows extra ordinary effects in glucose metabolism, lack of chromium leads to enhance plasma sugar, LDL, TC (total cholesterol), and triglycerides and reduced the amount of good cholesterol (HDL) and functions of insulin receptors either person is on normal diet (Sundaram *et al.*, 2012),(Vincent *et al.*, 2017). The results of our present study were consistent with a previous study that Conducted for 15 weeks to check HbA1c levels after using chromium picolinate. Results of their study showed significant reduction in the serum levels of HbA1C. CrPic can recover the function of B-cells and maintained the levels of HbA1c for T2DM rats (Huang S. *et al.*, 2014).

Combined usage of vitamin C and chromium gave parallel result to a 3 months study that show significant decrease in TG, LDL, cholesterol (Rafighi, *et al.*, 2011). Results of current study showed reduction in LDL from 116 to 105, TC from 221 to 198 and TGL from 202 to 191 mg/dl in treatment group compared to control. Levels of HDL increased from 33 to 38mg/dl after therapeutic period that disclosed the consent with 4 months controlled, single blind, randomized trial on 71 patients with T2DM in which increased serum chromium concentrations were significantly lowered total cholesterol and LDL-c, comparing pre- and post-treatment period, in the control group (Paiva, *et al.*, 2015). Administration of vitamin C and chromium induced a significant reduction in serum AST, ALT levels along with reducing oxidative stress induced by hepatotoxicity. Present article showed significant reduction in liver enzymes ALT (40 to 34) and AST (36 to 31) u/l that showed similarity with the studies that conducted for chromium and vitamin C supplementation on diabetes mellitus type 2 patients, this supplementation reduces liver damage including liver damage markers aspartate transaminase (AST) and alanine aminotransferase (ALT) elevation, and liver enlargement (Gonçalve, *et al.*, 2022), (Li, *et al.*, 2022).

Higher vitamin C and chromium consumption was significantly associated with lower BMI. (Namkhah *et al.*, 2021). Combination of vitamin C and chromium significantly reduced BMI for treatment group. body mass index significantly dropped from 29 to 26 kg/m2 in treated group as compared to placebo. There were no significant differences in BMI values for control group but serum vitamin C levels were significantly higher in subjects of treatment group in comparison with placebo that showed parallel result to a study on 17 diabetic participants who underwent vitamin C depletion and they were given a vitamin C dose range of 15-1250 mg daily. That supplementation showed positive effect on lowering BMI and obesity rate for diabetes patients (Ebenuwa I, *et al.*, 2022). Previous literature and studies support the

findings of the current study that vitamin C and chromium supplementations significantly improved the lipid profile, HbA1c, liver enzymes and BMI of participants. As discussed previously there is no study that evaluated the combined effects of these two essential nutrients. The present study presents the highest improvement in the lipid profile, HbA1c, liver enzymes of participants who were examined in the treatment group (vitamin C and chromium).

CONCLUSION

This study gives brief results about two nutrient supplements that exhibit significant effect on diabetic patient's lipid profile, blood glucose and liver function tests. The observation stated about significant glucose reduction plus improvement in impaired insulin action. Enhance insulin sensitivity that cause reduction in weight and eventually minimize BMI ranges. These results support the use of a 500mg Vitamin C and 200microgram Chromium picolinate as a convenient to improve insulin resistance, HbA1c, LFT's and LP.

REFERENCES

Aamir AH, Ul-Haq Z, Mahar SA, Qureshi FM, Ahmad I, Jawa A and Heald AH (2019). Diabetes prevalence survey of Pakistan (DPS-PAK): Prevalence of type 2 diabetes mellitus and prediabetes using HbA1c: A population-based survey from Pakistan. *BMJ Open,* **9**(2): e025300.

Al-Salameh A, Chanson P, Bucher S, Ringa V and Becquemont L (2019, February). Cardiovascular disease in type 2 diabetes: A review of sex-related differences in predisposition and prevention. *In*: Mayo Clinic Proceedings, **94**(2): 287-308.

Ashor AW, Werner AD, Lara J, Willis ND, Mathers JC, and Siervo M (2017). Effects of vitamin C supplementation on glycaemic control: A systematic review and meta-analysis of randomised controlled trials. *Eur. J. Clin. Nutr.,* **71**(12): 1371-1380.

Cheesbrough M (2018). District laboratory practice in tropical countries. *IJMS,* **1**(1): 65-68.

Dakhale GN, Chaudhari HV and Shrivastava M (2011). Supplementation of vitamin C reduces blood glucose and improves glycosylated hemoglobin in type 2 diabetes mellitus: A randomized, double-blind study. *Adv. Pharmacol. Sci.,* **2011**: 195271.

Dludla PV, Nkambule BB, Nyambuya TM, Ziqubu K, Mabhida SE, Mxinwa V and Tiano L (2022). Vitamin C intake potentially lowers total cholesterol to improve endothelial function in diabetic patients at increased risk of cardiovascular disease: A systematic review of randomized controlled trials. *Front. Nutr.,* **9**: 2524.

Ebenuwa I, Violet PC, Padayatty S, Wang Y, Wang Y, Sun H, Adhikari P, Smith S, Tu H, Niyyati M, Wilkins K (2022). Abnormal urinary loss of vitamin C in

diabetes: prevalence and clinical characteristics of a vitamin C renal leak. *Am. J. Clin. Nutr.,* **116**(1): 274-284.

El Sheikh WM, Alahmar IE, Salem GM and El-Sheikh M A (2019). Tumor necrosis factor alpha in peripheral neuropathy in type 2 diabetes mellitus. *EJNPN,* **55**(1): 1-7.

Gonçalve GM, Barros PP, da Silva GH, Watanabe JF and de Camargo Eisinger AB (2022). Interaction of Carthamus oil, chromium picolinate and glyburide in blood glucose and its impact on liver enzymes and lipid profile in diabetes-induced rats. *Rev. Colomb. Cienc. Quim. Farm.,* **51**(1): 230-242.

Huang S, Peng W, Jiang X, Shao K, Xia L, Tang Y and Qiu J (2014). The effect of chromium picolinate supplementation on the pancreas and macroangiopathy in type II diabetes mellitus rats. *J. Diabetes Res*., **2014**: 717219.

Jiang YW, Sun ZH, Tong WW, Yang K, Guo KQ, Liu G, and Pan A (2021). Dietary intake and circulating concentrations of carotenoids and risk of type 2 diabetes: A dose-response meta-analysis of prospective observational studies. *Adv. Nutr.,* **12**(5): 1723-1733.

Kebbe M, Gao M, Perez-Cornago A, Jebb SA and Piernas C (2021). Adherence to international dietary recommendations in association with all-cause mortality and fatal and non-fatal cardiovascular disease risk: A prospective analysis of UK Biobank participants. *BMC Medicine,* **19**: 1-9.

Król E, Krejpcio Z, Okulicz M and Smigielska H (2020). Chromium (III) glycinate complex supplementation improves the blood glucose level and attenuates the tissular copper to zinc ratio in rats with mild hyperglycaemia. *Biol. Trace Elem. Res.,* **193**: 185-194.

Li R, Guo C, Lin X, Chan TF, Su M, Zhang Z and Lai KP (2022). Integrative omics analysis reveals the protective role of vitamin C on perfluorooctanoic acid-induced hepatoxicity. *J. Adv. Res.,* **35**: 279-294.

Namkhah Z, Ashtary-Larky D, Naeini F, Clark CC and Asbaghi O (2021). Does vitamin C supplementation exert profitable effects on serum lipid profile in patients with type 2 diabetes? A systematic review and dose-response meta-analysis. *Pharmacol. Res.,* **169**: 105665.

Ngala RA, Awe MA and Nsiah P (2018). The effects of plasma chromium on lipid profile, glucose metabolism and cardiovascular risk in type 2 diabetes mellitus. A case-control study. *PloS One,* **13**(7): e0197977.

Paiva AN, de Lima JG, de Medeiros AC, Figueiredo HA, de Andrade RL, Ururahy MA, Rezende AA, Brandão-Neto J and Almeida MD (2015). Beneficial effects of oral chromium picolinate supplementation on glycemic control in patients with type 2 diabetes: A randomized clinical study. *J. Trace Elem. Med. Biol.,* **32**: 66-72.

Rafighi Z, Arab S, Yusof RM and Shiva A (2011). The effect of vitamin C and E on lipid profile in people with type 2 diabetes mellitus. *Glob. J. Health Sci.,* **3**(2): 69.

Sundaram B, Singhal K and Sandhir R (2012). Ameliorating effect of chromium administration on hepatic glucose metabolism in streptozotocin induced experimental diabetes. *Biofactors,* **38**(1): 59-68.

Vincent JB (2017). New evidence against chromium as an essential trace element. *J. Nutr.,* **147**(12): 2212-2219.

Vincent JB, Neggers Y and McClung J (2019). Roles of Chromium (III), Vanadium, Iron and zinc in sports nutrition. *In*: Nutrition and Enhanced Sports Performance. Academic Press, pp.653-664.