Journal of Food and Nutrition Research, 2016, Vol. 4, No. 8, 535-542
Available online at http://pubs.sciepub.com/jfnr/4/8/8

DOI:10.12691/jfnr-4-8-8

Effect of Chromium Picolinate Supplementation on Diabetic Profile and Nutritional Status of the Type-2 Diabetic Adult Population – A Randomized Controlled Trial

Hajra Ahmad[1], Zaheer Ahmed[1,*], Rezzan Khan[2]

[1]Department of Home & Health Sciences, Allama Iqbal Open University Islamabad, Pakistan
[2]Consultant Nutritionist, Shifa International Hospital, Sector H-8/4, Islamabad, Pakistan
*Corresponding author: zaheer_863@yahoo.com

Abstract The health impacts of Chromium Picolinate (CrP) have been searched by various researchers particularly focused on management of Type-2 Diabetes Mellitus (T2DM) with the conflicting results. The objective of the present study was to investigate the role of CrP on management of T2DM. It was a randomized controlled trial (RCT). Two groups of newly diagnosed Type -2 diabetics between the age brackets of 40-65 years were randomly selected from diabetes clinic. One group was exposed to 200 µg of CrP per day and the other was given a capsule of inert material as placebo having no impact on diabetic profile. The intervention duration was 03 months followed by one month as washout period. The outcome variables were biochemistry related to diabetic profile, clinical signs symptoms and toxicity if any. Dietary profile and anthropometrics were used for nutritional assessment. The study revealed that 82.7% of the subjects had family history of diabetes among which 59.6% were close relative. 98.1% were suffering from some kind of stress. Diabetic profile such as FPG, HbA1c and insulin levels improved in terms of normality after three months in treatment group, but did not come to the normal acceptable range e.g. The FPG dropped from142.85±17.71 to 130.42±32.68 mg/dl with a significant P value of 0.003 within the phases. Other health indicators such as lipid profile, blood pressure and clinical signs symptoms also improved and more in treatment group. Dietary counseling showed positive effects on food intake. Renal and hepatic profile showed no signs of toxicity in treatment group. The study concluded that CrP combined with dietary counseling had positive effect on diabetic profile of the newly diagnosed T2DM patients. The clinical signs and symptoms were improved. No hepatic and renal toxicity was observed.

Keywords: *chromium, HbA1c, Fasting blood glucose, lipid, liver, profile*

Cite This Article: Hajra Ahmad, Zaheer Ahmed, and Rezzan Khan, "Effect of Chromium Picolinate Supplementation on Diabetic Profile and Nutritional Status of the Type-2 Diabetic Adult Population – A Randomized Controlled Trial." *Journal of Food and Nutrition Research*, vol. 4, no. 8 (2016): 535-542. doi: 10.12691/jfnr-4-8-8.

1. Introduction

Chromium in its different forms is a commonly utilized mineral supplement also used by the T2DM patients for its management and control as its role is attributed to glucose homeostasis [1,2]. Chromium Picolinate (CrP) is a synthetic salt form of Chromium Chloride, in which Picolinic acid may serve to improve chromium absorption [2].

CrP has been used in varying doses to improve diabetic profile of the T2DM patients. Supplemental dose of CrP up to 100-1000 µgms per day has been safely given to human subjects [3,4]. Since CrP is absorbed better therefore, picolinic acid has been approved as a chelator for better utilization of chromium. This is synthesized from an amino acid (Tryptophan) in kidney cells and brewer's yeast and is also present in intestinal cells and human milk. Thus, picolinic acid may be a naturally produced molecule that facilitates the absorption and transport of ions and has become a popular nutrient as well as therapeutic agent for T2DM[5].

Type 2 Diabetes Mellitus (T2DM) affects 95% of the diabetic population [6]. It refers to a group of metabolic disorders characterized by elevated blood glucose levels, and is one of the leading five causes of mortality world over. It may lead to multi organ dysfunction. Its etiology among humans is multifaceted, starting from genetics to lifestyle [7].

It is one of the chronic diseases and at present is strongly considered to be an outcome of the genetics and environmental factors [8]. Previously it was associated with affluence, but the concrete evidences are now contrary to it, as it is equally present in developing countries as well [9,10]. In 2013 about 382 million people suffered from T2DM over the globe and an upsurge of 592 million is expected by 2035 [11].

T2DM being a chronic & complication prone disease requires lifelong management, which puts a significant financial burden on the sufferers [12]. Positive change in lifestyle, dietary habits, cost effective drugs, efficient supplementary& complementary therapies are among current concerns, and therefore strategies are being designed to control it [13]. CrP supplementation is one among the options but the meta-analysis of studies on its supplementation in T2DM have contradictory statements related to its effect on lipid profile and glycemic management among diabetics [14]. Therefore further studies are needed to explore the issue.

Chromium is an essential nutrient involved in normal carbohydrate and lipid metabolism. It influences glucose metabolism by potentiating the action as taking part in insulin signal amplification mechanism [15]. It has been claimed to act by one way or the other by; (i) increase in the number of insulin receptors, (ii) increased binding of insulin to its receptor and (iii) increased activation of the receptor in the presence of insulin[16] Thus chromium can be claimed as one of the "master" nutrients for controlling blood sugar in diabetic individuals. It may also be responsible to reduce myocellular lipids and enhance insulin sensitivity in individuals with T2DM [17].

A Meta-analysis of seven RCTs, which met the criteria of RCT study design concluded that chromium lowers fasting blood glucose levels but have no effect on HbA1c, lipid profile and BMI of the diabetic patients [18]. The researchers from related reviews concluded that the data for individuals with diabetes are uncertain. Therefore RCTs in well-characterized, at-risk populations are necessary to determine the effects of chromium on glucose, insulin, and HbA1clevels. The present study was designed to evaluate the effect of CrP on diabetic profile and nutritional status of the newly diagnosed T2DM patients.

2. Materials & Methods

The study design was a Randomized Controlled Trial. The selected subjects were studied in three phases; i.e. at baseline, by the end of 90 days treatment period and at the end of 30 days washout period. A parallel placebo group was also studied on the same parameters. The flow diagram showing complete picture of the subjects enrolled, completers and dropouts in three phases of the study is depicted in Figure-1. Initially 60 patients were enrolled for intervention. Eight were dropped at the initial stage due to various reasons therefore fifty two were randomized for intervention i.e. 26 in each group. By the end of intervention 17 were dropped in total, 13 from placebo and only four from CrP group. The dropout rate was less in treatment group showing better impact of CrP on management of T2DM.

2.1. Locality and Population

The study was conducted at diabetes clinic of Medical Outpatient Department (OPD) of Pakistan Institute of Medical Sciences (PIMS), Islamabad, Pakistan. Male and female subjects falling within the age bracket of 40-65 years having newly diagnosed T2DM constituted the study population.

2.2. Sample Size and Sampling Technique

A sample size of 52 newly diagnosed T2DM patients not yet put on any treatment were included in the study population. The subjects were divided into two groups i.e., placebo and CrP; 26 subjects were allotted to each group. They were diagnosed as diabetic by the attending physicians, on the basis of fasting plasma glucose (FPG) according to the criteria given by American Diabetic Association (ADA) [19].

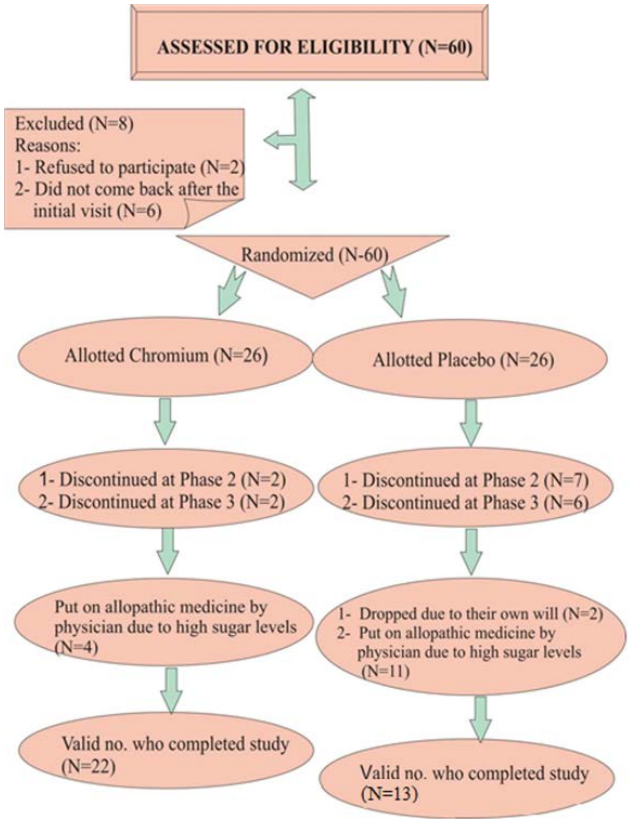

Figure 1. Flow diagram of participation of subjects in the study

2.3. Phases of the Study

The study was completed in three phases i.e. ***Phase- 1:*** This included collection of baseline data related to, assessment of nutritional status: such as Anthropometric, Biochemical, Clinical signs symptoms Dietary information and life style. ***Phase -2:*** It was based on the Intervention to see the effect of CrP on diabetic profile and related variables in relation to placebo. A capsule of CrP weighing 200 µg/day after breakfast was advised to the cases while controls were given a capsule of inert material after breakfast, which had no known impact on diabetic status of the patients. This period comprised of three (03) months. ***Phase -3:*** It comprised of one month in which effect of stopping the intervention on diabetic profile and other parameters was studied. This period was labeled as "washout period".

The data collection in all three phases was based on the Information related to life style, diabetic profile such as FPG, HbA1c percentage and fasting insulin levels. Some lab parameters were studied for possible complications of the T2DM and to record the side-effects of CrP if any. These included, complete lipid profile such as total

cholesterol, High Density Lipoproteins (HDL), Low Density Lipoproteins (LDL), Very Low Density Lipoproteins (VLDL) and Tri-Glycerides (TG) levels. These were conducted with standard techniques for possible forth coming lipid disorder. The toxic effects of the selected nutraceuticals was assessed with the help of biochemistry related to hepatic and renal profile. This included Alanine Transaminase (ALT), Alkaline Phosphatase (ALP) and Micro-albumin content of the urine, urinary proteins (total) & urinary creatinine levels. Selected anthropometrics, clinical assessment and dietary assessment were also recorded.

2.4. Anthropometric Assessment

Height and weight was taken to calculate BMI of the subjects at three phases of the study. The standard procedures accepted internationally were used to take the body measurements [20].

2.5. Clinical Assessment

Basic clinical data such as blood pressure, and pulse rate was also recorded. American Heart Association (AHA) standards were used to determine a deviation from the normal. Some other related clinical signs and symptoms were recorded on a nominal scale according to subject's perception and feelings [21]. These included visual status, tingling sensation, body aches & pains, burning feet, fatigue, and status of wound healing and diabetic foot. The values obtained were then analyzed for any change in clinical signs and symptoms from one phase to another.

2.6. Dietary Assessment

Dietary information was collected with the help of seven (07) days Food Diary (FD) and Food Frequency Questionnaire (FFQ). This information was collected at two stages i.e. before and after the intervention [22,23].

Initial seven days FD was filled by each patient as baseline information followed by same information at the end of three months intervention period. It helped to evaluate the impact of dietary counseling throughout ninety (90) days intervention period. The dietary information from FD was later on converted into macronutrients (Carbohydrates, fats and proteins) and energy intake and was compared with the recommended intake of healthy population of same age group [24].

Fortnightly education/counselling for dietary advice focused on guidelines of American Diabetic Association (ADA) were provided to each patient for necessary compliance to the restricted diet for diabetics.

2.7. Ethical Considerations

The study was approved by the Ethical Committee of Pakistan Institute of Medical Sciences (PIMS), Islamabad for its implementation and execution. Informed written/ consent was taken from each patient before enrolling them as study subject.

3. Results & Discussion

The initial work on role of chromium on T2DM started in 50's .The overview of researches up till now has proven that chromium supplementation is effective in lowering blood pressure and plasma cholesterols, enhancing insulin sensitivity, facilitating weight loss, increasing lean body mass, and reducing metabolic syndrome related risk factors. Besides all these positive effects undeniable research results indicate an important role of CrP in the intervention of T2DM and other Metabolic Syndrome related conditions [25]. A recent study based on CrP supplementation revealed reduction in FPG and HbA1c values with no change in lipid profile [26].

In this RCT, sixty newly diagnosed Type -2 diabetic patients were assessed for eligibility, among which eight were excluded due to various reasons (Figure-1), while fifty two were randomized for intervention. They were randomly divided into two equal groups. Each group was exposed to separate treatment i.e. CrP and Placebo as per procedure described in research design and methods section. It was tried to have all subjects from same Socio-demographic profile

The number of male and female subject enrolled for the study was equal. Most of them (82.7%) were educated with varying levels of education. Since Islamabad is capital city and most of the residents are involved in government jobs, so as expected many (34.6%) of the subjects were in government jobs. Majority (82.7%) had family history of diabetes, most of them (59.6%) were having a diabetic near relative i.e. either parents or siblings or both. Smoking was not common; it is good to note that majority (90.6%) had left smoking on health care provider's advice. Socio-demographic profile of subject is depicted in Table 1.

Table 1. Socio-demo graphic profile of the subjects

Attributes	Profile	Number	Percentage
Gender	Male	26	50
	Female	26	50
Educational status	Illiterate	9	17.3
	Under matric	17	32.7
	Matric to intermediate	16	30.8
	Graduation	4	7.7
	Post graduate	6	11.5
Occupation	Govt job	18	34.6
	Private job	6	11.5
	Looking after home	3	5.8
	Miscellaneous	25	48.1
Family history of diabetes	Yes	43	82.7
	No	9	17.3
Relationship /history	No history of diabetes	9	17.3
	Near relative (parents and siblings	31	59.6
	Distant	12	23.1
Present smoking status	Yes	5	9.6
	No	47	90.4
Presence of stress	Yes	51	98.1
	No	1	1.9
Stress status	Mild	3	5.8
	Moderate	12	23.1
	Moderately sever	26	50.0
	Sever	11	21.2
Sleep status	Yes	46	88.5
	No	6	11.5
Hours of sleep	<5	5	9.6
	5-8	44	84.6
	>8	3	5.8
Mean age of the subjects	Male	50 years	
	Female	47 Years	

Stress was the major problem faced by majority (98.1%), but level of stress varied from mild to severe. About half of the population was having moderately severe level of stress. A latest review article supports this finding which says people exposed to stressful working conditions, traumatic events, depression and conflicting situations increases the risk of T2DM [27]. Similarly another systematic review suggest link between depression and diabetes in low and middle income countries [28,29]. The finding of the present study verifies this phenomenon.

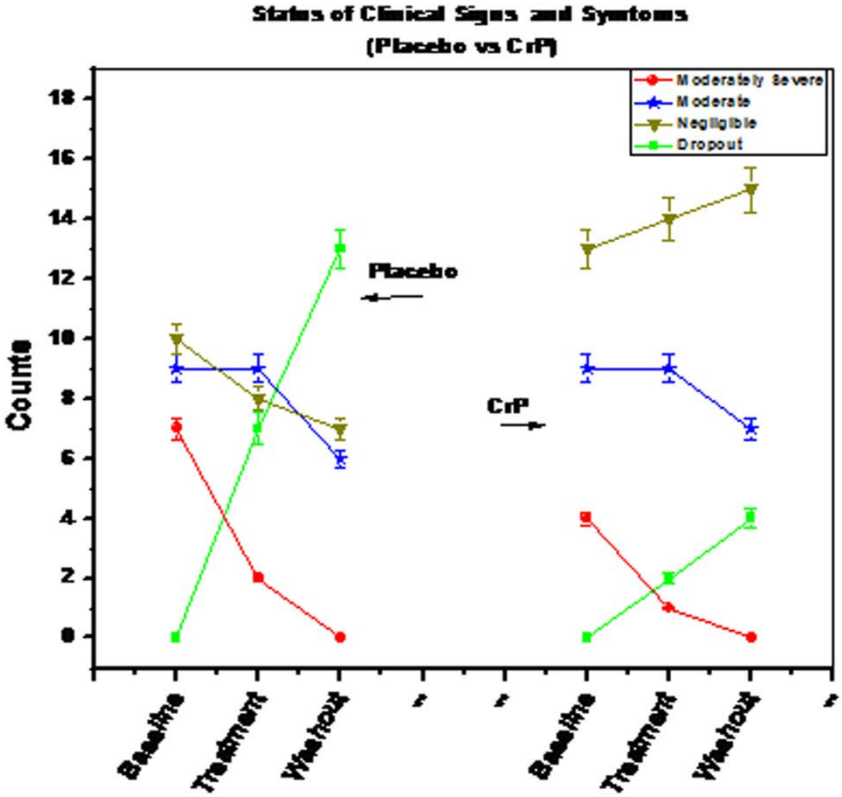

Figure 2. Effect of Chromium Picolinate on Clinical Signs and symptoms of Type-2 diabetics

The clinical signs and symptoms of the diabetic patients were studied on a nominal scale purely based on patient's subjective feelings. These included body aches and pains, tingling sensations, visual defects, feelings of being fatigued, burning feet, heeling of the wounds and diabetic foot if any. The intervention group was compared with the placebo. It was recorded that generally these clinical signs and symptoms reduced in severity after the intervention and in wash out period. The reduction was more in CrP group as compared to placebo. Also the dropout rate was more in Placebo. (Figure 2)

Previous studies also support these findings for example a survey to assess the effect of chromium on fasting glucose, postprandial glucose, and diabetic symptoms of 833 people with T2DM was conducted. The patients were monitored for up to ten months following supplementation with CrP with a dose of 500 µg/day. Symptoms of diabetes including fatigue decreased from 443 people who reported feeling fatigued before supplementation to 52 people after supplementation. Subjects reporting symptoms of thirst decreased from 334 to 47; frequency of urination episodes dropped from 322 to 40 people after Chromium supplementation for 1 month or longer. Similar effects were observed in women and men. There were no established negative side effects of supplemental Cr. The data from this survey endorses the safety and positive effects of supplemental Cr and reveals that beneficial effects of supplemental Cr observed in a few months are also present after 10 months [30].

CrP had beneficial effect on diabetic profile and clinical signs and symptoms of the subjects. One among such was Systolic and Diasystolic blood pressure. This improved towards normal by the end of three months intervention in the both groups and the impact was more in CrP treated group. The improvement in the placebo group was attributed to the dietary counseling which was same in the two groups. The hypertension status of the subjects was defined as per classification given by American Heart Association i.e. Normotensive, Prehypertensive, Hypertension stage-1, stage-2 and stage-3 (Figure 3). According to one study systolic blood pressure improved significantly in Chromium treated patients .while the same trend was observed for lipid profile as it reflected in improved values of cholesterol, triglyceride and LDL [15].

The subjects were assessed for their dietary intake with the help of seven days food diary before and after the intervention (Table 2). In between they were educated about the appropriate diet for diabetics keeping in view the American Diabetic Association (ADA) guidelines.

The average intake of all macronutrients and energy was reduced in both groups as outcome of the education and dietary counseling. Table-2 shows the dietary intake in terms of nutrients before and after study. Since dietary counseling was provided to both the groups put on placebo and chromium, therefore both the groups seem to have a check on their diet therefore the difference was not statistically significant. An article based on cohort studies suggests that healthy dietary patterns tend to reduce the

risk of diabetes and improve the health status of patients suffering from T2DM.[31], which supports the finding of our study as patients reduced their dietary intake in terms of total calories and type of carbohydrates.

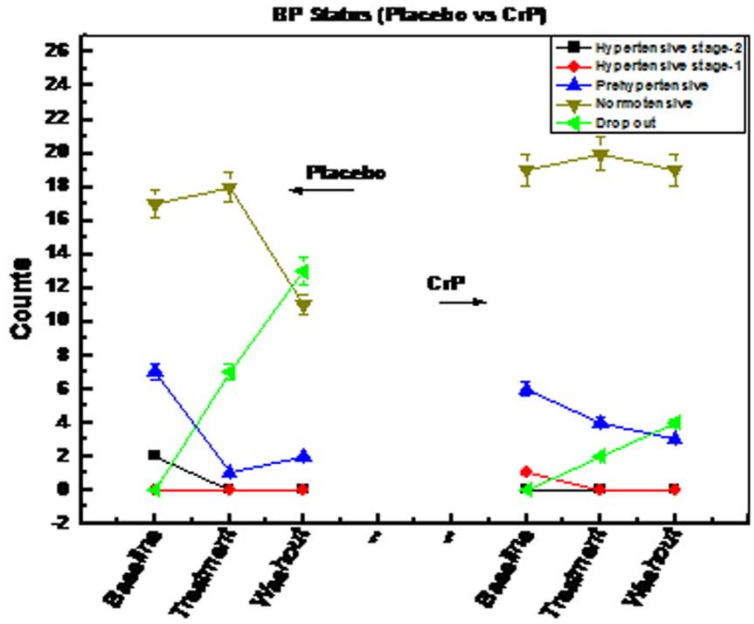

Figure 3. Status of hypertension at baseline, intervention and washout period, Control VS Treatment group

Table 2. Intervention wise nutrient intake at baseline and after 03 months

Nutrients	Placebo			Chromium		
	Baseline	Intervention	P-value	Baseline	Intervention	P-value
Energy (Kcal)	2378±392	2123±288	0.236	2405±414	2163±251	0.237
Carbohydrates (gms)	387±72	322±37	0.236	372±74	326±26	0.241
Proteins (gms)	72±12	65±7	0.236	76±17	70±17	0.241
Fats (gms)	68±18	65±15	0.236	67±18	66±11	0.237

The Body Mass Index (BMI) was calculated at three phases of the study to see and impact of intervention on nutritional status in terms of BMI. The results are depicted in Figure 4.

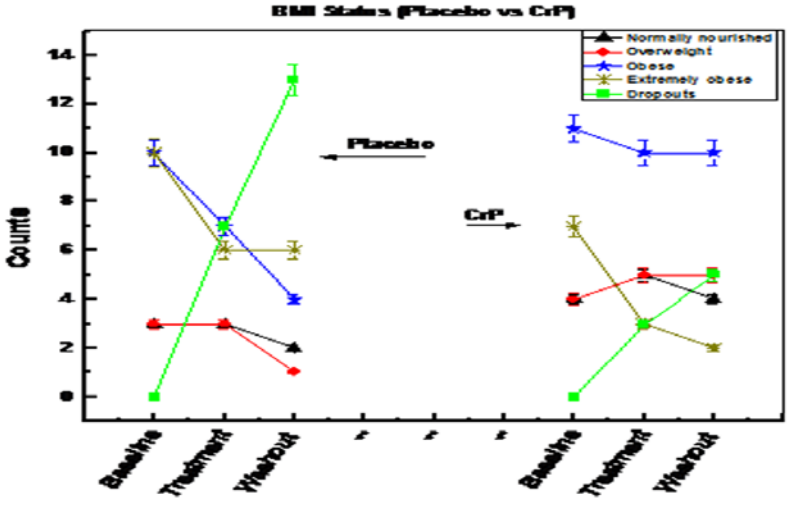

Figure 4. BMI status at baseline, after intervention and at the end of washout period

Obesity is one of the major risk factors for mortality among diabetics [32]. In present study the subjects were assessed for BMI at three phases of the study. Figure 4 indicates the number of overweight and obese people at three phases of the study. The prevalence of overweight and obesity was more at baseline, which decreased after three months intervention in both groups. This decrease was more in CrP treated group as compared to placebo. The review of literature has conflicting results. A meta-analysis of the randomized control trials to see the effect of chromium on glucose and lipid profiles in patients with T2DM concluded that Cr although lowers the FPG but had no effect on other parameters including BMI [18].

The subjects were assessed for their lipid profile at three phases of the study in two groups. It was interesting to note that that values of cholesterol, triglycerides, HDL and LDL were within the normal range in majority of diabetics accept for VLDL which were higher at baseline and remained higher throughout the study with little decline towards normal (Table 3). The findings of this

study are consistent with previous studies as CrP have no effect on lipid profile of the Type 2 diabetics. The meta-analysis of 13 studies which met the criteria of clinical trials also indicated that Cr has no effect on lowering TC, HDL, LDL, VLDL , and TG [18].

Table 3. Intervention wise diabetic, lipid, hepatic & urinary profile in three phases of the study

Parameters	Baseline			After 3 months intervention			Washout period			Overall effect within group	Overall effect between group
	Placebo	chromium	P. value within group	Placebo	Chromium Picolinate	P. value within group	Placebo	Chromium Picolinate	P. value within group		
Diabetic Profile											
FPG (mg/dl)	149.58 ±22.90	142.85 ±17.71	0.209	143.26 ±36.07	130.42 ±32.68	0.38	128.38 ±26.39	129.14 ±22.40	0.281	0.003	0.000
Insulin (µIU/mL)	24.47 ±16.49	33.37 ±28.3	0.394	22.66 ±12.01	24.72 ±23.2	0.472	20.18 ±11.88	24.33 ±22.7	0.474	0.037	0.000
HbA1C (%)	7.78 ±0.92	7.98 ±1.28	0.432	6.50 ±0.76	6.12 ±0.89	0.337	6.02 ±0.82	6.04 ±0.81	0.538	0.000	0.000
Lipid Profile											
Cholesterol (mg/dl)	179.4 ±31.4	189.2 ±40.1	0.387	177 ±34.8	167±34	0.473	168 ±21.6	165.2 ±32.2	0.429	0.102	0.612
Triglyceride (mg/dl)	180.4 ±83.1	193.2 ±158.4	0.418	192.2 ±71.3	148.4 ±46.3	0.323	163.54 ±34.14	163.50 ±45.7	0.429	0.131	0.923
HDL (mg/dl)	38.2 ±9.2	38.6 ±12.8	0.445	43.4 ±11.07	42 ±11.4	0.446	46.4 ±10	44.6 ±11.5	0.613	0.645	0.565
LDL (mg/dl)	109.5 ±30.2	111.7 ±42.4	0.335	104 ±29.8	98.1 ±38.6	0.489	103.8 ±24.03	97.09 ±46.1	0.363	0.119	0.861
VLDL (mg/dl)	36.08 ±16.62	38.63 ±31.67	0.418	32.70 ±6.82	32.70 ±9.14	0.429	32.70 ±6.82	32.70 ±9.14	0.429	0.414	0.504
Hepatic Profile											
ALT (IU/L)	43.42 ±28.12	52.88 ±42.7	0.485	39.16 ±27.32	42.67 ±27.3	0.440	32 ±19.58	40.36 ±24.1	0.283	0.007	0.000
ALP (IU/L)	105.85 ±24.1	108.77 ±34.2	0.546	105.43 ±31.42	92.64 ±22.7	0.489	109 ±33.13	84 ±19.5	0.428	0.025	0.000
Urinary Profile											
UMA (mg)	24.34 ±24.84	25.17 ±27.7	0.473	26.82 ±43.48	26.11 ±27.5	0.428	28.83 ±43.46	24.94 ±26.8	0.420	0.393	0.999
Urinary Protein (mg/dl)	32.84 ±30.30	106.5 ±336	0.434	20.28 ±17.57	50.46 ±62.4	0.395	27.3 ±16.8	19.34 ±10.4	0.301	0.209	0.450
Urinary creatinine (mg/dL)	112.4 ±61.01	126.8 ±86.3	0.433	93.63 ±55.73	83.91 ±60.3	0.476	108 ±48.8	119.2 ±54.2	0.392	0.215	0.099

FPG= Fasting Plasma Glucose, HbA1C= Glycated Hemoglobin, HDL = High Density Lipoprotein, LDL = Low Density Lipoprotein, VLDL = Very Low Density Lipoprotein, UMA =Urinary Micro Albumin

The three variables of diabetic profile included FPG, HbA1c and Insulin levels were recorded at three phases of the study. The treatment group was compared with placebo. The FPG levels were above normal range at baseline both in placebo and treatment group. After three months intervention these levels dropped towards normal range in treatment group from 142.85±17.71 mg/dl to 130.42±32.68 mg/dl but did not come to the normal range of 70-110 mg/dl. Similarly the FPG levels dropped to some extent in placebo group as well but this drop was not significant. The drop in both groups was also attributed to dietary counseling and 30 minutes daily walk as well. These levels further dropped at the end of one months' washout period showing compliance of the subjects to dietary advice and long term effect of CrP on diabetic profile.

Insulin levels and HbA1c were also recorded at three phases of the study. The insulin levels decreased in both groups but more in treatment as compared to placebo showing better uptake of the glucose from blood. The case to case observation shows no specific trend of insulin levels at baseline as it varied from low to high in both groups. The intervention brought more subjects towards normal levels of below 5 µIU/mL, which were more obvious in CrP group. This trend continued even after one month's washout period. The HbA1c levels also decreased in both groups from baseline to intervention and this decrease was proportionally better in treatment group as compared to placebo. It came to the normal levels of 6.12±0.89 percent from 7.98±1.28 percent. This decrease was maintained even after stoppage of treatment.

The effect of treatment was almost same on HbA1c percentage as for insulin levels. The treatment group shows mprovement with P value of 0.000 after all phases of the udy and between the groups. Few other studies also support these findings such as clinical trials with CrP have reliably shown that it can increase insulin sensitivity and improve the health of diabetics. Chromium supplementation appears to improve glycemic control in type 2 diabetic patients, which seems to be due to an increase in insulin action rather than stimulation of insulin secretion [5, 33]

The subjects had varied levels of FPG, and HbA1c at baselines mostly above the normal cut off values as recommended by ADA for two i.e. FPG 126 mg/dL (7.0 mmol/L) HbA1C 6.5% (48 mmol/mol) [19]. These dropped after the intervention, and which was more obvious in treatment group. Insulin levels were also decreased by the end of intervention showing less insulin resistance. There is growing evidence that chromium may facilitate insulin signaling and chromium supplementation therefore may improve systemic insulin sensitivity [34]. The present study proved this concept.

A systematic review of randomized controlled trials evaluating chromium supplementation revealed that in such studies subject description is important to consider. A meta-analysis of 41 studies showed that "among

participants with T2DM, chromium supplementation improved glycosylated hemoglobin levels by −0.6% (95% CI, −0.9 to −0.2) and fasting glucose by −1.0 mmol/L (−1.4 to −0.5) but had no effect on lipids. There was no benefit in individuals without diabetes" [14]. Few other studies also support these findings such as a dietary intervention of organic chromium supplements resulted in improved glycemic control. The reduction in HbA1C and mean blood glucose reveal the ability of chromium to maintain euglycemia. Chromium supplementation demonstrated as an effective regimen for newly onset type-2 diabetic patients [15,35].

The group treated with CrP shows improvement trend in diabetic indicators as compared to placebo after the intervention, this trend is more obvious after intervention, which is maintained by the end of washout period in treatment group showing lasting impact on FPG as compared to placebo. Statistically significant results were observed between the placebo and chromium group at P- Value 0.000. Significant results were also observed among the subjects at different phases of intervention with P- Value 0.003. There were insignificant results at different phases of intervention between the groups for insulin levels. However insulin levels were significantly dropped from base line to washout period at P=0.037. The treatment group depicts improvement in glucose uptake from blood by decreasing the insulin levels at baseline from 33.37±28.3 to 24.72±23.2 and 24.33±22.7 after 03 months intervention and at the end of wash out period of one month at P = 0.000 as compared to placebo group. These results coincide with the a previous study which proves that chromium is one of the most popular supplements among researchers and a majority found its positive effect on FPG and related diabetic profile [36].

In intervention studies it is important to evaluate overall impact of intervention on management of disease and functioning of the organs such as liver and kidney which are involved in metabolic and secretory process of the digested food.

CrP supplements had no negative effect on liver function test as in this study ALT levels on the average were above normal range (4- 42 IU/L)at baseline in both groups. The status of ALT levels improved after three months of intervention and continued to improve even in washout period, showing no liver toxicity by CrP intake. Similarly for ALP levels which were high at baseline, reduced after intervention and this reduction was more in CrP treated subjects as compared to placebo i.e. 105.43±31.42 IU/L in placebo and 92.64±22.7 in CrP group. This continued to reduce even in the washout period in CrP treated group, while increased in Placebo group showing positive effect of CrP on liver function.

Chromium supplements are also known to have positive effect on insulin levels; triglycerides total body fat mass and central obesity without any side effects [37] Its supplemental dose doesn't negatively affect renal or liver function [5,34].

In vitro study findings showed that chromium picolinate may improve insulin sensitivity by enhancing intracellular insulin receptor. The treatment for 10 weeks significantly improved changes in metabolic risk factors including favourable changes in histopathology of the liver, kidney and pancreas suggesting its potential role in the management of diabetes [38,39].

4. Conclusion

The study concluded that CrP have positive effect on Diabetic profile of the T2DM patients. It improved clinical signs and symptoms including blood pressure. CrP supplementation along with dietary education, improves dietary intake. It has positive effect on weight management thus positively effecting BMI. It had no effect on Lipid profile. No renal and hepatic toxicity was observed. Further studies in varying doses of CrP on population with same characteristics are recommended to find out the best and safe dose of CrP on human subjects.

Acknowledgement

The authors are obliged to Diabetes Clinic of Pakistan Institute of Medical Sciences (PIMS), Islamabad for providing volunteers as subjects. The Pathology lab of same hospital for providing standard labs for conducting biochemical tests involved in this research project.

The authors' contributions are as follows: H.A. Conducted the study as part of her PhD project and wrote the original draft of manuscript. Z.A. & R.K act as supervisor & co-supervisor and also gave technical input to improve the manuscript.

Conflict of Interest

None of the authors has any conflicts of interest to declare.

References

[1] Doddigarla Z., Parwez I., Ahmad J, "Correlation of serum chromium, zinc, magnesium and SOD levels with HbA1c in type 2 diabetes: A cross sectional analysis", D*iabetes & Metabolic Syndrome: Clinical Research & Reviews*, 2015.

[2] Yin, R.V., Phung, O.J, "Effect of chromium supplementation on glycated hemoglobin and fasting plasma glucose in patients with diabetes mellitus", *Nutrition journal*, 14:1. 2015.

[3] Joseph, E., DiSilvestro, R., de Blanco, E.J.C, "Triglyceride lowering by chromium picolinate in type 2 diabetic people" *International Journal of Nutrition and Metabolism*, 7.24-28. 2015.

[4] Rocha, N.R., Carrara, M.A., Stefanello, T.F., Teixeira, C.J., Oliveira, A.C.P., Batista, M.R, "Effects of chromium picolinate supplementation in type 2 diabetic patients", *Acta Scientiarum Health Sciences*, 36.161-164.2014.

[5] Ghosh, D., Bhattacharya, B., Mukherjee, B., Manna, B., Sinha, M., Chowdhury, J, et al. "Role of chromium supplementation in Indians with type 2 diabetes mellitus" *The Journal of nutritional biochemistry*, 13.690-697. 2002.

[6] Xie, W., Zhao, Y., Zhang, Y, "Traditional chinese medicines in treatment of patients with type 2 diabetes mellitus" *Evidence-Based Complementary and Alternative Medicine*, 2011, 2011.

[7] Nolan, C.J., Damm, P., Prentki, M, "Type 2 diabetes across generations: from pathophysiology to prevention and management", *The Lancet*, 378,169-81.2011.

[8] Raghavan, S., Porneala, B., McKeown, N., Fox, C.S., Dupuis, J., Meigs, J.B, *Metabolic factors and genetic risk mediate familial type 2 diabetes risk in the Framingham Heart Study*, *Diabetologia*, 58. 988-96. 2015.

[9] Alwan, A, "Global status report on noncommunicable diseases 2010" *World Health Organization*, 2011.

[10] Shaw, J.E., Sicree, R.A., Zimmet, P.Z, "Global estimates of the prevalence of diabetes for 2010 and 2030", *Diabetes research and clinical practice*. 87. 4-14. 2010.

[11] Guariguata, L., Whiting, D., Hambleton, I., Beagley, J., Linnenkamp, U., Shaw, J, "Global estimates of diabetes prevalence for 2013 and projections for 2035", *Diabetes research and clinical practice*, 103.137-49. 2014.

[12] Parkin, C.G., Davidson, J.A, "Value of self-monitoring blood glucose pattern analysis in improving diabetes outcomes", *Journal of diabetes science and technology*. 3:500-508.2009.

[13] Somineni, H.K., Boivin, G.P., Elased, K.M, Daily exercise training protects against albuminuria and angiotensin converting enzyme 2 shedding in db/db diabetic mice, *Journal of Endocrinology*, 221.235-251. 2014.

[14] Balk, E.M., Tatsioni, A., Lichtenstein, A.H., Lau, J., Pittas, A.G, "Effect of chromium supplementation on glucose metabolism and lipids a systematic review of randomized controlled trials", *Diabetes care*, 30. 2154-2163. 2007.

[15] Sharma, S., Agrawal, R.P., Choudhary, M., Jain, S., Goyal, S., Agarwal, V, "Beneficial effect of chromium supplementation on glucose, HbA 1 C and lipid variables in individuals with newly onset type-2 diabetes", *Journal of Trace Elements in Medicine and Biology*, 25. 149-153. 2011.

[16] Anderson, R.A, "Chromium and insulin resistance", *Nutrition research reviews*, 16. 267-275. 2003.

[17] Cefalu, W.T., Rood, J., Pinsonat, P., Qin, J., Sereda, O., Levitan, L., Anderson, R.A., Zhang, X.H., Martin, J.M., Martin, C.K. and Wang, Z.Q, Characterization of the metabolic and physiologic response to chromium supplementation in subjects with type 2 diabetes mellitus. Metabolism. 59. 755-762. 2010.

[18] Abdollahi, M., Farshchi, A., Nikfar, S. and Seyedifar, M, "Effect of chromium on glucose and lipid profiles in patients with type 2 diabetes; a meta-analysis review of randomized trials", *Journal of Pharmacy & Pharmaceutical Sciences*, 16. 99-114. 2013.

[19] American Diabetes Association, Classification and Diagnosis of Diabetes. *Diabetes Care*, 39. S13-S22. 2016.

[20] Marfell-Jones, M.J., Stewart, A., de Ridder, J, *International standards for anthropometric assessment*, 2012.

[21] Streiner, D.L., Norman, G.R., Cairney, J, *Health measurement scales: a practical guide to their development and use*: Oxford University Press, USA; 2014.

[22] Crozier, S.R., Inskip, H.M., Godfrey, K.M., Robinson, S.M, "Dietary patterns in pregnant women: a comparison of food-frequency questionnaires and 4 d prospective diaries", *British journal of nutrition*, 99. 869-875. 2008.

[23] Tyrovolas, S., Pounis, G., Bountziouka, V., Polychronopoulos, E., Panagiotakos, D.B, "Repeatability and validation of a short, semi-quantitative food frequency questionnaire designed for older adults living in Mediterranean areas: the MEDIS-FFQ", *Journal of Nutrition for the Elderly*, 2010;29:311-24.

[24] Manual A. Dietary guidelines for Indians. Nat Inst Nutrition. 2. 89-117. 2011.

[25] Lau, F.C., Bagchi, M., Sen, C.K., Bagchi, D, "Nutrigenomic basis of beneficial effects of chromium (III) on obesity and diabetes", *Molecular and cellular biochemistry*, 317. 1-10. 2008.

[26] Paiva, A.N., de Lima, J.G., de Medeiros, A.C., Figueiredo, H.A., de Andrade, R.L., Ururahy, M.A., Rezende, A.A., Brandão-Neto, J. and Almeida, M.D.G, "Beneficial effects of oral chromium picolinate supplementation on glycemic control in patients with type 2 diabetes: A randomized clinical study", *Journal of Trace Elements in Medicine and Biology*, 32. 66-72. 2015.

[27] Kelly, S.J., Ismail, M, "Stress and type 2 diabetes: a review of how stress contributes to the development of type 2 diabetes", *Annual review of public health*, 36. 441-462. 2015.

[28] Mendenhall, E., Norris, S.A., Shidhaye, R., Prabhakaran, D, "Depression and type 2 diabetes in low-and middle-income countries: a systematic review", *Diabetes research and clinical practice*, 103. 276-285. 2014.

[29] Tabák, A.G., Akbaraly, T.N., Batty, G.D., Kivimäki, M, "Depression and type 2 diabetes: a causal association?" *The lancet Diabetes & endocrinology*, 2. 236-245. 2014.

[30] Cheng, N., Zhu, X., Shi, H., Wu ,W., Chi, J., Cheng, J., and Anderson, R.A, "Follow-up survey of people in China with type 2 diabetes mellitus consuming supplemental chromium" *The Journal of Trace Elements in Experimental Medicine*, 12. 55-60. 1999.

[31] Alhazmi, A., Stojanovski, E., McEvoy, M., Garg, M, "The association between dietary patterns and type 2 diabetes: a systematic review and meta-analysis of cohort studies" *Journal of Human Nutrition and Dietetics*, 27. 251-60. 2014.

[32] Costanzo, P., Cleland, J.G., Pellicori, P., Clark, A.L., Hepburn, D., Kilpatrick, E.S., Perrone-Filardi, P., Zhang, J. and Atkin, S.L, "The obesity paradox in type 2 diabetes mellitus: relationship of body mass index to prognosis: a cohort study", *Annals of internal medicine*, 162. 610-618. 2015.

[33] Zhang, Q., Xiao, X., Li, M., Li, W., Yu, M., Zhang, H., Ping, F., Wang, Z., Zheng, J. and Xiang, H, "miR-375 and miR-30d in the effect of chromium-containing Chinese medicine moderating glucose metabolism", *Journal of diabetes research*, 2014. 2014.

[34] Hummel, M., Standl, E., Schnell, O, "Chromium in metabolic and cardiovascular disease", *Hormone and metabolic research*, 39. 743-751. 2007.

[35] Wang, Z.Q., Qin, J., Martin, J., Zhang, X.H., Sereda, O, Anderson RA, Pinsonat, P. and Cefalu, W.T, "Phenotype of subjects with type 2 diabetes mellitus may determine clinical response to chromium supplementation", *Metabolism*, 56. 1652-1655. 2007.

[36] Bartlett, H.E., Eperjesi, F, "Nutritional supplementation for type 2 diabetes: a systematic review", *Ophthalmic and physiological optics*, 28. 503-523. 2008.

[37] Aghdassi, E., Arendt, B.M., Salit, I.E., Mohammed, S.S., Jalali, P., Bondar, H., Allard, J.P, "In patients with HIV-infection, chromium supplementation improves insulin resistance and other metabolic abnormalities: a randomized, double-blind, placebo controlled trial", *Current HIV research*, 8. 113-120. 2010.

[38] Jain, S.K., Rains, J.L., Croad, J.L, "Effect of chromium niacinate and chromium picolinate supplementation on lipid peroxidation, TNF-α, IL-6, CRP, glycated hemoglobin, triglycerides, and cholesterol levels in blood of streptozotocin-treated diabetic rats", *Free Radical Biology and Medicine*, 43. 1124-1131. 2007.

[39] Sundaram, B., Aggarwal, A., Sandhir, R, "Chromium picolinate attenuates hyperglycemia-induced oxidative stress in streptozotocin-induced diabetic rats", *Journal of Trace Elements in Medicine and Biology*, 27. 117-121. 2013.