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# AMELIORATING EFFECT OF TURMERIC ON KIDNEY FUNCTION IN PATIENTS WITH TYPE 2 DIABETES MELLITUS

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#### Keywords:

Chronic kidney disease, creatinine, diabetes mellitus, Nephropathy, Plasma proteins, Urea

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ABSTRACT: Background: Diabetes mellitus is one of the most common metabolic disturbances associated with carbohydrates, lipids, proteins, and relative or absolute insulin depletion. Various long-term complications of diabetes develop due to chronic hyperglycemia and insulin resistance. Chronic kidney disease (CKD) and diabetes mellitus (DM) are major public health problems worldwide. Turmeric is one of the medicinal herbs studied for antioxidant, antibacterial, and antifungal effects. Curcumin has been established to be defensive against nephropathy. Objective: The purpose of this study was to assess turmeric's effect on different kidney function parameters in patients with type 2 diabetes mellitus (T2DM). Materials and Methods: Two hundred patients with T2DM were selected in randomized control trial, of which 100 subjects were enrolled in the study group, were given 500 mg of raw turmeric powder in capsule form daily along with their antidiabetic drug medication (Metformin) for 3 months period while 100 subjects on medication of antidiabetic drug (Metformin) were selected as a control group. Serum levels of urea, creatinine, total protein, albumin, and globulin were measured at baseline and after 3 months intervention period. **Results:** Showed a significant reduction in serum creatinine and significant improvement in total proteins and albumins in the study group by the end of 3 months of turmeric supplementation. Conclusion: Supplementation of turmeric leads to improved plasma proteins and decreased serum urea and creatinine levels in T2DM patients and could be useful in the improvement of kidney function in T2DM.

**INTRODUCTION:** Diabetes is a metabolic disorder that leads to hyperglycemia due to impaired insulin secretion, insulin function, or both. Type 2 diabetes affects 90-95% of people<sup>1</sup>. Disturbances in insulin production and action, a hormone secreted by the islets of langerhans in the pancreas, are implicated in the disease<sup>2</sup>.



The signs and symptoms of this disease are the elevated level of blood glucose, decreased peripheral absorption of glucose due to impairment of insulin secretion, and peripheral resistance to insulin <sup>1</sup>. Several pathological processes are involved in the development of diabetes.

Various long-term complications of diabetes develop due to chronic hyperglycemia and insulin resistance. These complications are macro and microvascular abnormalities such as autonomic neuropathy, peripheral neuropathy, retinopathy, cardiovascular symptoms and nephropathy <sup>3-5</sup>. Chronic kidney disease (CKD) leads to decreased

kidney function and/or evidence of kidney damage Kidney disease, especially in glomerular diseases such as diabetic kidney disease (DKD), is reproduced by increased blood generally concentrations of kidney function test (KFT) parameters such as albumin, urea, creatinine, etc.<sup>7</sup>. CKD and DM are major public health problems, and both have worldwide distribution. Diabetic nephropathy is the most common cause of the development of CKD. Approximately 30% of patients with DM have diabetic nephropathy, and with the growing number of DM patients and the aging population, there is likely a parallel increase in CKD incidence. According to the International Diabetes Federation Diabetes Atlas 2014, the number of patients with DM in India is expected to rise to 101.2 million by 2030 unless urgent precautionary measures are taken<sup>8</sup>.

A common complication of DM is diabetic nephropathy (DN), which is a main universal health problem <sup>9</sup>. Chronic inflammation and oxidative fundamental providers stress are of the development of DN<sup>10</sup>. A variety of preventable factors, including hypertension, alcoholism, and smoking, also speed up DN progression <sup>11</sup>. Oxidative stress is responsible for developing chronic complications of diabetes mellitus and results from chronic hyperglycemia, increased oxidants and thereby decreased antioxidants<sup>12, 13</sup>.

Diabetic individuals are often started on medication such as Metformin and are seen commonly by their providers, therefore increasing medical expenses. Hence to reduce the long-term cost of medication to control diabetes, new cost-effective alternative supplementation help to reduce long-term side effects and expenses for diabetes <sup>14-16</sup>. Many plants have been tested and used in the prevention and management of diabetes and associated complications. Spices form an important class of food adjunct in the human diet. Besides increasing the taste and flavor of foods, spices illustrated a broad range of physiological and pharmacological properties <sup>17-20</sup>. Earlier studies have shown that curcumin's anti-inflammatory and antioxidant treatments may delay the development of glomerulopathy<sup>11</sup>. Curcumin is an active phenolic compound derived from the rhizome of the herb Curcuma longa. It has been shown to possess various valuable including effects. antiinflammatory and antioxidant activities <sup>19</sup>. Curcumin has been established to defend against nephropathy in animal models <sup>21, 22</sup>. Previously, curcumin was accounted to be efficient supplement to prevent glucose-induced oxidative stress in the endothelial cells of diabetic animals <sup>12, 23</sup>.

Currently, DN is the main cause of CKD and one of the most significant long-term complications in terms of morbidity and mortality for individual patients with diabetes. There are multiple mechanisms by which curcumin may ameliorate renal damage. Curcumin increases blood urea nitrogen and promotes clearance of creatinine and urea. In addition, curcumin decreases levels of albuminuria and enzymatic, including levels of lactate dehydrogenase (LDH), aspartate transferase, alanine transferase and alkaline and acid phosphatases<sup>24</sup>.

Therefore, this study aims to evaluate the effects of curcumin on serum urea, creatinine, total protein, albumin, and globulin in patients with type 2 diabetes mellitus.

MATERIAL AND METHODS: The study was carried out in the Department of Biochemistry, Krishna Institute of Medical Sciences, Karad (Western Maharashtra). The study was approved by Institutional Ethics Committee (Letter Ref: KIMSDU/IEC/244/2013 Dated 06/12/2013). This study was carried out in the form of randomized control trial, which includes all type 2 diabetic patients referred to Krishna Hospital and Medical Research Centre, Karad. A total of 200 subjects with type 2 diabetes were enrolled for the study. They were further categorized into two groups with 100 subjects, including one study group and one control group. The study's objectives and risk factors were explained to volunteers after their written informed consents were obtained.

**Inclusion Criteria:** Non-insulin-dependent type 2 diabetics aged 35-65 years, with a single drug schedule for this treatment.

**Exclusion Criteria:** Patients with pregnancy, breastfeeding, using tobacco, alcohol, consuming thyroid, hypolipidemic, antihypertensive, and anticoagulant drug medications were excluded. The study group was given one capsule of 500 mg raw turmeric powder daily post-lunch for 3 months

period. During the study period, antidiabetic drug medication (Metformin) was sustained as usual, and subjects were advised to maintain their normal diet and physical activity.

The blood sample was collected from each subject at baseline and after 3 months intervention period. The collected samples were immediately centrifuged at 3000 rpm for 10 minutes and analyzed for serum urea, creatinine, total protein, albumin, and serum globulin concentrations. Data were analyzed using paired, and unpaired't' tests and values were expressed as Mean  $\pm$  Standard Deviation.

**RESULTS:** The results from table 1 indicated that no significant difference in serum urea was observed in controls when compared between baseline and after turmeric intervention for 3 months period (P=0.0621). Also, no significant difference was found in serum urea in the study group when compared between baseline and after 3 months of turmeric intervention (P=0.0523) **Table 1**.

Further, no significant difference in serum urea was observed when compared between the control and study group at baseline (P=0.3059) and after 3 months of intervention of turmeric (P=0.5472) **Table 1**. It was found to be a significant decrease in serum creatinine in both controls (p<0.0001) and the study group (P=0.0407) when compared between baseline and after 3 months intervention period **Table 1**. Whereas no significant decrease was found in serum creatinine of the control and study group when compared between baseline (P=0.2247) and after 3 months of intervention (P=0.2290) **Table 1**.

TABLE 1: SHOWING LEVELS OF SERUM UREA AND SERUM CREATININE IN CONTROL AND STUDYGROUP AT BASELINE AND AFTER 3 MONTHS INTERVENTION OF TURMERIC

Variable	Parameter	Baseline	After 3 Months	Difference	Paired	Paired
		Mean ± SD	period Mean ± SD	Mean ± SD	't'	<b>'P'</b>
Control Group	Serum Urea	$25.15 \pm 4.84$	24.55±3.84	$0.61 \pm 2.80$	4.234	0.0621
Study Group		$25.63 \pm 5.34$	24.93±4.99	$0.70 \pm 2.81$	3.283	0.0523
Unpaired 't' & 'P'		t= 1.027	t = 0.6030			
		P= 0.3059	P=0.5472			
Control Group	Serum	$1.15\pm0.21$	$1.06 \pm 0.12$	$0.088 \pm 0.19$	4.730	< 0.0001
Study Group	Creatinine	$1.12\pm0.20$	$1.08 \pm 0.11$	$0.037 \pm 0.18$	2.073	0.0407
Unpaired 't' & 'P'		t= 1.218	t= 1.207			
		P=0.2247	P=0.2290			

# TABLE 2: SHOWING LEVELS OF SERUM TOTAL PROTEIN, ALBUMIN AND GLOBULIN IN CONTROL AND STUDY GROUP AT BASELINE AND AFTER 3 MONTHS INTERVENTION OF TURMERIC

Variable	Parameter	Baseline	After 3 Months	Difference	Paired	Paired
		Mean ± SD	period Mean ± SD	Mean ± SD	't'	<b>'P'</b>
Control Group	Serum Total Protein	7.08±0.21	7.15±0.41	$0.067 \pm 0.30$	2.217	0.0289
Study Group		$7.09 \pm 0.42$	7.14±0.24	$0.049 \pm 0.32$	1.541	0.0126
Unpaired 't' & 'P'		t = 0.7084	t = 0.7578			
		P=0.4795	P= 0.4495			
Control Group	Serum Albumin	$4.00 \pm 0.25$	4.38±0.58	$0.37 \pm 0.55$	6.665	< 0.0001
Study Group		4.03±0.23	4.37±0.57	$0.34 \pm 0.55$	6.132	< 0.0001
Unpaired 't' & 'P'		t = 0.1234	t = 0.6454			
		P=0.9019	P= 0.5194			
Control Group	Serum Globulin	$3.08 \pm 0.65$	2.77±0.22	$0.30 \pm 0.10$	6.907	< 0.0001
Study Group		3.06±0.62	2.77±0.25	$0.29 \pm 0.06$	6.393	< 0.0001
Unpaired 't' & 'P'		t = 0.5809	t = 0.05895			
-		P=0.5620	P= 0.9531			

We found a significant difference in serum total protein in control group when compared between baseline and after 3 months of intervention (P=0.0289). Also significant decrease in serum total protein was observed in the study group when

compared between baseline and after 3 months of intervention (P=0.0126) **Table 2**. No significant difference was found in serum total protein in the control and study group at baseline (P=0.4795) and after 3 months intervention period (P=0.4495).

Table 2. In the case of serum albumin, we found extremely significant differences in both controls (p<0.0001) and the study group (p<0.0001)compared between baseline and after 3 months turmeric intervention period Table 2. However, no significant difference was observed in serum albumin in the control and study group at baseline (p=0.9019) and after 3 months of intervention of turmeric (p=0.5194) Table 2. The extremely significant difference in serum globulin was observed in controls when compared between baseline and after turmeric intervention for 3 months (P<0.0001). Also, an extremely significant difference was found in serum globulin in the study group when compared between baseline and 3 months of turmeric intervention (P<0.0001) Table 2. Further, no significant difference in serum globulin was observed in the control and study group at baseline (P=0.5620) and after 3 months of intervention of turmeric (P=0.9531) Table 2.

DISCUSSION: According to the result, no significant difference in serum urea was observed in controls when compared between baseline and turmeric intervention for after 3 months (P=0.0621). Also, no significant difference was found in serum urea in the study group when compared between baseline and 3 months of turmeric intervention (P=0.0523). Significant decreases in serum creatinine in both control (p<0.0001) and study group (P=0.0407) were observed when compared between baseline and after 3 months turmeric intervention period. Zein Shaban Ibrahim et al. found that urea and creatinine, the main indicators of DN were increased in rats of the diabetic group compared with levels of the control group. This increase was reversed when the rats were treated with curcumin

Radhia Khan *et al.* found no significant difference in blood urea levels in type 2 diabetes patients treated with curcumin <sup>24</sup>. Curcumin is an active phenolic compound derived from *Curcuma longa*, *mainly used in Asia as a spice, pigment*, and additive. Several studies have shown that curcumin has wide biological functions, predominantly antioxidant and anti-inflammatory. It has been established as a bi-functional antioxidant; it showed antioxidant activity by scavenging reactive oxygen species and inducing an antioxidant response. The

protective effect of curcumin has been assessed in different experimental models, including nephrotoxicity, chronic renal failure, ischemia, and diabetic nephropathy <sup>25-28</sup>. DN is the main cause of end-stage renal disease. Sharma et al. found that administration curcumin protects diabetic nephropathy and oxidative stress in animal models <sup>29</sup>. In addition, Soetikno *et al.* assessed the effect of curcumin administration oral in diabetic nephropathy models. They found that curcumin prevents the development of kidney disease in diabetic rats <sup>30</sup>. Treatment of curcumin improves creatinine clearance. In addition, it decreases oxidative stress by scavenging superoxide and hydroxyl radicals. Furthermore, it also boosts the activity of the antioxidant enzymes <sup>31, 32</sup>. Curcumin exhibits a multifunctional antioxidant activity, including the prevention of lipid peroxidation.

Furthermore, it has been found that the phenolic groups present in the structure of curcumin react directly with reactive oxygen species and reactive nitrogen species, leading to the expression of various antioxidants such as superoxide dismutase, glutathione catalase. glutathione reductase, peroxidase etc. <sup>33-36</sup>. In the present study, we found a marginal increase in serum total protein and serum albumin in both control and study groups before and after supplementation of turmeric, which clearly indicated that turmeric intervention in type 2 diabetic patients improved protein concentration in blood. But we found a decrease in serum globulin in both the groups before and after turmeric supplementation. Diabetes is characterized by increased plasma glucose levels, which in turn modify blood plasma proteins by a non-enzymatic reaction called glycation.

Protein glycation leads to the formation of toxic molecules called advanced glycation end products (AGEs). Accumulation of AGEs has been accelerated in diabetes and contributes to the pathogenesis of diabetic complications <sup>37, 38</sup>. In diabetes, albumin synthesis and secretion is decreased due to insulin deficiency <sup>39</sup>. In the present study, supplementation of turmeric for 3 months was found to be effective in diabetic patients to improve plasma protein concentrations, which will help improve kidney function in type 2 diabetic patients. This study agrees with the findings of Garkuwa *et al.* <sup>30</sup> and Shatadal *et al.* <sup>31</sup>.

who reported the reno-protective effect of curcumin in diabetic rats.

**CONCLUSION:** Various *in-vitro* and *in-vivo* studies have reported strong supportive evidence for investigating curcumin efficacy against type 2 diabetes mellitus. The data reported in the present study concluded that turmeric has therapeutic potential to counteract diabetes and its complications related to kidney function.

The supplementation of turmeric effectively reduces the blood concentrations of urea and creatinine and improves plasma proteins in type 2 diabetes patients. As a food adjunct, turmeric can be a useful supplement to improve kidney function in type 2 diabetes, which ameliorates associated diabetic complications, including diabetic nephropathy. However, further clinical trials will be needed to evaluate the effects of curcumin and its specific dosage in pre-diabetes and T2DM patients associated with kidney diseases.

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