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RESEARCH ARTICLE

The Effect of Turmeric and Ginger on Oxidative Modulation in end stage renal disease (ESRD) Patients

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Abstract

Background: End-stage renal disease (ESRD) is a state of oxidative stress (OS) due to uremic oxidant mediator's accumulation, Various herbs are recognized as sources of natural antioxidants and thus play an important role in the chemoprevention of diseases resulting from lipid peroxidation. This study aim to investigate the effect of Turmeric and Ginger on oxidative modulation in chronic renal failure (ESRD) Patients.

Methodology: Forty-five ESRD Patients were randomly assigned into 3 groups, group 1: control placebo group received starch, group 2: received turmeric and group 3: received ginger for 8 weeks. Plasma malondialdehyde (MDA), red blood cell (RBC) antioxidant enzyme activities including glutathione peroxidase (GPX), glutathione reductase (GR), and catalase (CAT), Plasma total cholesterol, high-density lipoprotein-cholesterol, low-density lipoprotein-cholesterol, triglyceride, albumin, and hemoglobin were also measured before and after study.

Results:

MDA level was significantly reduced ($P<0.05$) in both turmeric and ginger groups after trial and as compared with the control group, the ratio of decrease was significantly higher in the turmeric group. The enzyme activity of GPX, and CAT in RBCs were significantly increased ($p<0.05$) in both turmeric and ginger groups after trial and as compared with the control group.

Conclusion: Regular ingestion of turmeric and ginger reduce plasma MDA and increases RBC GPX, and CAT activity in CRF patients.

INTRODUCTION

Chronic kidney disease (CKD) is characterized by progressive loss of kidney function, which decreases the ability of the body to eliminate soluble waste resulting in the accumulation of "uremic toxins" [1,2]. It is now well documented that CKD is an inflammatory disorder and uremic toxins play a major role in creating the inflammatory milieu [1,2]. CKD is defined by either a reduction in glomerular filtration rate (GFR) and/or the presence of abnormalities in the urine such as protein, red blood cells or white blood cells. The GFR is mathematically derived from serum creatinine and is used to classify the severity of CKD into five stages (Table 1).

Although CKD often leads to the development of end stage renal disease (ESRD) it is more importantly an independent risk factor for the development of cardiovascular disease (CVD). Indeed, the most common cause of death in patients with CKD relates to this high incidence of CVD. The high risk of CVD in CKD patients is attributable to a number of other risk factors that accompany CKD such as diabetes mellitus, hypertension, obesity,

tobacco abuse and dyslipidemia [3]. An underlying abnormality that unites all of these disorders is the presence of inflammation and oxidative stress

Therefore, therapeutic approaches, which inhibit inappropriate inflammation and tolerance of oxidative stress, have a potential therapeutic value in ameliorating CKD.

Kidney damage is defined as pathologic abnormalities or markers of damage, including abnormalities in blood or urine tests or imaging studies.

Natural products and their active principles are sources for new drug discovery and treatment of diseases have attracted attention in recent years. Medicinal use of spices/herbs has been gradually increasing in developed countries [4].

Turmeric (Curcuma longa) is a wild plant native to tropical South Asia. Its dried rhizomes are ground into a deep orange-yellow powder commonly used as a spice, that is the key ingredient for many Asian dishes. Curcuminoids, a mixture of curcumin (diferuloylmethane), demethoxy- curcumin, and bisdemethoxycurcumin, are vital constitu- ents of turmeric [5]. Curcumin is perhaps the most active and nontoxic component of turmeric (constitutes 2–5% of turmeric), [6] which has been extensively studied for its therapeutic benefits, such as antioxidant, [7] anti-inflammatory, [8] cardioprotective, [9] renoprotective, [10] immunomodulatory, [11] cancer chemopreventive, [12] antide- pressant, [13] and neuroprotective activities. [14]

The other two constituents of the curcuminoid mixture also contribute significantly to the effectiveness of cur-cuminoids. Also, the curcuminoid mixture represents turmeric in its medicinal value better than curcumin alone. [5]

Ginger (Zingiber officinale) is a nontoxic spice with negligible side effects and is generally recognized as safe by the FDA [15].

Ginger is completely sterile and is propagated exclusively by vegetative means using rhizome [16]. Ginger has been recognized to have potent antioxidant properties being an effective forager of superoxide radicals, which has been regarded as a promising protective mechanism against stress [17]. Ginger is reported to be a carminative, diaphoretic, antispasmodic, peripheral circulatory stimulant, astringent, appetite stimulant, anti- inflammatory agent in addition to being useful in treating cold, headaches, arthritis, rheumatological conditions, and muscular discomfort. Studies have shown that ginger possesses antimicrobial, antischistosomal, anti- inflammatory, antipyretic, hypoglycemic hepatoprotective, diuretic and hypocholesterolemic effects [18]

In recent years, it has been proven that ginger consumption can reduce fasting serum glucose [19, 20] and systemic inflammation markers, such as C-reactive protein, in patients with type 2diabetes mellitus [19]. Additionally, some in vitro and animal studies indicated that ginger could result in the reduction of AGEs(advanced glycosylation end product) [21], vascular inflammation markers [22] , and oxidative stress [23].

This study was designed to investigate the effects of turmeric and ginger supplementation as pure plants on oxidative modulation in chronic renal failure (CRF) patients.

Patients and methods

The study was a prospective and double blind randomized clinical trial. All patients provided informed consent form before participating in the study. Participants were recruited from among 50 CRF stage 5 on regular Hemodialysis in Northern Area Armed Force Hospital, Hafr Albatin , KSA . Inclusion criteria consisted of having the age of 18 years and more and be stage 5 ESRD on regular Hemodialysis for 3 month at least and administering no other antioxidant medications.

Forty-five patients who met the study criteria were enrolled to the study and randomized into 3 groups group 1 of trial (N = 15), group 2 of trial (N=15) and controls (n = 15). Each patient in the first trial group (G2) received a dose of turmeric (1 capsule with each meal containing 500 mg turmeric, the second trial group (G3) each patient received (1 capsule with each meal containing 500 mg ginger; 3 capsules daily), whereas the control group (G1) received starch capsules for the same 8 weeks. The type and dose of the individualized drugs remained unchanged during the

study. Each patient was given an order number and received the medications in the corresponding prepacked bottles. All drug and placebo tablets were similar in size, shape, weight, and color. Patients were followed regularly for detection of any side effects related to the turmeric or ginger supplementation. Clinical investigators, laboratory personnel, and patients were all masked to the treatment assignment.

Turmeric and ginger were obtained from local market and powder was encapsulated by using hard gelatin capsules. Also, starch capsules were made by using hard gelatin capsules at the clinical pharmacy department.

Blood samples were drawn from each patient just before and at the end of the trial from the arterial line during haemodialysis session

Samples were immediately centrifuged and frozen at −70°C.

Analytical procedures

Plasma malonyldialdehyde (MDA), an indirect index of lipid peroxidation, was assayed as thiobarbituric acid reactive substances (TBARS) using colorimetric method [24]. Results are expressed as nmol/mL. The red blood cell glutathione peroxidase (RBC GPX) activity was measured in RBC hemolysate according to the method of Paglia and Val- entine 23 [25] by a decrease in absorption at 340 nm due to oxidation of NADPH to $NADP^+$. GPX activity in RBC was expressed as IU/g Hb.

The RBC CAT activity was assessed by Aebi method [26] and red blood cell glutathione reductase (RBC GR) activity in red blood cells was calculated by the method of Massey and William and expressed in units/g Hb. The hemoglobin concentration was determined using an autoanalyzer SE-9000. Serum creatinine was measured by an autoanalyzer using the Jaffé method [27]; Commercial enzymatic tests were used for determining serum total cholesterol (TC), triglycerides (TG), and HDL-C concentrations. Serum Albumin levels were measured using a bromocresol purple dye- binding method.

Statistical analysis

Data were analyzed using Statistical Package for the Social Sciences software version 20 (SPSS)
Inc, Chicago, IL). Chi-square test was used to analyze categorical variables such as age, gender.
Quantitative data were presented as mean ± standard deviation and compared by samples t –test before and after administration of turmeric and ginger.
Also, we performed data variations and analysis between control, turmeric and ginger groups on SPSS version 20. Means and standard deviation (SD) was computed. ANOVA was used to compare multiple independent groups
P value less than 0.05 were considered significant.

RESULTS

Table 1
Comparison of the Baseline demographic data between control and trial groups in studied patients

Groups / Characteristics	Group 1 Placebo (n . 15)	Group 2 Turmeric (n . 15)	Group 3 Ginger (n . 15)
Age (y)*	49 ± 2.97	51.87 ± 2.94	51 ± 1.36
Serum urea (mg/dL)*	81.78± 1.57	81.95 ± 1.6	80.53 ± 1.54
Serum creatinine (mg/dL)*	6.75 ± 0.11	7.87 ± 0.14	6.74 ± 0.13
Sex			

Men (%) Women (%)	9 (60) 6 (40)	10 (66.7) 5 (33.33)	9 (60) 6 (40)
History of diabetes, n (%)	4 (26.7)	6 (40)	5 (33.3)
History of smoking, n (%)	1 (6.7)	2 (13.3)	2 (13.3)
History of hypertension, n (%)	4 (26.7)	3 (20)	4 (26.7)

* Presented as mean ± SD.

The baseline characteristics of the patients did not differ significantly between the two groups (Table 1).

Table 2 Comparison of the oxidative parameters between control and trial groups in studied patients

Groups / Factors	Group 1 Placebo (n . 15)	Group 2 Turmeric (n . 15)	Group 3 Ginger (n . 15)
MDA (nmol/mL) Before trial	**9.68 ± 0.66[a]**	**8.07 ± 0.37 [a]**	**8.42 ± 0.35 [a]**
After trial	**8.77 ± 0.86**	**6.80 ± 0.54**	**7.47 ± 0.95**
P Value	**0.002**	**0.000**	**0.002**
RBC GR (units/g Hb) Before trial	**30.91 ± 2.68 [a,b]**	**29.52 ± 2.14 [a]**	**31.25 ± 1.55 [b]**
After trial	**32.32 ± 8.26 [a]**	**37.53 ± 8.66 [a]**	**35.49 ± 9.48[a]**
P Value	**0.542**	**0.04**	**0.093**
RBC CAT (kilounits/g Hb) Before trial	**112.47 ± 14.74 [a]**	**113.55 ± 15.02 [a]**	**109.34 ± 10.21 [a]**
After trial	**131.77 ± 19.02**	**152.67 ± 18.26 [a]**	**148.80 ± 17.83 [a]**
P Value	**0.003**	**0.000**	**0.000**
RBC GPX (units/g Hb) Before trial	**27.08 ± 7.34 [a]**	**34.01 ± 7.66 [b]**	**29.17 ± 5.89 [a,b]**
After trial	**39.33 ± 9.63**	**62.14 ± 12.47 [a]**	**61.86 ± 11.67[a]**
P Value	**0.000**	**0.000**	**0.000**

MDA = plasma malonyldialdehyde; n = number; RBC CAT = red blood cell
Catalase activity; RBC GR = red blood cell glutathione reductase activity; RBC GPX = red blood cell glutathione peroxidase activity.

MDA level was significantly reduced (P<0.05) in both turmeric and ginger groups after trial and as compared with the control group, the ratio of decrease was significantly higher in the turmeric group. The enzyme activities of GPX, and CAT levels were significantly increased (p<0.05) in both turmeric and ginger groups after treatment and as compared with the control group.

Table 3 Comparison of Hb and Albumin between control and trial groups in studied patients

	Group 1 Placebo (n . 15)	Group 2 Turmeric (n . 15)	Group 3 Ginger (n . 15)
Hb (g/dL) Before trial	11.36 ± **2.04** [a]	12.49 ± **2.23** [a]	11.69 ± **2.28** [a]
After trial	**11.99 ± 2.13** [a]	**13.45 ± 2.20** [a]	**13.41 ± 2.16** [a]
P Value	0.453	0.275	0.146
Albumin (g/dL) Before trial	3.96 ± **0.88** [a]	4.26 ± **1.02** [a]	3.96 ± **0.97** [a]
After trial	**3.99 ± 0.69** [a]	**4.41 ± 0.49** [a]	**4.28 ± 0.57** [a]
P Value	0.816	0.467	0.064

There was no significant difference in serum albumin and Hb between the different treatment groups.

Table 4 Comparison of lipid profile between control and trial groups in studied patients

	Group 1 Placebo (n . 15)	Group 2 Turmeric (n . 15)	Group 3 Ginger (n . 15)
Cholesterol (mg/dL) Before trial	179.67 ± **28.98** [a]	182.49 ± **34.09** [a]	180.53 ± **29.71** [a]
After trial	**179.74 ± 31.89**[a]	**159.07 ± 24.67** [b]	**172.10 ± 20.14** [a, b]
P Value	0.993	0.009	0.452
Triglyceride (mg/dL) Before trial	204.13 ± **39.28** [a]	210.93 ± **36.96** [a]	207.33 ± **34.40** [a]
After trial	**202.19 ± 32.71** [a]	**184.74 ± 29.53** [a]	**198.27 ± 27.53** [a]
P Value	0.873	0.041	0.476
HDL Cholesterol (mg/dL)			

Before trial After trial	34.90 ± **6.09** **33.67 ± 8.80** [a]	35.73 ± **9.17** **28.94 ± 6.92** [a]	33.71 ± **10.31** **30.63 ± 8.96** [a]
P Value	0.625	0.009	0.478
LDL Cholesterol (mg/dL) Before trial After trial	103.94 ± **23.93** [a] **105.74 ± 19. 10** [a]	104.58 ± **19.60** [a] **93.18 ± 13.70** [b]	105.35 ± **17.57** [a] **101.82 ± 13.96** [a,b]
P Value	0.791	0.008	0.581
V-LDL Cholesterol (mg/dL) Before trial After trial	40.83 ± **7.86** [a] 40.44 ± **6.54** [a]	42.19 ± **7.39** [a] **36.95 ± 5.91** [a]	41.47 ± **6.88** [a] **39.65 ± 5.51** [a]
P Value	0.873	0.041	0.476

Total- cholesterol, LDL-, VLDL- cholesterol and Triacylglycerol levels were significantly reduced ($P<0.05$) in turmeric group after trial and as compared with the control group. In contrast HDL -Cholesterol levels were significantly increased ($p<0.05$) in turmeric group after treatment and as compared to the control group.

Discussion

End-stage renal disease (ESRD) is a state of oxidative stress (OS) due to uremic oxidant mediator's accumulation [28] the activation of phagocytic oxidative metabolism by the dialysis membrane, intravenous iron therapy, and the antioxidant depletion [29]. Oxidative stress in these patients leads to a state of malnutrition and accelerated atherosclerosis [30]. Some trials showed a significant benefit from antioxidant therapy on cardiovascular outcome.

It has been recognized that ROS production in cells leads to an intracellular tyrosine phosphorylation cascade by two district protein families the Mitogen Activated Protein Kinase (MAPK) and the redox sensitive kinases [31]. The MAPK signaling pathways modulate gene expression, mitosis, proliferation, motility, metabolism, and programmed cell death [32]. Furthermore, curcumin is reported to inhibit proliferation and induce apoptosis in T lymphocytes and Jurkat cells [33].

The present study showed that, in comparison to placebo, turmeric and ginger supplementation were significantly more effective in attenuation of OS and increased in antioxidative markers in ESRD patients.

Oxidative stress is an imbalance between generation of reactive oxygen species (ROS) and antioxidants. A decrease in oxygen tensions and hypoxia-inducible transcription factors of the kidney was demonstrated in a number of experimental models of chronic kidney disease (CKD).

The present study indicated that oral supplementation of turmeric or ginger to CRF Patients. Decreased MDA level significantly more than placebo, the results also showing that turmeric is more effective in decreasing MDA as a marker of lipid peroxidation after trial in this study

Similar to our results, Acar et al. also reported that curcumin reduced the MDA and OS index levels in the brain and sciatic nerve tissues in the diabetic group [34].

In the present study, the enzymes of GPX, and CAT levels were significantly increased ($p<0.05$) in both turmeric and ginger groups after treatment and as compared with the control group. Antioxidant systems, both enzymatic and nonenzymatic, are naturally present and counteract free radicals. Enzymatic antioxidants include catalase, superoxide dismutase, and glutathione peroxidase. Nonenzymatic antioxidants contain glutathione, vitamin E and vitamin C, transferrin, and albumin [35].

Various herbs are recognized as sources of natural antioxidants and thus play an important role in the chemoprevention of diseases resulting from lipid peroxidation [36].

Curcumin is a cheap nutritional ingredient with negligible side effect. It is also clear that curcumin has significant anti-inflammatory, anti-oxidant and various other features which make it a strong candidate to be included in therapeutic armamentarium for treating CKD. Curcumin is a unique molecule which can prevent inflammation by acting at multiple sites. By preserving intestinal barrier function curcumin can prevent inflammation at the gut level and prevent systemic inflammation if adequate concentration is achieved in the circulation. [37]

Concerning turmeric herb, it was reported that the active principle of turmeric (curcumin) ameliorated diabetic nephropathy in rats and the antioxidant activity is being responsible for the nephroprotective action of curcumin [38]. Curcumin might be potentially useful in kidney diseases by preventing renal inflammation. Moreover, turmeric extract was found to possess multiple therapeutic activities that block the cardiac, hepatic, and renal toxicities induced by doxorubicin ; arsenic trioxide [39], [40] and acetaminophen. [40]. Moreover, it was suggested that curcumin might be useful in kidney diseases via preventing renal inflammation induced by lipopolysaccharide. [41].

Sankar et al. reported that curcumin decreased lipid peroxidation and increased the reduced glutathione, catalase, and glutathione peroxidase level and protected the normal histological architecture of the liver, kidney, and brain [42]. Iqbal et al. showed increased activities of glutathione peroxidase, glutathione reductase, glucose-6- phosphate dehydrogenase and CAT in the liver, in the curcumin fed mice as compared to the normal diet fed-matched mice.[43].

A previous study indicated that curcumin protects mitochondria against OS both in vitro and in vivo [44]. Curcumin has a strong potential for scavenging superoxide radicals, hydrogen peroxide, and inhibition of oxidative enzymes such as cytochrome P450, and chelating and disarming oxidative properties of metal ions such as iron [45] Alternatively, in vitro and in vivo studies have shown that curcumin activates the appearance of some intracellular antioxidative defense systems for free radicals [46]. González-Salazar et al. suggested that the ROS scavenging ability of curcumin is involved in the cardioprotective effect [47].

Curcumin has been reported to show antioxidant properties by one or more of the following interactions: Scavenging or neutralizing free radicals by oxygen quenching and making it less available for oxidative reaction and/or inhibition of oxidative enzymes like cytochrome P450, interacting with oxidative cascade and preventing its outcome and chelating and disarming oxidative properties of metal ions such as iron [48]. Dietary curcumin is reported to inhibit superoxide anion generation and hydroxyl radical generation through preventing the oxidation of Fe in Fenton's reaction, which generates OH radicals [49]

The efficacy of turmeric in decreasing high-sensitivity C-reactive protein and uremic pruritus in end stage renal disease patients was demonstrated.

Natural products and their active principles are sources for new drug discovery and treatment of diseases have attracted attention in recent years. Medicinal use of spices/herbs has been gradually increasing in developed countries [50]. Ginger, (Zingiber officinale Rosc.), an herbaceous perennial of the family Zingiberaceae is an important export-oriented spice crop with high medicinal value. Ginger is completely sterile and is propagated exclusively by vegetative means using rhizome [51]. Ginger has been recognized to have potent antioxidant properties being an effective forager of superoxide radicals, which has been regarded as a promising protective mechanism against stress [52]. Ginger is reported to be a carminative, diaphoretic, antispasmodic, peripheral circulatory stimulant, astringent, appetite stimulant, anti-inflammatory agent in addition to being useful in treating cold, headaches, arthritis, rheumatological conditions, and muscular discomfort. Studies have shown that ginger

possesses antimicrobial, antischistosomal, antiinflammatory, antipyretic, hypoglycemic hepatoprotective, diuretic and hypocholesterolemic effects [53].

In the fresh ginger rhizome, the gingerol (polyphenol) was identified as the major active component. The volatile oil consists of mainly mono sesquiterpenes; camphene, beta-phellandrene and curcumin. [54]

Nasri et al., (2013) demonstrated that, high levels of polyphenolic and flavonoid compounds with high antioxidant activity for ginger. The presence of polyphenols and flavonoids in the Z. officinale extract might be responsible for the antioxidant and nephroprotective activities. [54,55]

Ginger might have a beneficial effect for removal of urea from plasma and it should be considered as a therapeutic herb to manage renal function in patients with uremia [56].

A study was conducted by Maghsoudi et al. on 30 adult male rats [57]. They found that, ginger was a useful agent for the prevention of renal ischemia reperfusion-induced injury [57]. It was suggested that ginger extracts could be used as a nephro-protective supplement particularly to reverse diabetic-induced complications.[58]

In agreement to the results of the present study, Mahmoud et al. conducted a study to evaluate the effects of Zingiber officinale on both acute and chronic renal failure (CRF) and the mechanisms underlying their effects. [59]. Ginger showed renoprotective effects in both models of renal failure [59]. These protective effects may be attributed at least in part to their anti-inflammatory properties as evident by attenuating serum C-reactive protein levels and antioxidant effects as evident by attenuating lipid peroxidation marker, malondialdehyde levels, and increasing renal superoxide dismutase activity [60].

Ginger could be beneficial adjuvant therapy in patients with acute renal failure and CRF to prevent disease progression and delay the need for renal replacement therapy. Uz et al. analyzed the possible protective effect of dietary ginger against the damage inflicted by reactive oxygen species (ROS) during renal I/R on thirty rats using histopathological and biochemical parameters [61]. Ginger supplementation in the diet before I/R injury resulted in higher total antioxidant capacity and lower total oxidant status levels than I/R group. The ginger supplemented diet prior to I/R process demonstrated marked reduction of the histological features of renal injury. Their findings imply that ginger exerts renoprotective effects probably by the radical scavenging and antioxidant activities [61]. Hence, it is assume that oxidative stress due to abnormal production of ROS is believed to be involved in the etiology of renal toxicities [62, 63].

All the above-mentioned studies demonstrated that concurrent administration of ginger could prevent nephrotoxicity induced by oxidative stress.

Ginger was reported to have a significant reduction effect in lipid peroxidation (MDA) and serum CRP levels. It may be possible that 6- gingerol, one of the active constituents of ginger, due to its potential antioxidant properties, [64] improves renal functions by attenuating oxidative stress-mediated decline in glomerular filtration rate (GFR) and renal hemodynamics. Ginger was found to scavenge hydroxyl, superoxide, and other free radicals in a dose-dependent manner in vitro [65]. In human aortic endothelial cells, zingerone and 6-gingerol demonstrated significant antioxidant effects on low-density lipoproteins.[66] Previous studies showed that ginger ameliorated cisplatin-induced nephrotoxicity either by preventing cisplatin-induced decline of renal antioxidant defense system or by its direct free radical scavenging activity.[67] It was also proved that ginger exhibits anti-inflammatory effects [68].

There was no significant difference in serum albumin and Hb between the different treatment groups.

Increased triglyceride concentration is a general feature of kidney disease whereas increased cholesterol is not. Lipids are insoluble in blood plasma and therefore they can circulate only in the form of lipoproteins. On the other side increased TG alone is an important warning sign of the presence of highly atherogenic triglyceride rich lipoprotein particles (TRL).[69]

Lipoproteins are complex particles consisting from lipids transferred from and to the tissues and a phospholipid envelope containing different proteins. They are not passive containers of TG and cholesterol but dynamic particles with variable composition. Both lipoprotein turnover and composition is altered in kidney diseases [70].

Lipoproteins are divided into three families: Chylomicrons and their remnants, the VLDL, IDL- LDL family and the HDL family.
Chylomicrons produced in enterocytes are carriers of lipids from guts to liver. There are much bigger than the other lipoproteins and during ultracentrifugation they do not sediment at all. Chylomicrons contain one molecule of apoprotein is B48 and some apoprotein molecules A I, A II and A IV. During their life span they acquire apo E and apo C from HDL particles. In contact with muscle and fat tissue capillary endothelial cells they release fatty acids through triglyceride lipolysis catalyzed by endothelium-bound lipoprotein lipase. Remnants of chylomicrons are removed by the liver [70].

Cardiovascular disease is a leading case of mortality not only in the whole population but also in groups with different, non cardiovascular chronic conditions. Kidney disease is one of these and many patients with kidney disease paradoxically do not die from end stage kidney failure but from cardiovascular causes. Already mild or moderate renal impairment represents a considerable excess risk of cardiovascular mortality, that chronic kidney disease (CKD) and chronic renal insufficiency (CRI) is associated with accelerated atherosclerosis and abnormal lipid/lipoprotein metabolism [71, 72] .

There is substantial evidence that excess renal lipids can cause injury in animal models of metabolic disease (obesity, metabolic syndrome and diabetes mellitus), chronic kidney disease, acute renal injury of several etiologies, as well as aging [73]. Lipotoxic cellular dysfunction and injury occur through several mechanisms such as release of proinflammatory and profibrotic factors [73].

The results of the present study demonstrated that, total- cholesterol, LDL-, VLDL- cholesterol and Triacylglycerol levels were significantly reduced ($P<0.05$) in turmeric group after trial and as compared with the control group. In contrast HDL -Cholesterol levels were significantly increased ($p<0.05$) in turmeric group after treatment and as compared to the control group.

It was reported that, curcumin may prevent the absorption of cholesterol and lipids by disrupting micelle formation and promote fecal excretion of total steroids and bile acids [74]. When excretion of bile acids increases, conversion of cholesterol to bile acids in the liver will be enhanced in order to replenish the loss in bile acids. Conversion of cholesterol to bile acids is the major pathway of cholesterol elimination and accounts for about 50% of daily cholesterol excretion [75]. Curcumin was reported to decrease the serum cholesterol via enhanced CYP7A1 enzyme activity, which controls cholesterol homeostasis [76].

It was demonstrated that supplement with ginger extract at 50 mg/kg attenuates chronic fructose consumption-induced kidney injury in rats by suppressing renal overexpression of proinflammatory cytokines. These findings provide evidence supporting the benefit of ginger supplement for the metabolic syndrome-associated kidney injury.[77]

Mehrdad et al. [78] who stated that ginger has a beneficial effect for removal of urea and creatinine from plasma of normal mice treated with its alcoholic extract and considered as a therapeutic herb to manage renal function.

It has been reported that, treatment of CCl4 -induced oxidative stress with ethanol or Chloroform extract of ginger recorded Improvement of the GSH, LPO, and SOD, ethanol extract recorded the highest improvement levels due to its higher concentration of flavonoids, tannins, and alkaloids, the naturally occurring antioxidants. Preventive effects of ginger against CCl4 -induced oxidative stress could be attributed to its high level of polyphenol compounds (6-gingerol and its derivatives), which have a high antioxidant activity [79] .

It has been demonstrated that, oral administration of ginger along with adenine caused a significant improvement in renal function, represented by the significant decrease in serum creatinine, urea, and BUN. It also reduced serum LDH levels and attenuates ultrastructural changes. Electron microscopic examination showed relatively normal proximal tubules. The mechanisms of these renoprotective effects may involve reduction of both oxidative stress and inflammation in renal cells [80].

CONCLUSIONS

In conclusion, the results of this study indicate that short-term oral turmeric supplementation is a beneficial, safe, and effective adjuvant therapy for CRF patients. However, long-term trials with higher doses of turmeric are needed to clarify its effect on the renal function of such patients and the rate of progression of CKD of various origins.

Ginger significantly protects the renal cells and reduces oxidative damage however; further detailed studies are required to establish its clinical application.

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