The effects of new polyherbal Unani formulation AJMAL06 on serum creatinine level in chronic renal failure

Muhammad Shakil Ahmad Siddiqui[1*], Aftab Saeed[1], Allah Nawaz[1], Safila Naveed[3] and Khan Usmanghani[2,3]

[1]Faculty of Eastern Medicine, Hamdard University, Karachi, Pakistan
[2]Research and Development Department, Herbion Pakistan (Pvt.) Limited, Korangi industrial Area, Karachi, Pakistan
[3]Department of Clinical Pharmacy and Health Care, Faculty of Pharmacy, Jinnah University for Women, Karachi, Pakistan

Abstract: This study was conducted to evaluate the efficacy of Unani Ajmal06, an herbal formulation for management of chronic renal failure (CRF). The therapeutic evaluations of three different formulations such as *Itrifal Kashneezi*, *Jawarsih Zarooni Sada* medicines were conducted on number 35 CRF patients clinically diagnosed cases of chronic kidney failure. It was found that herbal coded Ajmal06 was effective for the treatment of CRF in 70% of the patients treated. SPSS tests on sign and symptoms indicated the efficacy of Ajmal06 in lowering serum creatinine level in 70% of patients of chronic renal failure. In clinical response of BUN exhibited 75% of patients improved where as in case of fatigue (70%), edema (90%), leg pain (76%) improved these types of conditions with significant *p* value.

Keywords: Polyherbal Unani formulation, serum creatinine, CRF, dialysis.

INTRODUCTION

The chronic kidney disease is quite prevalent and spreading epidemically all over the globe. The kidney failure is eighth leading cause of death in Unites State in 2009 (Sievert, *et al*. 2013). CRF is a life threatening serious medical, social, economic problem for patients and their families and the government. CRF is a condition in which the kidneys functions worsen slowly without developing any signs and symptoms. CRF can be hidden or undiagnosed many years. In CRF urine may pass normally without disturbance but passing of urine normally is not a parameter to judge the efficiency of kidney functions (Isakova *et al*., 2011). According to an estimated about 10% of the population in U.S. are suffering from chronic kidney disease (CKD) (Nugent, *et al*. 2011). Approximately 450,000 patients with CRF need hemodialysis in developed countries; only 33% dialysis patients survive for five-year, this a very worse survival rate than cancer, obesity, hypertension and malnutrition. Still there is no proper treatment option available except hemodialysis, the peritoneal dialysis or the renal replacement therapy (RRT). The replacement of kidney is costly procedure and it depends upon the availability and matching of organ. The cost of post replacement medication and regular dialyses 2 to 3 times per week are also unaffordable to every patient. The replaced kidney may fail or reject by the body any time. Renal failure is a complex disease which involves multiple organs of the body (Humphreys, *et al*. 2005).

More often CRF is associated with one or more organic diseases e.g. heart failure, chronic liver disease, bone and muscles diseases etc. It may due to complications of diabetes, blood pressure or due to immunological disorders for example systemic lupus erythromatus (SLE), Immunoglobulin A (IgA). Structural/anatomical changes may develop in kidneys congenitally or due to some other diseases (Jafar and Agarwal 2012) . Here, we described the efficacy and safety of herbal coded Ajmal06 that was prescribed to CRF patients and the patients were observed for specified time period. We found that this Poly herbal Unani formulation(PHUF) Ajmal06 is very effective in this chronic ailment without any side effects.

Aims and objectives benefits of study

To prove the efficacy and safety of these PHUF Ajmal06 in managing the CRF. There are many herbs and herbal combinations (*according to Unani Philosophy of temperament and humors*) available that have been tested and proven to improve renal health and even reverse renal damage.

MATERIALS AND METHODS

Dosage formed design

AJMAL06 formulation and selection criteria

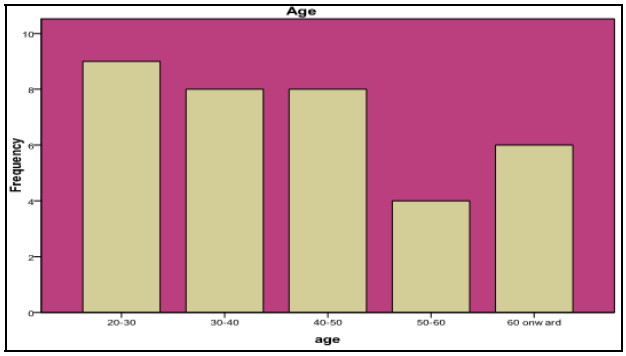
Herbal coded formulation consists of different herbal medicines in the form of aqueous extract and compound preparations. The drug design and collection of herbs according to herbal pharmacopoeia, monographs of Unani medicine on scientific basis. All patients had been treated with herbal coded *AJMAL06* formulations.

STATISTICAL ANALYSIS

All the data was collected at clinic Rafah-e-Aam Dawakhana Ajmali, Liaqatabad, Karachi, was subjected

**Corresponding author:* e-mail: rafaheaam@gmail.com

to analyze the statistical analysis, significant p value (p=<0.05) by using Anova and Chi-square test.



Graph 1: Distribution of age

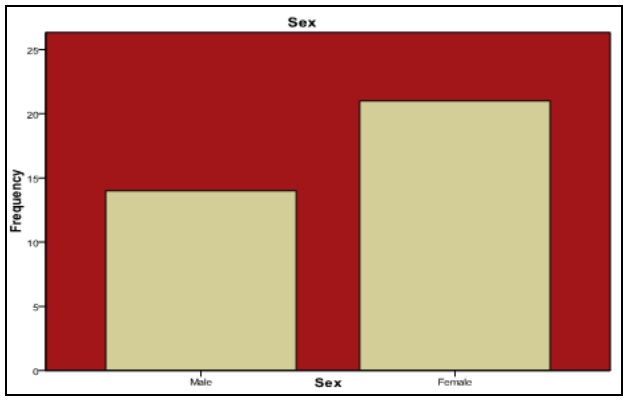


Fig. 2: Distribution of sex

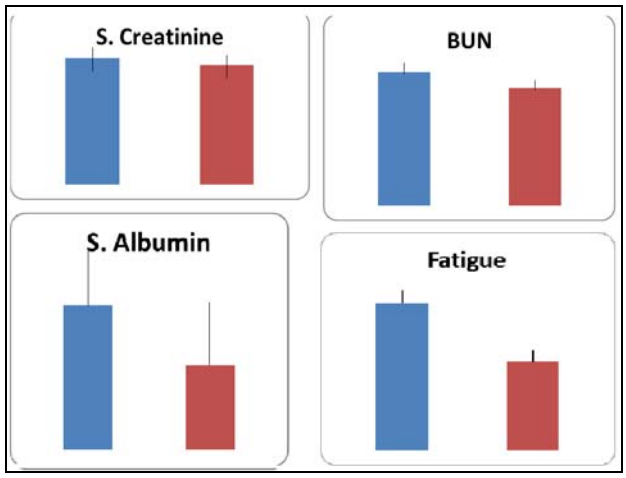


Fig. 3: Comparison of pre and post S. creatinin, BUN, S. Albumin and fatigue

Methods used to collect data

The study was experimental, randomized, clinical trial. Detailed history interviews, physical examinations, and blood, urine samples analysis and ultrasonography reports was taken prior to start the therapy. The patients of age between 20 to 70 years were prescribed the test drug for 3 month. Initially the consent was taken from all 35 patients enrolled prior to start the therapy. The patients were randomly selected according to inclusion criteria irrespective of socio-economic status at different medical health care centre including Rafah-e-Aam Dawakhana (Herbal Laboratories) Ajmali, Karachi. Prior to start this study, all the methods and consent form including clinical trial proforma for data record was approved by ethical committee at Hamdard University.

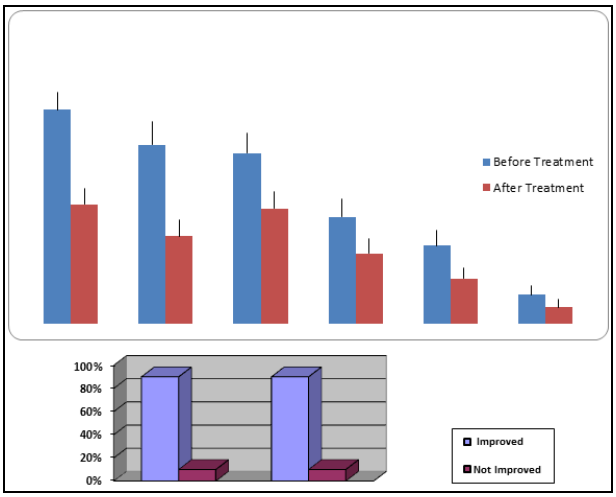


Fig. 4: Comparison of pre and post treatment

Inclusion criteria

Adults (age 20 years and older) with CRF, if the serum creatinine level increased above 2.0mg/dl, diabetes mellitus, hypertension with or without cardiovascular disease (CVD), mild or moderate renal insufficiency, defined as eGFR less than 60ml/min/1.73m^2 but greater than 30ml/min/1.73m^2.

Exclusion criteria

Acute renal damage, medical conditions that might interfere with the interpretation of results e.g. Cancer or pregnancy

Unani (Herbal) medicine

The Ajmal06 formula is based on the following preparations

Preparation 01 *Vitex nigundu* 5 grams, *Piper nigrum* make joshanda filtered for oral administration.

Preparation 02 *Itrifal Kishnizi*: *Terminalia chebula* Retz 0.43 mg, and *Terminelia chebula* Retz. uripe fruit 0.21 mg and *Coriandrum sativum* Linn 0.21mg.

Prescription 03 *Jawarish Zarooni Sada*: Piper longum 206mg, *Piper nigrum* 206mg, *Plumbago zeylanica* 206 mg, *Terminalia belerica* 206mg, *Terminalia chebula* 206 mg, *Zingiber officinale* 206mg, *Cyperus rotundus* 206 mg, *Emblica officinalis* 206mg, *Allium ascalonium* 82 mg, *Peucedanum graveolens* 82 mg.

RESULTS

All the patients were directed to continue with the no red meat, low sodium and potassium diet, limited quantity liquid intake and for diabetes the glucose content foods

Table 1: Paired samples correlations

		N	Correlation	Sig.
Pair 1	Before Treatment_S.Cr & After Treatment_S.Cr	31	.889	.000
Pair 2	Before Treatement_BUN & After Treatment_BUN	28	.662	.000
Pair 3	Before Treatment_S ALB 1 & After Treatment_S ALB	22	.539	.010

Table 2: Paired samples test

		Paired Differences					T	df	Sig. (2-tailed)
		Mean	Std. Deviation	Std. Error Mean	95% Confidence Interval of the Difference				
					Lower	Upper			
Pair 1	Before Treatment_S.Cr - After Treatment_S.Cr	.23097	2.06914	.37163	-.52800	.98993	.622	30	.539
Pair 2	Before Treatement_BUN - After Treatment_BUN	7.932	22.073	4.171	-.627	16.491	1.902	27	.068
Pair 3	Before Treatment_S ALB 1 - After Treatment_S ALB	.011	.442	.094	-.185	.207	.121	21	.905

allowed but in limited quantity according to plasma glucose values. Instructions were given to avoid other medicinal chemical agents during the treatment. Instructions to maintain hygiene were given to all the patients to prevent reinfection.

Assessment of effectiveness

Effectiveness of the treatment was assessed on the basis of:

1. Clinical improvement disappearance or relief of symptoms, improvement in general health.
2. For the effective assessment and evaluation, disease intensity scores were also maintained. After completion of treatment, disease intensity of the post treatment scores were compared with the pretreatment disease intensity score and statistically evaluated.

Distribution of age

Age distribution of the patients was given in fig 1 and 2.
In a trial, effect of coded herbal formulations AJMAL06 daily depending on the age and severity of infection was investigated on a total of 35 patients suffering from CRF.

DISCUSSION

Various medical scientist and researcher are owing to develop treatment strategy for CRF but still it is not possible to get relief from this ailment except dialysis that can give support for survival but not cure. Zhong and colleagues reported traditional Chinese medicinal herbs (MSCT) are often used in combination with western drug therapy for the treatment of chronic kidney disease (CKD) in China and many other Asian countries used. However, the level of the throat TCHM is limited to small non-randomized studies. Due to variations in prescribing patterns TCHM and the need for frequent dose adjustments, which are inherent in the practice of traditional Chinese medicine, which has been a challenge to design and implement large-scale randomized clinical trials TCHM. TCHM number associated with significant side effects, including nephrotoxicity. However, the reporting of adverse effects associated with TCHM has been inadequate (Zhong *et al*. 2013).

Kara has indicated that a number of drugs and herbal products that are used by patients with chronic renal failure in treating some symptoms such as high blood pressure, insomnia, or muscle cramps (Kara, 2006).

Nowack and coworkers reported that induced remission of nephrotic syndrome due to membranous nephropathy (MN) Astragalus membranaceus by nephrologists have drawn attention medicinal plants as an alternative treatment of glomerulonephritis. Most of these herbs are in current clinical use in China and looks promising for modifying immune processes have components in glomerulonephritis. However, its use in patients who are not yet represented clinical trials in accordance with international quality standards have not been conducted and toxic risks have not ruled out with sufficient control (Nowack, *et al*. 2011).

Peng reported that the accumulated evidence that some Chinese medicinal herbs including Astragalus and a mixture of Astragalus and Angelica, Ligusticum, triptolide and rhubarb, a device for slowing the progression of CKD paper. This effect is multi-functional and multi-specific and is often associated with a reduction in proteinuria and dyslipidemia relief but not to changes in systemic blood pressure. These mechanisms include anti-inflammatory and inhibition of TGF-b. On the other hand, some herbal medicines can be dangerous for patients with renal disease. In this paper we discuss recent advances in the study of some Chinese herbs for pharmacological intervention of progressive kidney disease and kidney damage (Peng *et al*., 2005).

Chronic renal failure is a major problem in modern society. Herbal medicine used to prevent the need for dialysis addition to treating the causes and effects of kidney failure as well as reducing the many negative effects of dialysis itself. Botanicals are to be treated for kidney failure: *Rheum palmatum* (Chinese rhubarb, since Huang), *Distachya ephedra* (Ephedra) strain, *thunbergii Geranium* (Geranium Thunberg) root, *Cinnamomum cassia* (Cassia) cortex, *Da Huang Bao Yuan Tang* (Decoction Panax ginseng [Asian ginseng] root, *Astragalus membranaceus* [talus] root, cassia bark, *Glycyrrhiza uralensis* [licorice] root and Chinese rhubarb), *Lespedeza capitata* (lespdeza round head), milk thistle (*Silybum marianum*) of seeds, *Urtica dioica* (nettle) seeds, *Parietaria judaica* (glass grass-de-la-wall) grass, (Java tea) *chinensis Cordyceps* (Cordyceps, Cordyceps), *Centella asiatica* (Gotu Kola) and Capsicum spp. (Cayenne) (Peesa, 2013).

It was reported that WH30 + is more effective in preventing acute renal failure, chronic renal failure (Ruggenenti, Cravedi *et al*. 2012). It was observed that there is a marked improvement in overall subjective signs and symptoms when treated with AJMAL06. There was a noticeable improvement in leg pain, nausea/ vomiting, fever and fatigue, which are the most common symptoms of CRF. According to the statistical analysis total 35 patients of Chronic Renal Failure were put on the coded formulation AJMAL06 improvement found in 20 or (70%) and 15 or (30%) patients did not respond to the therapy. Chi-Square test was applied and two-tailed p-value was calculated as 0.0452 (<0.05) which indicates that the efficacy of the Ajmal06 in the lowering of serum creatinine in Chronic Renal failure Patients.

Clinical response

BUN

It was found that test drug shown 75% improvement and 25% of the patient with complain of BUN did not show any improvement. The overall effect of AJMAL06 was satisfactory and significant *p* value when compared before and after treatment as shown in table 1and graph 3.

Whiteheads are commonly found in the patients of CKD. The values presents that the complaint of Fatigue was improved. The use of AJMAL06 was effective in 70% patient and ineffective in 30% patients (p=<0.05).

Edema

Complain of Edema completely improved in 90% of the patient and not improved in 10% of the patients were noticeable. Overall the result and data showed that herbal formulation AJMAL06 is effective (p=<0.001) as shown in table 2 and graph 3.

Leg pain

The complaint of Leg pain shows that 82% of the patients treated by the AJMAL06 were completely improved and no response shown in about 18% of the patients. The control drug was completely effective in 76% of the patients while in 24% of the patients there was no noticeable effect shown. It was analyzed that AJMAL06 was more effective than control drug in patients having complain of pustules (*p*=<0.05) as shown in table 8, Graph 8.

By comparing all these sign and symptoms of CKD and being treated with coded herbal formulation AJMAL06 observed that the drug has shown efficacy in treating the CKD. The *p* value calculated is 0.2971. It is shown in the table 2.

To lower high creatinin level is enormously cared about by the kidney diseases patients can be achieved by diet, monitoring blood chemistry, immunotherapy treatment. A careful analysis is obtained before the predialysis such as creatinin estimation urea estimation and it is advisable that before taking any step, it is always better to opt for poly herbal treatment. Advise patients with renal failure to discuss their condition with any herbal physician who intends to prescribe a new medication for their inter actions. The potentially useful herbal interventions, it is important to note that there are other important considerations in treatment of patients with renal failure low-protein diets, blood pressure control and use of anti-inflammatory and anti-oxidant herbal medicaments. In a difficult condition when in the renal complication are in compound form with other malaise, this therapy can be hopeful and promising. In fact many of these herbs as have been used have novel mechanism of action that could yield benefit results.

CONCLUSION

It is concluded that alternate hypothesis (H2) was accepted for this clinical evaluation study. The coded herbal formulation AJMAL06 showed efficacy and exhibited significant improvement and p value was found to be >0.05. There were no untoward side effects or drug reaction in case of AJMAL06.

REFERENCES

Humphreys BD, Forman JP, Zandi-Nejad K, Bazari H, Seifter J and Magee CC (2005). Acetaminophen-induced anion gap metabolic acidosis and 5-oxoprolinuria (pyroglutamic aciduria) acquired in hospital. *Am. J. Kidney Dis.*, **46**(1): 143-146.

Isakova T, Xie H, Yang W, Xie D, Anderson AH, Scialla J, Wahl P, Gutiérrez OM, Steigerwalt S, He J, Schwartz S, Lo J, Ojo A, Sondheimer J, Hsu CY, Lash J, Leonard M, Kusek JW, Feldman HI and Wolf M (2011). Fibroblast growth factor 23 and risks of mortality and end-stage renal disease in patients with chronic kidney disease. *Jama.*, **305**(23): 2432-2439.

Jafar TH and Agarwal SK (2012). A decade after the KDOQI CKD guidelines: A perspective from south Asia. *Am. J. Kidney Dis.,* **60**(5): 731-733.

Kara B (2006). The effect of herbal products on chronic renal failure. *Gulhane Medical Journal*, **48**(3): 189-193.

Nowack R, Flores-Suarez F, Birck R, Scimitt W and Bank U (2011). Herbal treatments of glomerulonephritis and chronic renal failure: Review and recommendations for research. *Journal of Pharmacognosy and Phytotherapy*, **3**(9): 124-136.

Nugent RA, Fathima SF, Feigl AB and Chyung D (2011). The burden of chronic kidney disease on developing nations: a 21st century challenge in global health. *Nephron Clinical Practice*, **118**(3): c269-c277.

Peesa JP (2013). Nephroprotective potential of herbal medicines: A review. *Asian Journal of Pharmacy and Technology*, **3**(3): 115-118.

Peng A, Gu, Y and Lin SY, (2005). Herbal treatment for renal diseases. *Ann. Acad. Med. Singapore,* **34**(1): 44-51.

Ruggenenti P, Cravedi P and Remuzzi G (2012). Mechanisms and treatment of CKD. *J. Am. Soc. Nephrol.,*, ASN. 2012040390.

Sievert DM, Ricks P, Edwards JR, Schneider A, Patel J, Srinivasan A, Kallen A, Limbago B and Fridkin S (2013). Antimicrobial-resistant pathogens associated with healthcare-associated infections summary of data reported to the National Healthcare Safety Network at the Centers for Disease Control and Prevention, 2009-2010. *Infect. Cont. Hosp. Ep.,* **34**(01): 1-14.

Zhong Y, Deng Y, Chen, Y, Chuang PY, Cijian He J (2013). Therapeutic use of traditional Chinese herbal medications for chronic kidney diseases. *Kidney International*, **84**(6): 1108-1118.