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Ayurveda

AYURVEDIC MANAGEMENT OF CHRONIC RENAL FAILURE: A NON RANDOMIZED AYURVEDIC CLINICAL TRIAL

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ABSTRACT Chronic Renal Failure is a syndrome affecting the kidneys, in which there is a gradual, progressive and **irreversible decline in kidney function** over a period of time. A non randomized, open labeled Ayurvedic clinical trial was conducted on 50 study subjects of Chronic Renal Failure. A package of 13 Ayurvedic herbal drugs was given. There were 6 cycles of 28 days each were administered in 180 days. On the basis of eGFR calculated as per CKD-EPI equation there were 39/50 **(78%) study subjects having CKD stage 5**, there were 9 (18%) study subjects having CKD stage 4 & 2 (4%) study subjects with CKD stage 3B. Thus all the study subjects were having very poor renal function that is considered to be irreversible damage as per Modern medicine. On completion of 6 months Ayurvedic treatment, there was shift of CKD stage 5 to 29 & 30.76 % by MDRD & EPI equations respectively to stage 4, 3 B, 3A and 2. This study has proved that even with CKD stage 5, the kidney function was restored and CKD stage 5 subjects were maintained without dialysis in due course of treatment. This study has shown that Ayurvedic management of CRF is a noteworthy alternate therapy to the Renal Replacement Therapy. The modern science has to note that CRF is no more irreversible but just a myth. Ayurveda has got a specific answer to treat CRF effectively.

KEYWORDS : CRF, CKD-5, dialysis, irreversible, myth, Ayurveda,

INTRODUCTION:-

Chronic Renal Failure (CRF) is a syndrome characterized by progressive & irreversible deterioration of renal function due to slow destruction of renal parenchyma, eventually terminating in to death when sufficient number of nephrons are damaged [1] .That stage is termed as End stage Renal Disease (ESRD) which render the patient permanently dependent upon Renal Replacement Therapy -RRT (dialysis or transplantation) in order to avoid life threatening uremia[2]. Chronic Kidney Disease (CKD) is the most used term globally and CRF corresponds to 3-5 stages of CKD. Chronic renal failure is reported to be a silent epidemic[3]. It is a global threat to health in general and for developing countries in particular, because therapy is very expensive and life-long [4] It is a matter of concern for all of us that prevalence of diabetes, hypertension and associated risk factors such as obesity, hypercholesterolemia and the metabolic syndrome increasing [5]; which along with increased life span of persons facilitate sustained and explosive growth of this epidemic. India is a prospective global capital of Diabetes. Approximately 30-40% of patients with Diabetes mellitus develop in to diabetic nephropathy and with the growing number of DM patients and increasing life span of population, as prevalence of CKD is higher in older people [6]; there is likelihood of commensurate increase in the incidence of CKD. There was one study conducted by Singh Ajay Kumar et al across 12 cities in India & reported that 17 out of every 100 people living in cities were suffering from some form of kidney disease [7]. This study alerted everyone that the incidence of CKD had attained enormous proportion in India.

It is irony that though RRT is cheapest in India, 90% of Indian population does not afford it. Among those study subjects who start haemodialysis, 60% are lost to follow-up within 3 months[8-9]. Subjects on RRT have poor quality of life [10], and there is high mortality among subjects on Haemodialysis [11]. In India only 4% need of Kidney transplantation is met. Thus modern Medicine has very limited options & low capacity to treat ESRD. Therefore it is essentially required to develop an alternate line of treatment that will obviate the need for RRT.

AIM:- To break the established myth that CRF is irreversible.

OBJECTIVE:-To maintain CKD-5/ ESRD study subjects on Ayurvedic therapy without dialysis.

MATERIAL & METHODS:-

Type of Study:-Clinical trial:- Open labeled Prospective study design- a systematic non randomized clinical trial Phase- I.

Place of study:- This Clinical Trial was conducted at Seth Tarachand Hospital of Tilak Ayurved College, Pune.

Study period:- June 2012- Aug 2016

Sample size: 50

Approval by ethical committee: This Clinical trial for PhD research work was duly approved by Ethical committee of Tilak Ayurved College, Pune on 7.10.2010.

Case definition:- A case is labeled as C.R.F. when Serum Creatinine value was > 1.8 gm/dl & Blood urea > 50 mg/dl and the values were raised for at least 6 months.

Inclusion Criteria:-

1. Any patient of diagnosed CRF due to varied etiology for last 6 months duration.
2. Age: More than 18 years
3. Sex: Either sex
4. Serum Creatinine level: > 1.8 mg ,Blood Urea : > 50 mg% for last 6 months
5. Hypertension with Diastolic BP: < 130 mm
6. Study subjects with and without on Dialysis
7. Study subjects willing to participate in the research project:

Exclusion Criteria:-

1. Patient with malignant Hypertension having > 130 mm diastolic BP
2. Renal Artery Stenosis
3. Neoplasm of kidney
4. History of previous Kidney transplant
5. Adult polycystic Kidney disease.
6. Uncontrolled arrhythmia or severe cardiac disease within the past 6 months

Standardization of individual ingredients and combination products of Shodhan chikitsa (i.e. Mrudu virechan), Tikta ksheer basti, Kasnyadi yog choorna and other Anupan drugs was carried out at Centre for P.G. studies and Research in Ayurveda, Tilak Ayurved Mahavidyalaya. Pune as per API Guidelines on 25.5.2012.

Consent: Informed consent for as per ICMR guidelines (bilingual) was obtained from study subjects before trial.

Investigations:-

1. Baseline investigation Examination.

a. Following investigations were carried on zero day:-

I) Complete Haemogram
ii) Blood sugar fasting & P.P.
iii) RFT-Serum Creatinine, Blood urea
iv) LFT
v) Serum electrolytes-K^{+}Na+,Ca^{++}
vi) Lipid profile
vii) Urine RE & microscopic.
viii) USG abdomen- Kidney, Liver, etc

- Serum Ceatinine, Blood urea, Urine RE, urine output were repeated on 28, 84, 140th and 180th day.
- LFT, Lipid profile, blood sugar was repeated, only when found abnormal.
- USG abdomen was repeated after end of study period wherever possible.
- Clinical signs and symptoms of CRF were assessed at every follow-up visit.

Treatment procedure:-

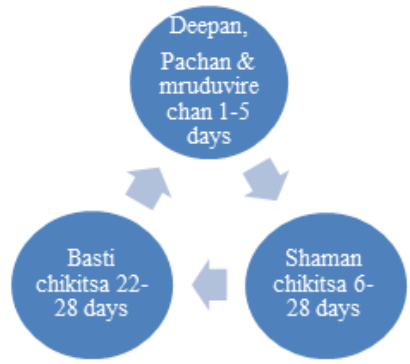
while giving treatment to patient, the Rog, Kosta, Rugna bal, Ayu, Desh, Kal etc. has to be taken in to account. In view of the Rog/advanced stage of CKD and weak Rugnabal in subjects, we avoided Rakta mokshanadi Shodhan chikitsa., Diet/Aahar, Lifestyle/Vihar, and following 13 drugs according to their therapeutic action have been used in the present study. The principles of therapeutic actions were *Agnipradeepak (Appetizer), Pachak, (Digestible),Virechak (Laxative) Raktashodhak/ Raktaprasadak (Blood purifier), Shothaghna, (Reducing oedema) Swedal (Sweating stimulator), Anulomak (Promoting downward direction of Vata)* and *Dhatu bal- vardhak (Nutritive & rejuvenating).*

Table No.1 Particulars of Ayurvedic drugs used in the clinical trial

Sr. No.	Name of Herb	Botanical name	Part used	Form	Proportion
1)	Pippali	*Piper longum*	Fruit	Choorna (Powdered form)	500 mg
2)	Erand patra	*Ricinuis communis*	Leaves	Swaras (Juice)	20 ml
3)	Ashmantak	*Bauhinia racemosa*	Bark	Bharad (Coarse) in Quath	Equal part in Quath 500 mg in Kasanyadi choorna
4)	Kasni	*Cichorium intybus*	Whole plant	Choorna & Bharad in Quath	
5)	Gokshoor	*Tribulus terrestris*	Fruit	Choorna Kasanyadi yog	500 mg
6)	Sariva /Anant mool	*Hemidesmus indicus*	Root	Choorna in Kasanyadi yog	500 mg
7)	Amra Haridra	Curcuma aromatica	Underground stem	Choorna in Kasanyadi yog	500 mg
8)	Amalaki	*Emblica officianalis*	Fruit	Choorna in Kasanyadi yog	500 mg
9)	Palash	*Butea monosperma*	Flower	Choorna in Kasanyadi yog	One part
10)	Punarnawa	*Berhaavia diffusa,roxb*	Root	Choorna in Kasanyadi yog & Bharad in Tiktakshir basti	500 mg One part
11)	Guduchi	*Tinospora cordifolium*	Stem	Bharad in Tiktakshir basti	One part
12)	Musta	*Cyperus rotundus*	Underground stem	Choorna & Bharad in Tiktakshir basti	One part
13)	Pashanbhed	*Coleus aromaticus*	Stem	Bharad in Tiktakshir basti	One part

All of them fall in one or other categotry of Aapya (Jala Mahabhut predominant), Srotoshodhaka & Bhedana Mutral drugs/ Diuretics [13].

Ayurvedic line of treatment in present study 28 days cycle × 6 cycles



Deepana, Pachan & Mrudu Virechan chikitsa:- Pippali (*Piper longum*) choorna 500 mg with tender Erand patra (*Ricinuis communis*) swaras 20 ml, early morning on empty stomach for 5 days. This was repeated for every consecutive month for a total period of 6 months.

Aahar:- The study subjects were asked to eat well cooked Moong dal / 5-10 g old Gud per day along with Jowar roti in these 5 days. They were asked to drink *Koshna jal (*warm water) panarth. This was repeated for every consecutive month till 6 months completed.

To Lekhan (pacify) Kapha & Pitta (Vamak, Virechak & Lekhaniya dravyas) the herbs to be used are to be administered only in the morning[14].

The properties of old Gud (jaggery) without chemicals are reducing Kapha dosha, helps to excrete mala- mutra easily, Ruchikar (Appetiser) and pathyakar (useful to the body).

b) Shaman/ Raktaprasadak chikitsa :-

Shaman:- It brings back *Visham doshas* in *Samaawastha*.

Shaman is caused by combined effect of Rasayan, Mutral, shothghna & Rakta prasadak dravyas.

Constituents of Kasnyadi yog choorna:-

Kasni (Cichorium intybus)	500 mg
Sariva (Anant mool/ Hemidesmus indicus)	500 mg
Punarnawa (Boerhaavia diffusa,roxb)	500 mg
Gokshoor (Tribulus terrestris)	500 mg
Amra Haridra (Curcuma aromatica).	500 mg
Amalki (Emblica officianalis)	500 mg
Palash (Butea frondosa Koen)	500 mg

Anupan- Ashmantak (*Bauhinia Racemosa)* & Kasni (*Cichorium intybus*) quath 50 ml twice daily from 6th to 28th day every month for 6 months

Above ingradients were used mixed with Ashamantak & Kasni quath 50 ml. twice daily from 6th to 28 th day every month for 6 months as Anupan.

c) Basti chikitsa (Medicated enema):- Basti chikitsa is unparalleled in elimination therapy, as it expels vitiated Doshas rapidly & easily from the body and also causes reducing as well as nourishing the body very quickly.

Vata is the main factor responsible for causation of many diseases and takes an important part in metabolic functions of the body. To alleviate Vata, Basti chikitsa (Medicated enema) is the best line of treatment. Basti chikitsa is very commonly used in many diseases; it is mentioned by granthkaras as half to full chikitsa.

Though *Vaman & Tivra virechan* also eliminate the vitiated doshas from the body, the drugs used in those therapies contain *Katu-rasa, Ushna & Tikshna gunas*, which may not be advised to children & old persons. But basti chikitsa can be given to all age groups without any risk.

Tikta Kshir Basti:- Ingradients:- Guduchi (*Tinospora cordifolia*),

Punarnawa (*Boerhaavia diffusa,roxb*), Musta (*Cyperus rotundus*), Pashan Bhed (*Coleus aromaticus*) siddha kshir was prepared as per text. We took Guduchi (*Tinospora cordifolia*), Punarnawa (*Boerhaavia diffusa,roxb*), Musta (*Cyperus rotundus*), Pashan Bhed (*Coleus aromaticus*) . Tiktakshir for basti was prepared as per Kshir pak method as follows:- 1 part crude ingredients + 100 ml. cow's milk +400ml. water boiled & reduced to 100 ml. This 100 ml tiktakshir (medicated milk) was given slowly per rectum by drip method through No.9 catheter.

Procedure of Tiktakshir basti

Pathya- apathya:-

The study subjects were asked to consume warm water **(Ushnodak pan)** as per need as mentioned by **Sharangdhar**[15]**.** Warm water is pacifying *kapha, Aamvata, Meda*, acts as *Deepniya* increases the Agni (*Kshudha*/Appetite), and Basti-*shodhana.* It acts to reduce cough, Dyspnoea & fever. Similarly, **Vagbhat** also mentioned the effect of *Ushnodak*. [16]Ushnodak acts as *Deepak, pachak, laghu, mutrashodhak & beneficial to kanthrog, uchaki, (hiccough) udar adhaman, Vat, kaph, navjwar, kas, Pinus, Ajeerna, shwas, parshwa shool* etc as well who take *virechaniya dravyas*. Therefore *Ushnodak* was used for all study subjects in the present study. In CRF there are symptoms of *Mandagni, Pandu*/ Anemia, *Shoth*/Oedema commonly seen. Therefore restriction of water was advised.

Aahar/Diet:- *Laghu, Supachya* aahar i.e. easily digestible was directed to be consumed. Lahya (puffed jowar), Moong dal, Jowar bhakri/roti, vegetables growing on creepers like pumpkin, snake gourd, sponge gourd, Bitter gourd, Shigru (drumstick) baked cereals were asked to be consumed along with Jawar bhakri.

ASSESSMENT CRITERIA:-

1) **Criteria for Clinical Improvement:-** Reduction in severity of symptoms
2) **Laboratory improvement**
1) Reduction in Serum Creatinine level & Blood urea level
2) Decrease in Proteinuria
3) Reduction in Anaemia

3) Follow-up shedule for Biochemical tests:-

There were 4 follow-ups on 28 days, 84 days, 140 days & 180 days

Evaluation of Treatment Outcome:-Management of study subjects without dialysis.

Excellent improvement: > 90% subjects with CKD 5 stage maintained without dialysis

Good improvement: 75-90% subjects with CKD 5 stage maintained without dialysis

Satisfactory improvement:- 50-74% subjects with CKD 5 stage maintained without dialysis

Average improvement: 10-49% subjects with CKD 5 stage maintained without dialysis

Poor improvement: <10% subjects with CKD 5 stage maintained without dialysis

Medication & Treatment permitted:- Study subjects stabilized on allopathic treatment of Diabetes and Hypertension, were permitted to continue the medication as advised by physician. The doses of these drugs were reduced later when there is visible improvement in patient's condition corroborated by biochemical tests.

Statistical analysis: All data analysis was carried out using the Statistical Package for Social Science (SPSS, version 20). $p < 0.05$ was considered as statistically significant.

RESULTS AND DISCUSSION:-

68 study subjects were enrolled for the study. one young subject opted out for kidney transplant, 2 subjects died one due to Heart failure & another due to multi organ failure. 50 study subjects successfully completed the treatment, with the treatment completion rate nearly 74%.

Table No 2: Age & sex-wise frequency distribution of study subjects

Age group	Male	Female	Total
18-25	1	2	3
26-33	3	2	5
34-41	7	1	8
42-49	3	2	5
50-57	4	5	9
58-65	7	8	15
66-73	4	0	4
73 & above	1	0	1
Total	30	20	50

Status of mean Age of study subjects:- In the present study, the mean age of the total study subjects was **49.8** years with **± 15.20** S.D. The range was 20 years to 81 years. As there is wide variation in the range, the **median was 54 years** and was adequately representative of the age of study subjects. The mean age group was lower than the studies conducted in developed countries. It is clarified here that the study subjects had a mean period of 1.735 years (nearly 21 months) of since they had suffered CRF when they were included in the study. Thus the mean age of study subjects while entering in CRF/ ESRD was 48.065±15.556 years and therefore, it was comparable to the findings of the many of the studies carried out in the country.

In the present study there were 30 (60%) of males while there were 20 (40%) of female study subjects. In many studies it was a common finding denoting male preponderance over females in CRF. **Dervla M. et al** [17]**,** reported similar finding in one study carried out in Ireland where they observed male preponderance of 59.5% in CKD patients.

In the present study majority of study subjects i.e. 94% belonged to Upper or upper middle class, only 6% belonged to middle middle class. There were no study subjects from lower middle or lower class. These findings substantiate the findings of Sakhuja & Kohli [18], who observed that 90% study subjects with CKD do not report and those include mostly the under privileged & persons below poverty line. This is probably the reason why lower middle & lower class study subjects were not represented.

Duration of CRF:- The mean period of suffering from CRF was 1.735 year (20.82 months) with range 6 months to 8 years and median was 1 year. The S.D. was ±1.61. There were 34% of study subjects were suffering from CRF for six months to 1 year, while 58% were suffering from 1-5 years and only 4 subjects (8%) suffering from >5 years.

Dialysis status of study subjects on admission:- There were 24 study subjects undergoing dialysis for a period from minimum 2 weeks to maximum 3 years. The average period on dialysis was 8.54 months. There were 7 study subjects who were advised to start dialysis but came to the researcher after knowing that there is an alternative to dialysis available in the form of Ayurvedic treatment & they willingly participated in the study.

There were 24 study subjects (48%) having diabetes. Out of them 15 study subjects were having diabetes for a duration less than 10 years of duration, while there were 9 study subjects having diabetes for more than 10 years. The mean duration of diabetes was 10.16 years, having range 1-28 years and median was 9.5 years. S.D. was ±6.64 years.

Hypertension:- The majority of study subjects, 32 (64%) were having H/o hypertension. There were 26 (52%) study subjects having Hypertension for duration less than or equal to 10 years, while The mean duration of hypertension was 4.36 years with range 0 to 28 years and median was 3 years, S.D. ±6.39.

A) Primary End points: 1) Reduction in Serum Creatinine & Blood urea:-

I) Reduction in Serum Creatinine level:- Serum Creatinine is the most important diagnostic tool to label a case as CRF. Measuring serum creatinine is a simple test, and it is the most commonly used indicator of renal function.

The normal serum value is 0.5 to 1.2 mg/dL. Any value above the normal value is indicative of deranged function of kidney. If Serum Creatinine is above 3 mg/dl the CRF is considered as irreversible & if it is more than 5-6 g/dl metabolic acidosis may ensue [17].In the present study minimum Serum Creatinine value of 1.8 mg/dl was decided to label a case as CRF as reported by Sakhuja & Kohli [18].

The mean Serum Creatinine value before start of treatment was 7.37 mg/dl, SD ±3.90, with range 2.19 to 21.6 mg/dl and Median 6.80 mg/dl. However, after 6 months of treatment Serum Creatinine mean value was reduced to 3.92 mg/dl, SD ± 1.88 with range 0.9 to 8.1 mg/dl and Median 4.265. Thus there was **46.81% net reduction** in mean value of serum Creatinine. We applied Student's paired't' test and the difference on 0 day & at 180 day was found to be statistically **highly significant as p < 0.001.** Not only this, there was statistically highly significant reduction in serum creatinine value noted from first follow up onwards itself on 28th day, second follow up on 84th day and 3rd follow up on 140th day.

Prashanth GS et al [19], reported increase in Serum Creatinine in group A & B, while there was no change observed in group C. Thus the superiority of Ayurvedic treatment could not be established. In the present study there was statistically highly significant reduction observed in Serum Creatinine and proved to be definitely effective line of treatment.

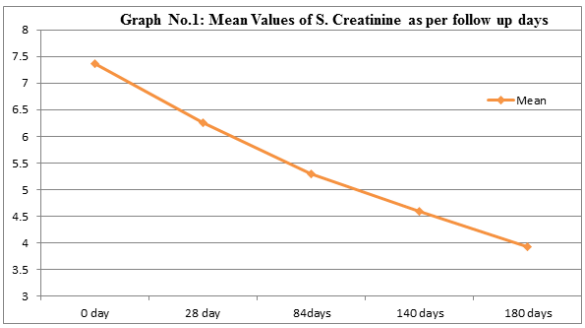


Table No. 3: Paired sample statistics of Serum Creatinine

Pair No.		n	Mean	Std. Deviation	t value	p value (2-tailed)
Pair 1	0 day	50	7.3732	3.90596	8.204	0.000
	28 day		6.2540	3.32565		Highly Significant
Pair 2	0 day	50	7.3732	3.90596	9.870	0.000
	84days		5.3012	2.73843		Highly Significant
Pair 3	0 day	50	7.3732	3.90596	9.695	0.000
	140 days		4.5988	2.25458		Highly Significant
Pair 4	0 day	50	7.3732	3.90596	10.231	0.000
	180 days		3.9290	1.87817		Highly Significant

ii) Reduction in Blood urea level:- In spite of its limitations, next to Serum Creatinine, Blood urea is an important indicator that gives fair idea of severity of CRF. In the present study the minimum Blood urea value to label a case as CRF was defined as ≥ 50 mg/dl. The mean Blood urea was 108.61 mg/ dl (more than double of normal value) with S.D. ±41.07. On initiation of present Ayurvedic treatment, the Blood urea started reducing, with the result that by 180 day Blood urea value was reduced to more than half, 53.31 mg/dl with S.D. ±.13.08. This reduction in Blood urea level was found to be statistically highly significant. Not only this, there is statistically highly significant difference in Blood urea at 0 day, at 28th day, at 84th day, at 140th day & at 180th day. It shows that the present line of Ayurvedic treatment started showing results from the first follow up itself.

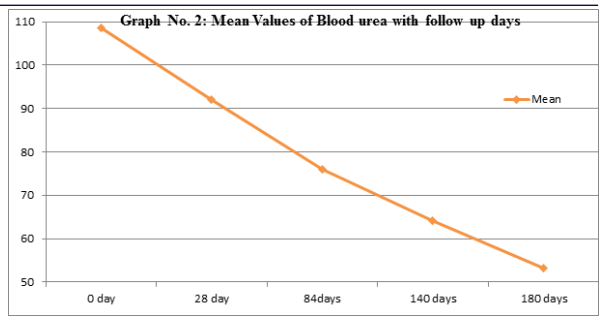


Table No. 4: Paired Sample statistics of Blood urea

Paired Samples Statistics						
		N	Mean	S.D. ±	't' value	'p' value
Pair 1	0 day	50	108.6120	41.07399	7.934	0.000 Highly Significant
	28 days	50	92.1440	37.23639		
Pair 2	0 day	50	108.6120	41.07399	11.572	0.000 Highly Significant
	84days	50	76.0500	28.27374		
Pair 3	0 day	50	108.6120	41.07399	12.577	0.000 Highly Significant
	140 days	50	64.1040	21.70729		
Pair 4	0 day	50	108.6120	41.07399	11.912	0.000 Highly Significant
	180 days	50	53.3160	13.07569		

df= 49

2) Decrease in Proteinuria, Reduction in Anemia, Restoration of Quality of life, Cost effective therapy:- There was statistically significant reduction in Proteinuria, Anemia, Restoration of QOL, Cost effective therapy 11.16 times cheaper than Haemodialysis, will be addressed separately in separate papers.

3) Reduction in symptoms:- In the present study, there were 12 study subjects who reported Ati mutra alpata/ **Anuria** at the time of their admission. They were already on dialysis for quite some time and their urine output was < 100 ml. There were 22 study subjects having Mutra-alpata/ **Oliguria** (Urine output < 400 ml) at the beginning of present study. There were none subjects with Mutra-alpata/ Oliguria from 112th day onwards. In the present study drugs that removed Strotorodh, increased urine production- mutra virechak drugs like Gokshur, Punarnawa, Erandpatra, Sariva, Pashanbhed, Amalki, Guduchi were used and they produced the desired effect by enabling the kidneys to raise its GFR and produce increased urine production. The present study has shown that Ayurvedic treatment has the potential to give the nephrons strength to recover from the so called irreversible damage and resume their function. Thus it has finally broken the myth that once kidney reached CKD stage 3- 5 it is irreversible. This study has proved that such irreversible stage can be reversed by Ayurvedic treatment and CKD -5 subjects were maintained without dialysis.

Table No. 5: Summary of Reduction in symptoms with test of significance

Sr. No.	Name of Symptom/ Sign	95% subjects free from symptom on day	Chi square value by Friedman's test	p value
1.	Thirst	112	287.422	.000
2.	Mutra- alpata/ Oliguria	84	93.668	.000
3.	Ati Mutra- alpata/ Anuria	56	72.545	.000
4.	Hematuria	112	64.998	.000
5.	Dysuria	56	83.764	.000
6.	Burning mocturition	112	269.267	.000
7.	Naktamutrata/ Nocturia	140	93.621	.000
8.	Fatigue	112	264.031	.000
9.	Paedal oedema	112	288.630	.000
10.	Puffiness over face	140	291.701	.000
11.	Anorexia	140	265.209	.000
12.	Dyspnoea	112	257.729	.000
13.	Nausea	140	271.149	.000
14.	Vomiting	84	251.732	.000
15.	Headache	84	204.105	.000
16.	Weakness	112	304.367	.000

17.	Lethargy	112	297.283	.000
18.	Drowsiness	84	181.751	.000
19.	Insomnia	84	212.116	.000
20.	Itching	84	229.598	.000
21.	Loss of Sweating	112 day	271.030	.000
22.	Quality of Life	180 day	322.920	.000
23.	Pallor	Significantly reduced on 180 day	204.724	.000
24.	Hypertension	Significantly reduced on 180 day	103.511	.000
25.	Proteinuria	Significantly reduced on 180 day	175.436	.000
26.	Anemia	Significantly reduced on 180 day	123.190	.000

n=50

Above table summarizes briefly the relief of 26 symptoms & signs on particular day of follow up with the statistical significance. It was observed that most of the symptoms were relieved by 112 days.

Increase in Urine output:- On 0 day, the mean urine output was 302.40 ml/ 24 hours ± S.D. 215.27, after completion of Ayurvedic treatment, mean Urine output was increased to 1063.50 ml/ 24 hours± S.D. 185.06. There was 251.68% increase in Urine output. This increase in urine output was found to be statistically highly significant during all the follow ups. t=26.99 on 180th day ($p < 0.001$).

Management of study subjects without Dialysis:-

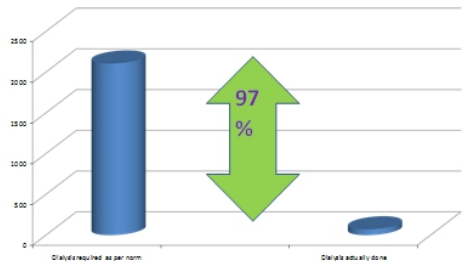
There were 24 study subjects undergoing dialysis for a period from minimum 2 weeks to maximum 3 years. The average period on dialysis was 8.54 months. There were 7 study subjects who were advised to start dialysis but rushed to the researcher after knowing that there is an alternative to dialysis available in the form of Ayurvedic treatment & they willingly participated in the study. Further, there were 8 study subjects in CKD stage 5 but were not put on dialysis. Their mean serum Creatinine was 6.09 mg/dl & median 5.95 mg/dl. All of them were having symptoms of Nausea, vomiting, anorexia which are early markers of uremia. They were maintained on Ayurvedic treatment without requiring a single dialysis. Out of those 24 study subjects who were on dialysis on admission, 13 study subjects did not require a single dialysis and were well maintained on Ayurvedic line of treatment in the present study. Thus there remained 11 study subjects, who required 70 episodes of dialysis. Out of these 11 study subjects, 9 were among those having Anuria & 2 of them were having Oliguria. They required minimum 3 and maximum 11 episodes of dialysis i.e. range 3-11 during the present study. The Average dialysis episodes required per study subject out of these 11 subjects was 6.36. It is clarified here that the study subjects were on dialysis for quite some period and their renal function was very poor. They were having mostly Anuria. Their body was adjusted to the dialysis for quite some time. The effect was Ayurvedic treatment was slow & steady. The Ayurvedic line of treatment made the kidneys to start their function in gradual manner. We extended the period of dialysis gradually & within 3 months all the study subjects were free from dialysis. In the present study it was noteworthy to mention that all the 39 study subjects of CKD grade 5 could be maintained without dialysis. Thus 2036 episodes (96.68%) of dialysis were prevented. if we assume cost of one dialysis is Rs 1500/-, the total cost saved was Rs. 3054000/- . Further study subjects were saved from the frustrating side effects of dialysis, that cannot be quantified in money.

The criterion for measuring outcome of treatment was maintenance of subjects without dialysis, was kept if >90% subjects maintained without dialysis to label the treatment as excellent improvement. It is noteworthy to mention that all the study subjects including those who were undergoing dialysis earlier and all 39 subjects in CKD stage 5 were maintained without dialysis during the treatment. As per Assessment criteria, if > 90% study subjects were maintained without Dialysis, the outcome would be considered as 'Excellent'. In the present study all study subjects were maintained without dialysis in due course of treatment & this outcome was assessed as **Excellent improvement**. Thus the treatment may be considered as best treatment, fulfilling objective of the study.

Table No.6 :No. of dialysis prevented in CKD stage 5 study subjects and cost saved

Category CKD 5	No.	No. of Dialysis required as per norm 2-3/wk in 6 months	No. of Dialysis done	No. of Dialysis avoided	Cost saved @ Rs 1500/- per episode of dialysis
Under dialysis	24	1326	70	1256	1884000
Dialysis advised but not willing @ 2/week	7	364	0	364	546000
CKD stage 5 not yet on dialysis but required as per norm @ 2/week	8	416	0	416	624000
Total	39	2106 100%	70 3.32%	2036 96.68%	3054000

Graph no. 3 : Episodes of Dialysis prevented



It is pertinent to note that not only the study subjects were maintained without dialysis but their urine output as well as eGFR was increased & there was shifting of CKD stages in upper (better stage of CKD), as mentioned below. There are 2 most commonly used methods of calculating eGFR i.e. by MDRD equation & by CKD-EPI equation. eGFR by both the methods is calculated & CKD stages of study subjects were calculated accordingly.

Table No. 7: Comparison of shifting of CKD stages by EPI & MDRD equations

		EPI equation		MDRD equation	
GFR ml/min	CKD stage	0 day	180 day	0 day	180 day
60-89	2	0	2	0	2
45-59	3A	0	8	0	7
30-44	3B	2	3	3	4
15-29	4	9	10	9	10
<15	5	39	27	38	27

This table compared the outcome of Ayurvedic treatment by estimating eGFR on the basis of using the most widely used EPI & MDRD equations. There were 39 subjects in CKD stage 5 as per EPI equation while there were 38 subjects in CKD stage 5 as per MDRD equation. There were 9 subjects each in CKD stage 4 in both the equations; however there were 3 subjects in CKD stage 3B as per MDRD while there were only 2 subjects in CKD stage 3B as per EPI equation.

Now if we compare the outcome distribution of study subjects by these two equations, it is clear from the above table that there was some similarities & differences noted in staging on 180th day; as there were 27 study subjects each in stage 5 in both the equation methods and 10 subjects each in stage 4, while there were minor differences in No. of study subjects in stage 3B & 3A study subjects. However in both of these methods, there was one similarity that, 2 study subjects could attain the stage 2 that may be considered as a great achievement of the study, as stage 2 is known as a very mild form of CKD.

Table No. 8: Comparison of eGFR by MDRD & EPI methods

eGFR by method	Mean on 0 day	Mean on 180 day	S.D. on 0 day	S.D. on 180 day	't' value	'p' value
MDRD	11	24.016	8.23	19.41	6.97	0.000
CKD- EPI	10.26	23.57	7.66	19.71	6.85	0.000

df=49

It was revealed that there was only slight of difference between the observations obtained in the eGFR values. It was observed that in the present study readings by both the methods were comparable. The present study established that EPI method works well even when the mean eGFR was < 15ml/min/ 1.73 m^2. Similarly MDRD equation did perform well when eGFR was more than 60 ml/min/ 1.73 m^2 and the figures for the 2 subjects who were shifted to CKD stage 2 were very much comparable by both the methods.

Table no. 9: Shifting of CKD stage 5 based on EPI equation

CKD stage 5 No.	39
Study subjects remained in same stage 5 after treatment	27
Study subjects after treatment shifted to CKD stage 4	9
Shifted to stage 3B	2
Shifted to stage 3A	0
Shifted to stage 2	1

According to CKD- EPI equation there were 39 study subjects in CKD stage 5, out of them there were only 27 study subjects remained in the same stage, though there was improvement in their eGFR value noted. It was clear from the table above that 12 (30.76%) study subjects shifted in upper stage i.e. 9 shifted to stage 4, 2 shifted to stage 3 B and one shifted to stage 2.

Table no. 10: Shifting of CKD stage 4 based on EPI equation

CKD stage 4 No.	9
Study subjects remained in same stage 4 after treatment	1
Shifted to stage 3B	1
Shifted to stage 3A	7
Shifted to stage 2	0

Similarly**,** there were 9 study subjects in CKD stage 4, out of them there was only one study subject remained in the same stage, though there was improvement in the eGFR value noted. It was clear from the table above that 8 study subjects (88.88%) shifted in upper stage i.e.1 shifted to stage 3B while, 7 shifted to stage 3 A and none shifted to stage 2

Table no. 11: Shifting of CKD stage 3B based on EPI equation

CKD stage 3B No.	2
Study subjects remained in same stage 3B after treatmen	0
Study subjects after treatment shifted to CKD stage 3A	1
Shifted to stage 2	1

Similarly**,** there were 2 study subjects in CKD stage 3B, out of them one study subject shifted to stage 3A, while, other shifted to stage 2. It is again substantiated & reconfirmed that if the present Ayurvedic line of treatment is started at an early stage- say at stage 3B, rather than starting it late at CKD stage 5 or 4, there are bright chances that kidney will respond more quickly & the damage is fully reversed.

Thus it is postulated that when the patient is detected at an early stage, the Ayurvedic treatment has a better prospects to bring the person in stage 2 that is considered as a very minor form of CKD.

It is mentioned by **William E. Mitch** [20] in Cecil Loeb textbook of medicine that one third of CKD stage 4 patients progress to ESRD within a period of 3 years. Due to the present Ayurvedic line of treatment 89% of study subjects in CKD stage 4 shifted to 3B & 3A. Thus the risk of landing in to ESRD in these subjects was totally prevented.

Similarly**,** there were 2 study subjects in CKD stage 3B, out of them one study subject shifted to stage 3A, while, other shifted to stage 2.

There were 21 study subjects having one/ both kidneys small in size. Only 5 study subjects of them repeated Sonography on completion of treatment, others did not repeat it. There was not much of a change noted in the size of kidney in 5 subjects on the post treatment sonography. So this indicator **did not prove to be conclusive.** However there was some encouraging improvement noted in the Cortico-Medullar differentiation**.** Where there was complete loss of CMD in 3 study subjects, before start of treatment, there was partial loss noted in 2 subjects & in one of them CMD seemed CMD well maintained as observed in post treatment sonography. This change in CMD is a pointer towards potential of present line of treatment on the reversal of microscopic changes in CKD stage 5, that what considered as irreversible by the Modern school of Medicine.

AYURVEDIC DISCUSSION:- In the present study Agnimandya (Anorexia) & Vat prakop were the two main factors responsible for the samprapti of CRF. The treatment outline was based on following lines:-

Nidan parivarjan /Remove cause
↓
Deepan- Pachan /Increase appetite & digestion
↓
Mrudu-virechan /Mild laxative
↓
Shaman (Langhan/ fast, Swedan,/Promote sweating/ Trishna nigraha/Water moderation)
↓
Vatanuloman (promote downward direction of Vata)
↓
Bruhan/ Rasayan Chikitsa (Rejuvenation therapy)

Samprapti bhang/ Reversal of pathology:- Factors causing dushti/ vitiated Rakta & Meda dhatu by *Aahar, Vihar, Aushdhi* and *Chinta, Shok, Bhayadi Mansik* hetus were dealt by Nidan parivarjan. In Samprapti of CRF *Agnimandya & Vatprakop* are the two crucial factors. The pathology behind renal diseases is disturbed Agni (metabolic Fire), due to which the food is not digested properly; undigested nutrients are toxic in nature and that is termed as Aam dosha. Aam dosha blocks micro channels, remains stagnant, accumulated in many sites giving rise to *Strotorodh*. Due to *Strotorodh*, formation of the vital components is disturbed.

Therefore the treatment was aimed to treat *Agnimandya (Jathragnimandya + Dhatvagnimandya*). Due to Agnimandya, *Aam nirmiti* occurs which creates *Strotorodh pradhan Vatprakop*. Therefore *Aam* was treated & *Strotorodh* was removed.

Charakacharya mentioned that Hetus / causes leading to *Agnimandya* are to be avoided by ***Nidan parivarjan.*** [21] This is *Upadesh tantra yukti* advocated by Charakacharya. As discussed earlier, the *Aahar, Viharaj & Pradhanik hetus* were pointed out to the subjects & were advised to make necessary changes in their lifestyle. Use of antibiotics, analgesics was stopped. Steroids were gradually withdrawn. It helped to reduce the Strotorodh.

In the present study*, Deepan, Pachan, Swedan, Virechan, Langhan and Tikta rasatmak- Raktaprasadak drugs (like Guduchi, Pippali, Musta, Sariva etc*), were used; *Tikta kshir basti* is *mrudu shodhan, Bruhan, Balya, Dhatuposhak, Dhatuvardhak chikitsa,* hence used in this study. The combined & synergistic use of them digested *Aam,* that helped to remove the Strotorodh. Due to removal of *Strothorodh in Rasvaha, Swedvah & Ambuvah strotas 'Vimargag Pitta returned to swasthan & Agni* was increased that removed the *Jathragni mandya & Dhatvagnimandya to create Sampraptibhang.* The Tiktakshir basti gave '*Abhyas tarpan*' to all Dhatus as mentioned by Charak.[22]. It was repeated of each cycle of 28 days for the treatment period of 6 months & that removed the *'Kha vaigunya*'of the Vrikka. In the present study we used *Deepaniya, Prameha- nashak, Raktaprasadak, Ruchya, Sar guna dravyas* that enhanced *sthanasth Agni* of Vrikkas (kidneys) to regain its function.

LIMITATIONS OF STUDY:- Measurement of Albumin & Creatinine in urine for calculating ACR (Albumin Creatinine Ratio) remained limitation of the study as guidelines were not there when the study was designed [23].

CONCLUSIONS:-

- There was 46.81% decrease in Serum Creatinine value & 51% decrease in Blood urea values. Both of these reductions in values were statistically significant from the first follow up. There was 251.68% increase in Urine output. This increase in urine output (more than 2.5 times) was found to be statistically highly significant.($p < 0.001$).
- On the basis of eGFR calculated as per CKD-EPI equation there were 39/50 **(78%) study subjects having CKD stage 5**, there were 9 study subjects having CKD stage 4 & only 2 study subjects

with CKD stage 3B. Thus all the study subjects were having very poor renal function that is considered to be irreversible damage as per Modern medicine**. This study has broken the myth that ESRD is irreversible**. There was shift of CKD stage 5 to the tune of 28.9 and 30.8% by EPI & MDRD equations respectively to stage 4, 3 B, 3A and 2. This study has proved that even with the CKD stage 5, the kidney function is restored with the result that all the study subjects with **CKD stage 5 were maintained without Dialysis in due course of treatment.**

- This study established that **when the patient is detected at an early stage, (say stage 3B or 4), the Ayurvedic treatment has a better prospects to bring the person in stage 3A & 2 .**
- It is pertinent to point out here that the both the study subjects who attained the stage 2 were Diabetics. It showed that the **Diabetic nephropathy was reversible & kidney function could be restored.**
- This study has given evidence that CKD-EPI equation works equally well with MDRD equation even when GFR was < 15 ml/ min/ 1.73 m^2.

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