

Treatment of early stage diabetic nephropathy using Siddha drug *Sirupeelai kudineer* - Single Case Study

Case Report

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Abstract

Background: Nephropathy is one of the major micro-vascular complications of Diabetes Mellitus, which can be detected in the earlier stage by the investigation of urinary microalbumin excretion level, estimation of ACR and GFR. The Siddha drug *Sirupeelai Kudineer* indicated for the complications of Diabetes Mellitus is selected for this Case study. The efficiency of the drug was reported by measuring the change in renal function over the period of study and the KD QOL assessment. **Case description:** A male patient of 62 years with the history of DM and hypertension since 20 years came to the hospital with complaints of bilateral pedal oedema, general weakness, frequent nocturnal micturition and weariness of limbs since last two months. His renal profile and glycaemic index was deranged (Serum Creatinine -1.42 mg/dl; Blood Urea -54.3 mg/dl; Urine Micro albumin -99.45mg/L; Urine Creatinine -74.8 mg/dl; ACR -15.02 mg/mmol; eGFR - 64.5 ml/min; BSL (Fasting) -157 mg/dl; BSL (Postprandial) -289 mg/dl). Patient was taking certain oral allopathic medicines and injection huminsuline 30/ 70 in the dose of 35 units before lunch, and 30 units before dinner subcutaneously. As per Siddha concept his three humours deranged and seen with the Clinical features of *Madhumega roga avathaigal* and *Neeradaippu*. He was given Siddha medicine *Sirupeelai kudineer*-120ml twice a day for the period of one month. Significant relief in symptoms and improvement in certain renal parameters was noted in the subject. **Conclusion:** The clinical and laboratory parameters in this case study suggest that this drug may be used along with other allopathic drugs in the treatment of Diabetic nephropathy patients.

Key Words: Siddha, Diabetic Nephropathy, *Sirupeelai kudineer*, Microalbumin, eGFR, Serum creatinine.

Introduction

Diabetic Nephropathy - impairment of renal function in Diabetic subjects is one of the challenging problems in the Medical field, increases the rate of mortality and morbidity. Approximately 20-30% of subjects with diabetes eventually develop Kidney disease (1). Diabetic Nephropathy is one of the micro-vascular complications of Diabetes leading to defective function of the kidneys with accumulation of waste products (particularly nitrogenous substances) in the blood. Renal insufficiency in chronic stage (for ≥ 3 months) is also known as Chronic Kidney Disease (CKD), persistence of which may results in end stage renal disease (ESRD); for which replacement therapy (dialysis or transplantation) becomes necessary, and is associated with complications in virtually of all organ

systems. Therapeutic interventions in the earlier stages may prevent or ameliorate some of these complications, as well as slows down progression to kidney failure.

Siddha Literature enlightens the complications of Diabetes (*Neerizhivu noi*) as ten types of *avathaigal* (2). The features mentioned in *avathaigal* depicts the clinical outcome of Chronic Kidney Disease. The manifestation of clinical features in final stage Diabetic Nephropathy includes oliguria, fatigue, anorexia, nausea, vomiting, itching and dryness of skin, drowsiness, numbness and swelling in the limbs, muscle twitching or cramps, bone pain, breathlessness, increased thirst, sleep disturbance and sexual problems.

The evidence for kidney damage is the reduction in Glomerular Filtration Rate (GFR) and identification of elevated levels of albuminuria or Proteinuria. Abnormal urinary albumin excretion and eGFR levels are being used to stage the Chronic Kidney Disease (CKD) as Stage A1, A2 A3 and G1 to G5 respectively (3). The prevalence of earlier stage CKD is higher and the treatment at these stages 1-3 is effective in slowing the progression towards kidney failure.

Abnormal albumin levels in urine can be detected in 30% of patients diagnosed with type 2 DM. Presence of protein in urine can speed up the development of the

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renal disorder and subsequently lead to end-stage renal failure. Albumin creatinine ratio in random urine samples is the most appropriate investigation to detect early renal impairment.

As there is lack of effective medicines in Conventional System, continuous search for agents which provide protection against the renal impairment caused by drugs is in progress. So it is better to seek for a safe and effective alternative remedy for the Management of Renal function in Diabetics. This fact intends to go for a native solution through 'Sirupeelai Kudineer for the management of Diabetic Nephropathy'.

The drug, *Sirupeelai (Aerva lanata)* is mentioned as *Pashana bedhi* and *Uppu chatthai nasamakki* in the Siddha text *Bohar Nigandu* 1200 (4). The other name of the herb in Siddha literature may also be an indicative of the removal of the metabolic waste products from blood. Hence the Nephro-protective activity of the herb *Sirupeelai (Aerva lanata)* has been pharmacologically evaluated in animals (5) after getting the acute toxicity study reports (6).

Review of Journals describes the antioxidant (7) and anti-diabetic activity (8) of the herb *Sirupeelai*. The major action of the herb *Sirupeelai* is Diuretic which is essential for the removal of stagnant impurities and water from circulation and functioning of kidney. Hence *Sirupeelai* drug is being selected for evaluation in this case of Diabetic nephropathy.

Case Presentation

A male patient of 62 years already diagnosed with Diabetes mellitus and hypertension since 20 years came to the outpatient department of Siddha Regional Research Institute, Thiruvananthapuram, Kerala in October 2021 with complaints of bilateral pedal oedema, general weakness, frequent nocturnal micturition and weariness of limbs (Refer Table no.1) since last two months. The patient was on following medications at the time of initial visit to our OPD. 1. Tab vidagliptin 50 milligram (mg), 2. Tab Dopaglyn 10 twice daily, 3. Injection Huminsuline 30/ 70 in the dose of 35 units before lunch, and 30 units before dinner subcutaneously, 4. Tab Telzen AM twice daily and 5. Tab Nebiset 5mg once per day. Patient was told to stop taking all medications except insulin.

Examination

- Pulse rate- 84/min
- Blood Pressure- 150/90 mm of Hg
- CVS, RS, and Abdomen- Normal.
- Vitals- Appetite: good; Bowels: clear and regular;
- Urine: normal; Sleep: sound.
- Habits- No abuse habits.
- Diet- Mixed & irregular interval

Table 1: Siddha assessment - Before and After Treatment

Envagai thervu (The Eight Methods of Examination)	Before treatment on 06/10/2021	After treatment 24/11/2021
<i>Neerkkuri</i> (urine examination)	Straw coloured	Straw coloured
<i>Neikkuri</i> (oil on urine sign)	Pearl Shaped, not spreading	Round pattern, Steady spread
<i>Naadi</i> (pulse)	<i>Pitha Vatham</i>	<i>Vatha Pitham</i>
<i>Sparisam</i> (palpation)	Mild warmth present	Normal
<i>Naa</i> (tongue examination)	Coating, Fissure, Dryness absent.	Coating, fissures-nil, taste perception -normal
<i>Niram</i> (colour of the body)	Dusky complexion	Dusky complexion
<i>Mozhi</i> (speech)	Low pitched	Medium pitched
<i>Vizhi</i> (eye examination)	Normal	Normal
<i>Malam</i> (stool examination)	Yellowish, Formation of stools normal, No constipation	Yellowish, Formation of stools normal, No constipation

Investigations

At the time of the baseline visit (06/10/2021), pathological findings were as follows: In Biochemical tests, values of Serum Creatinine, Blood Urea, Blood Sugar Level (BSL) (Fasting), Blood Sugar Level (Postprandial), Urine Micro albumin, Urine Creatinine, Urine albumin to creatinine ratio (ACR) & Estimated glomerular filtration rate (eGFR) are 1.42 mg/dl, 54.3 mg/dl, 157 mg/dl, 289 mg/dl, 99.45mg/L, 74.8 mg/dl, 15.02 mg/mmol & 64.5 ml/min respectively (Date: –refer table no.2). Urine examination showed 250 mg/dl sugar loss.

Table 2: Symptoms & Investigations - Before and After Treatment

Date	Subjective assessment (Symptoms)	Objective Parameters (Investigations)
Base line (Before treatment) 06/10/2021	Bilateral pedal oedema, General weakness, frequent nocturnal micturition, frothy urine and weariness of limbs	<ul style="list-style-type: none"> - Serum Creatinine -1.42 mg/dl. - Blood Urea -54.3 mg/dl. - Urea Creatinine Ratio - 38.2. - Blood Sugar Level (BSL) (Fasting) -157 mg/dl. - Blood Sugar Level (BSL) (Postprandial) -289 mg/dl. - Urine Micro albumin -99.45mg/L. - Urine Creatinine -74.8 mg/dl. - Urine albumin to creatinine ratio (ACR) -15.02 mg/mmol. - Estimated glomerular filtration rate (eGFR) - 64.5 ml/min. - Urine routine and microscopic – Frothy urine, showed 250 mg/dl sugar loss. - Blood Pressure – 150/90 mmHg
First follow up 23/10/2021	Relives symptoms of Bilateral pedal oedema, General weakness, frequent nocturnal micturition and weariness of limbs.	<ul style="list-style-type: none"> - Serum Creatinine -1.22 mg/dl. - Blood Urea -34.8 mg/dl. - Urea Creatinine Ratio - 28.5. - BSL (Random) -169.4 mg/dl. - Urine Micro albumin - 239.2mg/L. - Urine Creatinine -100 mg/dl. - ACR -27.03 mg/mmol. - eGFR – 76.4 ml/min. - Blood Pressure -150/ 90 mmHg
Second follow up 01/11/2021	Above symptoms are markedly relives. Including pedal oedema and weariness of limbs.	<ul style="list-style-type: none"> - Serum Creatinine -1.40 mg/dl - Blood Urea -39.5 mg/dl. - Urea Creatinine Ratio - 28.2. - BSL (Random) -183 mg/dl. - Urine Micro albumin - 361.40mg/L. - Urine Creatinine -65.5 mg/dl. - ACR - 62.35 mg/mmol. - eGFR – 66.5 ml/min. - Blood Pressure - 150/ 90 mmHg
Third follow up 08/11/2021	Showed significant relief in all above mentioned symptoms.	<ul style="list-style-type: none"> - Serum Creatinine -1.34 mg/dl. - Blood Urea -40.7 mg/dl. - Urea Creatinine Ratio - 30.4. - BSL (Random) -227.1 mg/dl. - Urine Micro albumin – 202.07mg/L. - Urine Creatinine -90.5 mg/dl. - ACR – 25.23 mg/mmol. - eGFR – 68.7 ml/min. - Blood Pressure -130/ 90 mmHg
Fourth follow up 17/11/2021	Showed significant relief in all above mentioned symptoms.	<ul style="list-style-type: none"> - Serum Creatinine -1.24 mg/dl. - Blood Urea -37.1 mg/dl. - Urea Creatinine Ratio - 29.9. - BSL (Random) -293.2 mg/dl. - Urine Micro albumin – 399.30mg/L. - Urine Creatinine -188.8 mg/dl. - ACR – 23.90 mg/mmol. - eGFR – 74.3 ml/min. - Blood Pressure – 130/ 80 mmHg
Immediately after completion of medication 24/11/2021	Symptoms relieved.	<ul style="list-style-type: none"> - Serum Creatinine -1.14 mg/dl. - Blood Urea -36 mg/dl. - Urea Creatinine Ratio - 31.6. - BSL (Fasting) -295.8 mg/dl. - BSL (Postprandial) -328.2 mg/dl. - Urine Micro albumin -353.95 mg/L. - Urine Creatinine -113.3 mg/dl. - ACR – 35.30 mg/mmol. - eGFR – 80.8 ml/min. - Urine routine and microscopic – Showed 250 mg/dl sugar loss. Froth in urine reduced. - Blood Pressure -140/ 80 mmHg

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First visit after completion of medication 24/12/2021	No specific symptoms present.	<ul style="list-style-type: none"> - Serum Creatinine -1.32 mg/dl. - Blood Urea -26.3 mg/dl. - Urea Creatinine Ratio - 19.9. - BSL (Fasting) -233 mg/dl. - BSL (Postprandial) -376.5 mg/dl. - Urine Micro albumin -367 mg/L. - Urine Creatinine -99 mg/dl. - ACR – 41.89 mg/mmol. - eGFR – 69.8 ml/min. - Urine routine and microscopic – Showed 30 mg/dl protein and 250 mg/dl sugar loss, froth in urine reduced well. - Blood Pressure - 130/ 80 mmHg
Second visit after completion of medication 09/02/2022	No specific symptoms present.	<ul style="list-style-type: none"> - Serum Creatinine -1.15 mg/dl. - Blood Urea -36.5 mg/dl. - Urea Creatinine Ratio - 31.7. - BSL (Fasting) -276 mg/dl. - BSL (Postprandial) -391.4 mg/dl. - Urine Micro albumin -442 mg/L. - Urine Creatinine – 81.6 mg/dl. - ACR – 61.21 mg/mmol. - eGFR – 78.2 ml/min. - Urine routine and microscopic – Showed 500 mg/dl sugar and mild protein loss, froth in urine reduced. - Blood Pressure -110/ 80 mmHg
Third visit after completion of medication 09/03/2022	No specific symptoms present.	<ul style="list-style-type: none"> - Serum Creatinine - 1.2 mg/dl. - Blood Urea - 37.3 mg/dl. - Urea Creatinine Ratio - 31.1. - BSL (Fasting) – 274.3 mg/dl. - BSL (Postprandial) – 371 mg/dl. - Urine Micro albumin – 378.8 mg/L. - Urine Creatinine – 130 mg/dl. - ACR – 32.93 mg/mmol. - eGFR – 75.8 ml/min. - Urine routine and microscopic – Showed 500 mg/dl sugar and 30 mg/dl protein loss, froth in urine reduced well. - Blood Pressure – 120/ 80 mmHg

Table 3: Assessment of CKD QOL questionnaire - Gradation of Symptoms (9)

Gradation of Symptoms		
1		Extremely bothered
2		Very much bothered
3		Moderately bothered
4		Somewhat bothered
5		Not at all bothered

Table 4: Assessment of CKD QOL questionnaire - Before and After Treatment

	Before treatment on 06/10/2021	After treatment on 24/11/2021
Fatigue, weakness	3	5
Muscle soreness	4	5
Excessive thirst	3	5
Joint pain	3	4
Sleep during day	3	5
Cramps in muscles	3	5
Joint stiffness	3	5
Numbness in hands or feet	2	5
Trouble with memory	3	5
Shortness of breath	3	5
Swelling of ankles	2	5

Diagnosis

Based on the history, physical examination and the clinical parameters of the patient like elevated blood pressure, persistent albuminuria and elevated ACR

values, the patient was diagnosed with Diabetic Nephropathy as per Modern Science. According to Siddha Medicine, the diagnosis is *Neerizhivinal erpatta Siruneeraga noi* (Kidney disease induced as a

complication of DM). Based on the signs and symptoms of the patient, the primary blood, urine investigation reports and renal ultrasound, other diseases like multiple myeloma, nephrotic syndrome and renal artery stenosis were ruled out.

Treatment

Sirupeelai Kudineer -120 ml - Morning and evening daily before food for 1 month duration. All other allopathic treatments for hypertension and Diabetes were stopped except injection huminsuline 30/70, and the patient did not take any medicine other than *Sirupeelai Kudineer* in Siddha for diabetic nephropathy. We aimed to check the efficacy of *Sirupeelai Kudineer* for a short duration of one month and to avoid other drug interactions, we stopped all other medicines except insulin injections during that period.

Results

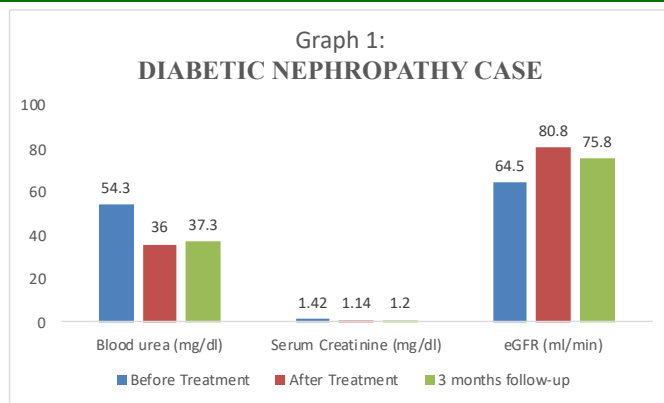
During one month of the treatment period and follow-up phase this patient of diabetic nephropathy got improvement in certain renal function tests; the signs and symptoms reduced as shown in **Table no. 1&2**. The severity of the subjective parameters such as bilateral pedal oedema, General weakness, frequent nocturnal micturition and weariness of limbs were significantly reduced after two weeks follow up and resolved completely after one month medication. The Glomerular filtration rate - eGFR percentage of the patient showed to be improving in the subsequent weeks of treatment. Blood urea and serum creatinine level was remarkably decreased after one month medication. But there is increase in the level of Urine Micro albumin and ACR during and after treatment. The improvement in CKD QOL was shown in **Table 4**. The renal parameters marked in Clinical Laboratory were tabulated as **Table 5** and charts prepared are illustrated below.

Table 5: Changes in biochemical parameters

Sl. No	Biochemical Parameters	Before Treatment	After Treatment	3 months follow-up
1	Blood urea (mg/dl)	54.3	36	37.3
2	Serum Creatinine (mg/dl)	1.42	1.14	1.2
3	eGFR (ml/min)	64.5	80.8	75.8
4	Urine Micro albumin (mg/L)	99.45	353.95	378.8
5	ACR (mg/mmol)	15.02	35.30	32.93

Discussion

As per Siddha concept, *Neerizhivu noi* (Diabetes) is due to the derangement of *Iyya* (One of the three types of bodily composition according to Siddha concept) humour initially affecting natural forces like *Keezhnokku kal* (excretory system), *Paravu kal* (circulatory system) and then the body constituents – Seven *Udal thadhukkal*



(*Saaram* or nourishing juice, *Cheneer* or blood, *Oon* or Muscles, *Kozhuppu* or Fat, *Enbu* or bone, *Moolai* or marrow, *Sukilam/ Sronitham* or Semen/ Ova) leading to emaciation and functional impairment (10). The drug *Sirupeelai* is indicated for *Thrithodam*, *Neeradaippu / Moothira Kiricharam* (Urinary disorders), *Pandu* (Anaemia), etc (10) which are all mostly found as the later stage complications of Diabetes mellitus. Hence the drug *Sirupeelai Kudineer* was selected for this Diabetic Nephropathy case study.

The Siddha drug *Sirupeelai (Aerva lanata)* used in this case study is of bitter (*Kaippu*) taste and hot potency (*Veppa veeriyam*) (11) having diuretic and lithotriptic action. The substances of *Kaippu* (bitter) taste can balance the elevated *Iya* humour and aggravate the *Vali* humour. Hence *Sirupeelai* can neutralize *Iyam* and arouse the *Abana Vayu* thereby supports in the elimination of deranged metabolic wastes and other impurities from the body. The major action of the herb *Sirupeelai* is Diuretic which is essential for the removal of stagnant impurities and water from circulation and functioning of kidneys.

On the other hand, *Phytochemistry of Aerva lanata* reveals that, it is a rich source of flavanoids such as kaempferol, quercetin, isorhamnetin, alkaloids, tannic acid, etc.(12) Previous studies reported that tannins and flavonoids in herbs are liable for the active antioxidant activity and may support for the regeneration of renal tubules. (13)

Pharmacological studies reported diuretic, Nephroprotective, antioxidant, anti-inflammatory, hypoglycaemic, anti-diabetic, anti-parasitic, antimicrobial, hepatoprotective, anti-urolithiasis, antiasthmatic, antifertility and hypolipidemic properties of *Aerva lanata*. The study on nephroprotective activity of *Aerva lanata* showed dose-dependent reduction in the elevated blood urea and serum creatinine and normalized the histopathological changes.¹¹ Moreover the antioxidant activity of the herb is the indicative of rejuvenate action in kidneys - regeneration of renal tubules and nephrons. This drug may be supporting for the maintenance of *thiridhodam* (The three types of pulse diagnosing tool and bodily composition according to Siddha concept) in equilibrium and prevent further injury at the cellular level.

In this study, the variations (increase or decrease) in haematological and bio-chemical parameters were observed during and after the intake of Medicine. Urine Micro albumin and ACR was increased after treatment

and in the follow-up Phase. This may be due to glomerular hyper filtration. Certain studies reported that albuminuria is a dynamic, fluctuating condition rather than a linearly progressive process. (14)

However the Blood urea level decreased by 50.83% after treatment and slightly increased in the follow-up Phase. The Serum creatinine also decreased from 1.42 to 1.14mg/dl after treatment and 1.12 mg/dl in the follow-up Phase. As the blood urea and serum creatinine level of the patients shows a significant improvement, the nephroprotective action of the drug may be considered. The glycaemic index of the patient is worsening over the course of the treatment. This may be due to the sudden stoppage of oral hypoglycaemic drugs which was being taken by the patient.

The estimated GFR also improved from 64.5 to 80.8 after treatment and 75.8 ml/min in the follow-up phase. Symptomatic betterment was also observed after treatment and in the follow-up phase. The assessment of CKD QOL also showed highly significant improvement after treatment and no signs/ symptoms reoccurred in the follow-up phase.

This case study with the improvement in GFR and significant reduction in Blood urea and Serum creatinine levels brought some new hope in the treatment of Diabetic Nephropathy which usually goes to end stage renal disease. Moreover further studies to get much more data is needed to find out the reason for elevation of Urine Microalbumin in this case and thereby establish the scientific facts.

In this Diabetic Nephropathy case study with the drug *Sirupeelai Kudineer*, no adverse effects were observed during and after the study. This therapy is found to be effective and probably safe for the patients of Diabetic Nephropathy. Hence this trial drug *Sirupeelai Kudineer* may be used as adjuvant therapy in Patients with Diabetic Nephropathy along with other treatment modalities.

Conclusion

In this Case study, Considering the symptomatic improvement of the patient and improvement in certain renal parameters, it is being concluded that, the drug *Sirupeelai Kudineer* may be beneficial to those patients with diabetic nephropathy if the glycaemic control is maintained in the patient. Moreover this case study shows that *Sirupeelai Kudineer* can be used as an adjuvant therapy in Diabetic Nephropathy patients in addition to the other allopathic medications of the patient. On the other hand, the study has created the pathway for further studies in the management of Diabetic Nephropathy.

Patient Perspective

The patient self-reported that he was highly satisfied with the treatment as he had considerable reduction in symptoms experienced and his quality of life was improved. Earlier, he used to get swelling in his legs continuously. Now the swelling subsided. Medicines for high blood pressure was discontinued when this drug was

started. And so far blood pressure is normal. So after that he did not have to take medicine for hypertension.

Informed Consent

Written informed consent was obtained from the patient. The patient has given his consent for his images and other clinical information to be reported in the journal. The patient understand that name and initials will not be published and due efforts will be made to conceal identity, but anonymity cannot be guaranteed.

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