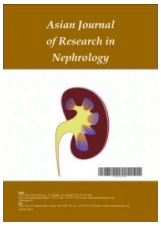

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# Assessment of Treatment Adherence and Its Predictors in Maintenance Hemodialysis Patients

**Edwin Antony[1], Maria James[1], Anjitha Roy[1] and Shaji George[2*]**

*[1]Nirmala College of Pharmacy, Muvattupuzha, Kerala, India.*
*[2]Department of Pharmacy Practice, Nirmala College of Pharmacy, Muvattupuzha, Kerala, India.*

***Authors' contributions***

*This work was carried out in collaboration among all authors. Author EA designed the study, performed the statistical analysis, wrote the protocol and wrote the first draft of the manuscript. Authors MJ and AR managed the literature searches along with analyses of the study. Author SG managed the overall work by providing guidance and corrections. All authors read and approved the final manuscript.*

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## ABSTRACT

**Introduction:** End Stage renal disease (ESRD) is an irreversible progressive condition responsible for high morbidity and mortality. Long term treatment and lifestyle modifications are difficult to adapt which significantly impairs treatment adherence and quality of life.
**Aim:** To assess the treatment adherence of ESRD patients undergoing maintenance hemodialysis.
**Methodology:** A prospective, observational, comparative, multicentre study was done for 10 months. Demographic and clinical parameters were collected from medical records and their treatment adherence was assessed using End-Stage Renal Disease-Adherence Questionnaire (ESRD-AQ). The responses were scored and identified the patients having low adherence.
**Results:** A total of 121 patients were enrolled in the study with a mean age of 62.14± 11.41 years. Dietary adherence and fluid restriction were observed at 63.33% and 60.33% respectively. Adherence to hemodialysis sessions indicated 97% while towards medication was 67.77%. A significant correlation existed between clinical biomarkers with specific adherence scores which suggest the validity of reported adherence scores. Awareness of patients regarding the diet, fluids, and, medications through patient counselling was found to be very effective in improving the adherence in ESRD populations.

**Corresponding author: E-mail: shajige@gmail.com;*

**Conclusion:** The study concludes that a huge number of hemodialysis patients are non-adherent to the treatment and the pharmacist role is pivotal in improving treatment adherence and patient compliance.

*Keywords: End-stage renal disease; chronic kidney disease; hemodialysis; adherence; ESRD-AQ.*

## 1. INTRODUCTION

Chronic Kidney Disease (CKD) is a global health problem, with escalating prevalence, incidence, economic burden, and unsatisfactory outcomes. Glomerular filtration rate (GFR), when falls below 15ml/min/1.73m$^2$ denotes the fifth stage of CKD and is often called an end-stage renal disease (ESRD). HD is the most common modality followed by transplantation and Peritoneal Dialysis is a distant third option. Hemodialysis (HD) was introduced in India in 1962, transplantation introduced in 1971, and peritoneal dialysis (PD) was introduced in 1991. As of 2017, Renal Replacement Therapy (RRT) is predominantly private health care–driven initiative. There are over 130,000 patients receiving dialysis, and the number is increasing by about 232 per million population, a reflection of increasing longevity in general [1].

End-stage renal disease is characterized by the requirement of renal replacement therapy to sustain life and it is often accompanied by uraemia, anaemia, acidosis, osteodystrophy, neuropathy, and is frequently accompanied by hypertension, fluid retention, and susceptibility to infection [2].

Dialysis replaces the normal kidney function by only about 10% and is mainly a lifesaving strategy [3]. One of the major risk factors in maintenance hemodialysis patients is non-adherence to the treatment regimen. The degree of non-compliance in maintenance hemodialysis patients varies with different views based on their treatment, which comprises adherence to medications, adherence to dietary and fluid restrictions. The risk factors contributing to the non-compliance to diet and fluid regimen include; older ages, male gender, lack of proper education and awareness, mental conditions, etc. Those patients who are undergoing hemodialysis may have many health-related complications which include; retention of salt and water, fluctuating serum levels of calcium and phosphorus, secondary hyperparathyroidism, hypertension, chronic anaemic conditions, elevated cholesterol levels, and cardiovascular diseases. [4]. Patients who show the failure of adherence, are at increased risk of morbidity and mortality and become a burden on the health care systems [5].

Patients who are on hemodialysis require about 10-12 regular medications including phosphate binders, vitamin preparations, calcium supplements, medications for hypertension, diabetes, and other comorbidities such as dyslipidemia, cardiovascular diseases, apart from the iron preparations and erythropoietin stimulating agents. This pill burden can lead to the multiplicity of the medication regimens and cost burden that can induce a high risk of adverse drug events, followed by non-adherence [6]. The psychosocial variables which influence the non – adherence are negative beliefs about medicines, health locus of control, and emotional barrier specific to the diseased condition. The proper compliance of these groups of patients can be improved by proper nutritional and psychosocial therapy [7].

## 2. METHODOLOGY

A prospective, longitudinal – observational, comparative study was designed to assess the medication adherence of ESRD patients on Maintenance Hemodialysis. The study was carried out for 10 months. Patients diagnosed with ESRD on maintenance HD for at least 3 months and patients aged above 20 years were included in the study. Patients with acute renal failure, psychiatric disorders, HIV, Hepatitis C, and patients who were not interested in receiving counselling were excluded from the study.

Baseline data regarding patient demographics, comorbidities, laboratory values, and data on dialysis were obtained from treatment records by using a predesigned data collection form. Medication adherence was assessed through direct patient or bystanders' interviews, by using the ESRD-Adherence questionnaire. The end-stage renal disease adherence questionnaire (ESRD- AQ) is a validated tool to assess the; degree of adherence, perception, and impact of counselling about HD treatment modalities. It contained questions to evaluate the patient history, adherence to hemodialysis sections,

adherence to medications, fluid restrictions, and diet recommendations [6]. Responses obtained were then scored and assessed to determine patient adherence. Mean ± standard deviation of pre- dialytic serum potassium and phosphorous levels were used along with interdialytic weight gain (IDW) as a biochemical marker for the clinical assessment of adherence to the diet, medication, and fluid restrictions respectively.

## 2.1 Statistical Analysis

The collected data were compiled using Microsoft Excel and statistical analysis was done using the IBM SPSS Statistics package, version 19. Karl Pearson's Correlation coefficient was used to study the correlation. Bivariate relationship between socio-demographic factors with adherence was analyzed using the Mann Whitney U test and Kruskal Wallis test. P-value of less than 0.05 was considered to be statistically significant.

## 3. RESULTS

A total of 124 patients were enrolled into the study as per the inclusion and exclusion criteria. However, 2 patients died during the study period and 1 went for transplantation hence they were excluded in the second phase of the study. Therefore, a total of 121 patients were included for analysis.

Table 1 depicts the demographic factors of the study population and it shows that the majority of the subjects (42.15%) fall under the age category of 61-70, followed by the 26.45% in the 51-60 age limit, 19.83% in age greater than 70 years and 5.8% belongs to 31-40 age category. As 61.98% of subjects were above 60 years of age, obviously the proportion of people not working has outnumbered the working people, and the analysis indicated 68% of the subjects were not working and 32% were working on a part-time basis in dialysis free days.

On analysing the gender distribution, a predominant male dominance (77%) was observed, with females at 23%. Considering the marital status, majority of the patients (93%) are married and a small fraction of about 7% belong to the category of the unmarried population. On comparing the educational status, it was

**Table 1. Demographic parameters of the study population (n = 121)**

| Demographic factors | | Study population (%) |
|---|---|---|
| **Age** | 20-30 years | 3.31 |
| | 31-40 years | 2.48 |
| | 41-50 years | 5.78 |
| | 51-60 years | 26.45 |
| | 61-70 years | 42.15 |
| | >70 years | 19.83 |
| **Gender** | Male | 73 |
| | Female | 27 |
| **Educational qualification** | High school or less | 63.63 |
| | Higher secondary | 24.79 |
| | College/university | 11.57 |
| **Annual income** | <1 lakh Rupees | 50 |
| | >1 lakh Rupees | 50 |
| **Work status** | Working | 32 |
| | Not working | 68 |
| **Insurance** | Insured | 25 |
| | Not insured | 75 |
| **Years on dialysis** | <1year | 14.05 |
| | 1-5 years | 62.80 |
| | 6-10 years | 18.18 |
| | >10 years | 4.96 |
| **Dialysis schedule** | Twice weekly | 61.16 |
| | Thrice weekly | 38.84 |
| **Co morbidities** | Hypertension (HTN) | 29.75 |
| | Diabetes Mellitus (DM) | 9.09 |
| | HTN+DM | 52.89 |
| | OTHERS | 2.48 |
| | NONE | 5.79 |

**Table 2. Scoring of the overall adherence**

| Overall adherence | | | |
|---|---|---|---|
| **Adherence behaviour** | **Scoring range as per ESRD-AQ** | **Number of patients** | **Median(Interquartile range) score** |
| Poor | <700 | 8 (6.60 %) | 662.5 (593.75- 675 ) |
| Moderate | 700-999 | 45 ( 37.19% ) | 875 (800-900) |
| Good | 1000- 1200 | 68 ( 56.20 % ) | 1100 (1050-1100) |

**Table 3. Correlation of adherence with pre-dialytic serum potassium, serum phosphorous, and interdialytic weight gain**

| **Specific adherence scores (Mean± SD)** | **Pre-dialytic potassium serum concentration (Mean± SD)** | **Pearson correlation coefficient (r)** | **P-value** |
|---|---|---|---|
| Medication (175.12 ±42.44) | 4.96 ± 1.01 | - 0.139 | 0.368 |
| Fluid (126.45±48.77) | | -0.020 | 0.0837 |
| Diet (126.85± 53.63) | | - 0.335 | 0.000** |
| **Specific adherence scores (Mean± SD)** | **Pre-dialytic phosphorus serum concentration (Mean± SD)** | **Pearson correlation coefficient (r)** | **P-value** |
| Medication (175.12 ±42.44) | 5.67±1.7 | - 0.306 | 0.001** |
| Fluid (126.45 ± 48.77) | | -0.41 | 0.654 |
| Diet (126.85± 53.63) | | - 0.407 | 0.000** |
| **Specific adherence scores (Mean± SD)** | **Inter dialytic weight gain (mean± SD)** | **Pearson correlation coefficient (r)** | **P-value** |
| Medication (175.12 ±42.44) | 2.95±1.19 | - 0.051 | 0.140 |
| Fluid (126.45 ± 48.77) | | -0.410 | 0.000** |
| Diet (126.85± 53.63) | | - 0.135 | 0.582 |

***.Correlation is significant at the 0.01 level (2-tailed).*

observed that 63.63% had the educational status of 10$^{th}$ grade or less, 24.79% had completed the higher secondary education and 11.57% had college/university education. About 25% of the study population had insurance while the remaining 75% were not having any kind of insurance. Of the study subjects, 61.16% were following the twice-weekly dialysis regimen and the remaining 38.84% were following the thrice-weekly regimen of hemodialysis. Among them, 62.80% of patients were on hemodialysis for 1-5 years, 18.18% of subjects were on dialysis for 6-10 years, 14.05% of subjects were on dialysis for less than 1 year and only 4.96% of the subjects were on dialysis for above 10 years. The main comorbidity observed was hypertension and diabetes mellitus.

The overall adherence behaviour of each patient was assessed by summing the scores of questions 14, 17, 18, 26, 31, and 46. Out of the 121 patients, a total of 68(56.20%) had good adherence behaviour, 45(37.19%) had moderate adherence and 8(6.61%) had poor adherence. Adherence to the four treatment modalities including dialysis schedule, medications, fluid, and diet was assessed. Out of 121 patients, most of the patients showed high adherence to dialysis sessions (97%), dietary adherence observed was 63.33% followed by fluids 60.33%, and medications 67.77%. Mean adherence score to medications, fluid restriction, and diet recommendations were also assessed out of a maximum score of 200 which was 175.12±42.44, 126.45±48.77, 126.85±53.63 respectively. The reason patients cited for medication non-adherence includes forgetfulness, cost of medication, difficulty in keeping track of medications, and side effects. The most commonly cited reason for fluid and diet non-adherence was inadequate knowledge about the recommended dietary modification and inability to control the restricted dietary and fluid modifications.

Pre HD serum potassium did not correlate with medication and fluid adherence. There was a negative correlation between pre-dialytic serum potassium and diet adherence score ($r = -0.335$, $p= 0.000$). The significant negative correlation between pre-HD serum potassium level and reported adherence indicates the validity of reported adherence scores.

Fluid adherence has no significant correlation with the pre-HD serum phosphorous level. There is a significant negative correlation between pre –dialytic serum phosphorous and diet adherence. Non- adherence to diet results in a considerable rise in the phosphorous level ($r = -0.407$, $p<0.00$) which also indicates the accuracy of reported adherence. Medication adherence has significant negative correlation with pre-dialytic serum phosphorous level (Pearson correlation $r = -0.306$ $p= 0.001$). Patients who were not adherent to medication and diet experienced hyperphosphatemia. There was no significant correlation between IDW with diet ($r= -0.135$, $p=0.582$) and medication adherence($r=-0.051$, $p= 0.140$). A significant negative correlation between adherence to fluid restriction and IDW ($r = -410$, $p= 0.00$) was identified. Those who were not adherent to their recommended fluid had significant fluid overload and weight gain.

Various Predictors of adherence were also analysed and the results obtained uplifts the fact that adults between the age group of 41-50 showed better adherence behaviour compared to older age and younger population. Age categorizations were analysed by Kruskal Wallis test to determine whether there were differences in the means of adherence scores with adherence behaviour. Statistical significance was observed between age and adherence pattern (diet = p0.003, medication =p 0.003, fluid = p 0.001, overall= p 0.000).

Patients who were educated were aware of the importance of treatment adherence and shows more adherence to the treatment modalities as compared with those who had the lowest level of education ($p =0.041$).

On the other hand, income was a significant contributing factor towards medication adherence since treatment cost is a perceived barrier for non-compliance. Because of the high cost for hemodialysis treatment, lack of adequate health insurance, and low economic status some patients ended up missing or withdrawing from the medication therapy. Income had no statistical significance with diet, fluid, and overall adherence ($p=0.236$, $0.174$, $0.096$).

The frequency of dialysis had no statistical difference with diet, medication, and overall adherence, however, there exists a difference in fluid adherence ($p=0.001$). Patients on dialysis with a thrice-weekly regimen were the least adherent to fluids restrictions compared to twice weekly regimen since they were confident that fluid overload will be corrected since dialysis was carried on alternative days.

As shown in Fig. 1 duration of dialysis had a significant impact on adherence behaviour. Better adherence was shown by those on HD for more than 10 years in each treatment modality ($p<0.05$) while high medication adherence was observed in participants with the least duration of dialysis ($p<0.05$). Patients who recently initiated dialysis were unable to restrict the diet and fluid intake and modify the lifestyle to accommodate the dialysis sessions. There was a significant difference between comorbidities with medication and overall adherence ($p=0.002$). Participants who were free of other diseases show better adherence patterns than those with chronic diseases.

As shown in Fig. 2 about half of the population (50.41%) were taking more than 10 pills/day which may be one of the major contributing factors for medication nonadherence. A significant negative correlation existed between total pill burden and medication adherence ($p<0.05$, $r = -0.349$). The increased number of pills raised the medication cost and drug interactions which results in a reluctance to adherence to the therapy. Therefore high pill burden is an independent predictor of medication nonadherence. Phosphate binders were a major contributing factor to the total pill burden (24.88%). The median intake of phosphate binders was 2 pills/day. Sevelamer, Calcium carbonate, Calcium acetate -monotherapy, or combination therapy were the phosphate binders being used in the study population. There was a significant inverse relationship between phosphate binders and medication adherence ($p<0.05$, $r = -0.307$).

## 4. DISCUSSION

The current study was aimed to assess the treatment adherence of ESRD on maintenance hemodialysis. From this study, it is evident that treatment adherence was significantly impaired. Adherence to various treatment options was investigated which implies that compliance pattern towards medications, dietary and fluid restrictions was less than optimum because of lack of adequate knowledge, ignoring lifestyle modifications, fear of side effects of drugs, medication cost, and forgetfulness. The majority of the study participants showed adherence to

dialysis sessions but some of them were shortening the scheduled time as per their inconvenience or medical reasons. Several sociodemographic and clinical variables such as age, qualifications, employment, financial status, frequency and duration of hemodialysis, comorbidities, and pill burden were associated with adherence whereas gender, marital status, and insurance do not possess any influence on adherence behaviour. A significant correlation existed between clinical biomarkers with specific adherence scores which suggested the validity of reported adherence scores.

A cross-sectional study in 220 hemodialysis patients conducted by Naalweh et al observed 81% medication adherence 31% adherence to fluid restrictions and 24% dietary adherence. He also observed that 55% of his study population had good adherence followed by 40.5% with moderate adherence and 9% with poor adherence. Our study data analysis also brought out similar results with the majority of our study population showing adherence to medication followed by adherence to diet and fluid restrictions [6].

Leggat et al conducted a study to evaluate the noncompliance in hemodialysis patients and his study results show that 8.5% of patients skipped their dialysis sessions while 20% shortened their sessions. Noncompliance with dialysis sessions was associated with a greater risk of mortality and adverse patient outcomes. But in our study, about 3% of the study population shortened their hemodialysis session three or more times per month, the majority of which was due to the occurrence of one or more health issues like muscle cramps, body pain, nausea [8].

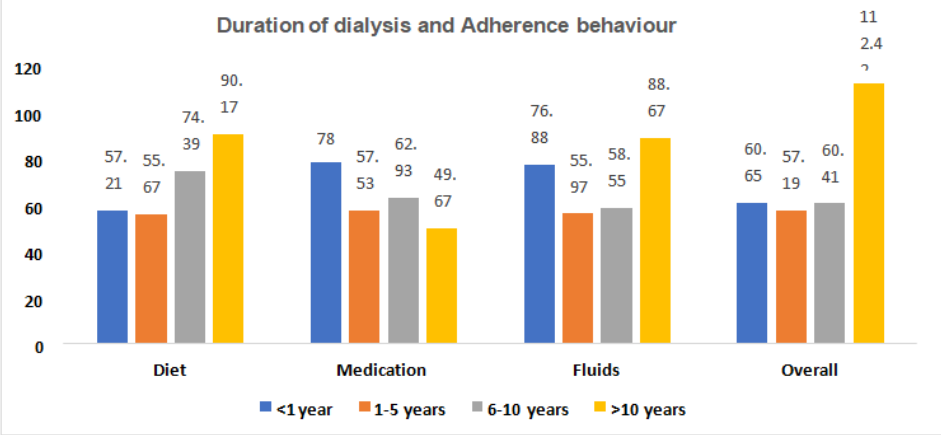


**Fig. 1. Duration of dialysis and adherence behaviour**

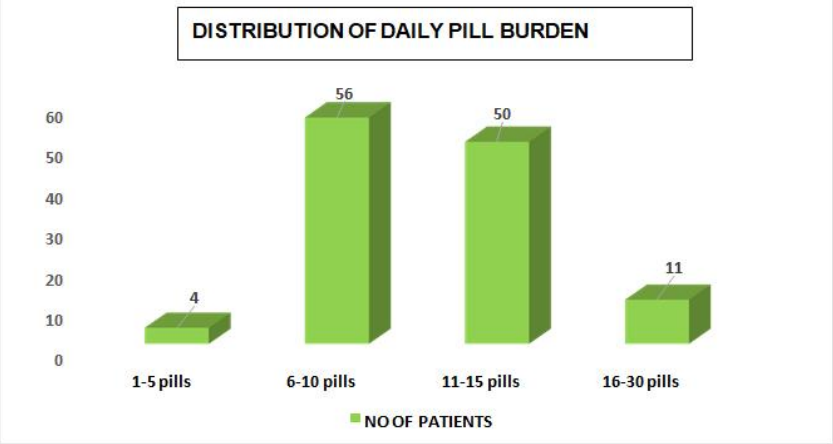


**Fig. 2. Frequency distribution of Total pill burden**

A study on phosphate control adherence in hemodialysis patients by Umeukeje EM et al concluded that suboptimal control of dietary phosphorus, phosphorus binders and dialysis were contributing factors that lead to hyperphosphatemia in chronic kidney disease patients. He also identified that hyperphosphatemia was a significant contributor to cardiovascular and all-cause mortality. Similarly in our study, we also observed that suboptimal patient adherence to diet and medications lead to the occurrence of hyperphosphatemia [9].

Naalweh et al from his study on treatment adherence on hemodialysis patients established a significant correlation between dietary adherence and pre hemodialysis potassium concentration. He also observed that adherence to fluid restriction was associated with reduced intradialytic weight gain in dialysis patients. Our study results also are in par with this study results, stating that patients adherent to diet and fluid restriction experience reduced intradialytic weight gain and lower incidence of hyperkalaemia [6].

Multiple studies have brought out the various factors associated with adherence in hemodialysis patients. Mukakarangwa et al conducted a cross-sectional study to detect the factors associated with hemodialysis in ESRD patients. This study found that the various factors associated with adherence to hemodialysis were age, religion, education, and experiencing discomforts during the dialysis procedure [10]. Schmid et al. in a review of available reports on medication adherence by HD patients, had concluded that age, lower cost of medication, and a higher level of education were factors associated with better adherence since they had more confidence in the benefits of their medication regimen [11]. Poor adherence to hemodialysis regimen can be a major threat towards achieving better patient outcomes, as stated by Chan et al in his study on adherence barriers to chronic hemodialysis in the US population [12]. A review done by Karamanidou regarding the determinants of non-adherence to medications concluded that employment status was not related with medication adherence which was contrary to our study results [13]. Income had no statistical significance with diet, fluid, and overall adherence (p=0.236, 0.174, 0.096). On the other hand, there was a significant difference in medication adherence since treatment cost is a perceived barrier for non-compliance [4]. There was a significant negative correlation between total pill burden and medication adherence (p=0.00, r = -0.349). The increased number of pills raised the medication cost and drug interactions which results in a reluctance to adherence to the therapy. Therefore high pill burden is an independent predictor of medication non – adherence [6]. Prevalence of comorbidities is an important predictor of the outcomes of ESRD patients on hemodialysis. Prichard et al in his study stated that increasing age, presence of cardiovascular diseases, diabetes, and poor nutrition are factors leading to poor patient outcomes in ESRD patients. There was a significant difference between comorbidities with medication and overall adherence (p=0.002). Participants who were free of other diseases show better adherence patterns than those with chronic diseases. Most of the dialysis patients have comorbidities such as diabetes and hypertension and are often prescribed with medications to treat those conditions in addition to the medications they take for ESRD which may result in medication non- adherence. The primary reason for fluid non – adherence was thirst and dry mouth - factors that may be linked to comorbidities such as diabetes and side effects of certain medications [13].

The current system of therapy only aims to improve the functional capacity of the patients for as long as possible, however, they were not bothered about the progression of health-related quality of life of the patients. It is imperative to improve education regarding various treatment modalities and misconceptions about disease conditions.

## 5. CONCLUSION

Compliance pattern towards medications, dietary and fluid restrictions was less than optimum because of lack of adequate knowledge, ignoring lifestyle modifications, fear of side effects of drugs, medication cost and forgetfulness. The majority of the study participants showed adherence to dialysis sessions but some of them were shortening the scheduled time as per their inconvenience or medical reasons. Factors like age, qualifications, employment, financial status, frequency and duration of hemodialysis, comorbidities, pill burden were associated with specific adherence whereas gender, marital status and insurance do not possess any influence on adherence behaviour. A significant correlation existed between clinical biomarkers with specific adherence scores, which suggest the validity of reported adherence scores.

## CONSENT

Written consent was obtained from each selected patient before the enrolment into the study. Patients were selected based on the eligibility criteria after obtaining their informed consent.

## ETHICAL APPROVAL

Before the initiation of the study, the study protocol was reviewed and approved by the Institutional ethics committee.

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## COMPETING INTERESTS

Authors have declared that no competing interests exist.

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