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COMPARATIVE STUDY ON HIGH FLUX AND LOW FLUX DIALYSIS ENHANCING DIALYSIS ADEQUACY AND SURVIVAL RATE

Noor Fatima[1], Meerab Younas[2], Yumaima William[3], and Dr. Manzoor Naeem[*4]

[1,2,3,*4] *Renal Dialysis, Department of Emerging Health Professional Technologies, Allied Health Sciences Superior University Lahore Pakistan*

[1]noorarshad940@gmail.com, [2]phoolrajputrajput@gmail.com, [3]yumaimawilliam173@gmail.com, [*4]paknephrologist@hotmail.com

MBBS; KE. MD FCPS; PHD. BERLIN
Associates Professor,
Nephrologist
AZRA NAHEED MED COLLEGE. LAHORE
paknephrologist@hotmail.com
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ABSTRACT

Background: *Kidney failure in its final stage, end-stage renal disease (ESRD), leaves patients completely dependent on haemodialysis just to stay alive. The type of dialysis membrane used in this process is not a small detail.*

Objective: *This study set out to compare dialysis adequacy and patient survival outcomes between those on maintenance haemodialysis using high-flux dialyzers and those using low-flux dialyzers.*

Methods: *An observational, analytical study was carried out over four months at Muhammad Sulman Khalid (MSK) Hospital, Lahore. The patients who were recruited were 27 in total and they had ESRD and were on maintenance haemodialysis for 3 months or more, via purposive sampling. The inclusion criteria were that patients had to be older than 18 years and have good conditions of health and informed consent, and that they were excluded if they were in active infections, recent hospitalizations, cancer or severe medical complications. Data was collected through a Literature-based and expert-developed structured questionnaire as well as the patient's medical records. Dialysis adequacy was measured through Kt/V, and associations between dialyzer type and eleven clinical variables were tested using Chi-square and Fisher's Exact tests, with the latter applied wherever expected cell counts dropped below five.*

Results: *The sample of 27 patients was split nearly evenly, with 14 on low-flux dialyzers (51.9%) and 13 on high-flux (48.1%). All of the patients were diagnosed with hypertension and diabetes mellitus was documented in 81.5%, while approximately 48% of them had cardiovascular disease. Most patients had access via arteriovenous fistula (77.8%) and serum albumin levels were normal in 96.3%. Of the seven variables tested with regards to the dialysis adequacy (Kt/V) ($p < .05$); cardiovascular disease, session time, blood flow rate, urea, creatinine, and potassium ($p < .05$) emerged as statistically significant variables among the associations considered. The strongest signal came from blood flow rate, $p < .001$.*

Conclusion: *High-flux dialysis produced significantly better dialysis adequacy and solute clearance compared to low-flux dialysis among ESRD patients in this sample.* ***Keywords:*** *haemodialysis,*

high-flux dialyzer, low-flux dialyzer, end-stage renal disease.
Keywords:

INTRODUCTION

The burden of chronic kidney disease (CKD) as a public health issue is rapidly rising as a leading cause of premature death and disability in the world, with an estimated prevalence of 9-13% of the global population. When the patient develops CKD and develops end-stage kidney disease (ESKD), renal replacement therapy (RRT), such as haemodialysis, peritoneal dialysis and transplantation of the kidneys becomes an option, but access to kidney transplantation is limited in many parts of the world, especially low or middle income countries. Consequently, maintenance haemodialysis is now the most common renal replacement therapy across the globe and in South Asia and many more people now rely on chronic dialysis for survival (1).

In spite of improvements in dialysis, dialysis membranes and water treatment, the overall life expectancy of all patients treated on maintenance haemodialysis (MHD) is still not satisfactory compared to many other chronic illness. Dialysis patients still have high death rates due to cardiovascular disease, infection and complications from chronic inflammation and malnutrition. The accessibility of haemodialysis has caught the eye, but also quality of haemodialysis (dialysis adequacy), typically encompassed by the term "dialysis adequacy", and treatment parameters, such as dialyzer membrane selection, and the effect of these on dialysis adequacy and long term survival of patients on haemodialysis(2).

Dialysis adequacy typically is a measure of the removal of uremic toxins and excess fluid in a haemodialysis session, most often represented by small solute clearance measures like Kt/V or the urea reduction ratio (URR). These indices are directed towards the excretion of urea and other small molecules which pass easily through the dialysis membrane and had traditionally been thought to be effective measures of how much toxins are excreted. However, the uremic milieu is not just characterized by urea clearance; there are various small, middle, and large molecules and protein bound toxins present that can be directly linked to inflammation, vascular damage, and organ dysfunction beyond the level of urea and may contribute directly to those processes(3).

These include solutes ranging in size from 500-60,000 Daltons (middle molecules), including beta-2 microglobulin, inflammatory cytokines and other peptides involved in the pathogenesis of cardiovascular disease, immune dysfunction, and dialysis-related amyloidosis. Traditional low flux membranes, as they are still often termed, are very effective at removing the urines and albumins that are small molecules, but much less good at removing larger molecules called "middle molecules. Conversely, high flux membranes have larger pores and more convective transport capacity that may facilitate greater removal of middle molecules, but these might also lead to greater loss of albumin through the membrane unless the performance of this membrane is appropriately controlled(4).

A buildup of middle molecules has been associated with poor clinical outcomes, such as dialysis-related amyloidosis–bone/joint disease, vascular calcification, left ventricular hypertrophy, and increased cardiovascular-related mortality. Observational and interventional studies have demonstrated that even in the modern era, with general use of high flux dialysis, high β2M has been shown repeatedly to remain a significant risk factor for death, emphasising the ongoing problem of middle molecule retention among many patients. The results have stimulated the interest in new dialyzer technologies based on improved ability to remove middle and larger uremic toxins, without inducing clinically meaningful protein losses; in addition, a biological argument has arisen in favour of the consideration of dialyzer flux as an actionable determinant of dialysis adequacy and dialysis survival(5).

Low flux dialyzers generally have a beta 2 microglobulin clearance of less than, say, 10 millilitres per minute and are used mainly for diffusive clearance of small utrafiltrated solutes with less capacity for ultrafiltrating middle size

molecules. The higher permeability of high flux dialyzers allows for higher beta-2 microglobulin clearance, in excess of 20–30 ml per minute, and facilitates both diffusion and convection to achieve good clearance of middle molecules as well as adequate removal of small molecules. In a few classification schemes, including Japanese, dialyzers are further categorized into different types: type I membranes have a low flux, type II to V membranes are classified depending on the clearance peak for Beta-2 Microglobulin (6).

A greater convective transport of solutes in the middle molecule range may result in improved clearance of substance associated with inflammation, oxidative stress, and vascular damage, for high flux membranes. Meanwhile, some have raised concerns that extreme permeability could allow something undesirable to be leaked – such as albumin, an important indicator of nutrition and a good predictor of patients' survival in haemodialysis. Therefore, designing a dialyzer to favor better clearance of middle molecules and sufficient control of albumin leakiness is an on-going challenge, and with different high-flux membranes, this balance can be obtained more or less adequately in the clinical setting(7).

LITERATURE REVIEW

End stage renal disease (ESRD) is the most advanced, or last stage of chronic kidney disease (CKD), which is characterized by permanent kidney failure. However, patients who suffer ESRD are completely reliant on renal replacement therapy, and haemodialysis is by far the most common method of RRT worldwide. A patient's haemodialysis success is greatly dependent on the type of haemodialysis membrane used, particularly how well it clears toxic solutes that build up in the blood if kidneys don't function and the permeability of the membrane.

In 2026, Yunyi Li et al. conducted a study with the title Comparison of Clinical Therapeutic Effects Between High-Flux Dialysis and Low-Flux Dialysis, which discusses that high-flux dialysis is significantly better than low-flux dialysis in removing small and middle molecular weight toxins, correcting metabolic acidosis, and reducing micro-inflammatory markers. This multicenter, retrospective cohort study of 187 patients receiving high-flux dialysis and 189 patients receiving low-flux dialysis comprised 374 and 378 dialysis sessions, respectively, revealed that significantly more Kt/V, URR, creatinine reduction ratio and phosphorus reduction ratio were seen with high-flow. Low-flow dialysis achieved a lower HbA1C level than high-flow, and post-dialysis levels of C-reactive protein and white blood cell counts were lower with high-flow. β2-microglobulin level drops significantly after high-flux dialysis. It was found that high-flux dialysis was better for solute clearance, control of micro-inflammation and acid-base correction, without causing any significant patient discomfort, and that patient profile individualized treatment is still important (21).

In 2025, Wang, et al. published a study titled Protein Loss With High-Flux and Medium Cut-Off Membranes: An Ex Vivo Comparative Analysis, in which they discuss that high-flux and medium cut-off (MCO) dialyzers remove very different and much larger amounts of protein, with total protein loss up to 9-fold higher with MCO membranes. An ex vivo haemodialysis simulation system was used to collect ultrafiltrates from two high-flux dialyzers and one MCO dialyzer simultaneously under the same conditions, and 244 proteins were identified, 113 of which were semiquantified, showing that the protein distribution in ultrafiltrates from MCO dialyzers was skewed toward higher molecular masses. Important, some removed proteins was those with the possible beneficial biological functions, such as vitamin D-binding protein and haptoglobin. The study found that although MCO membranes provide superior separation of large middle molecules, the lack of selectivity in their separation raises significant clinical concerns with regard to long-term effects on the patients (22).

In 2025, Bernard Canaud et al. published a study entitled: High-Volume Hemodiafiltration Versus High-Flux Haemodialysis in which they conclude "High-volume hemodiafiltration (HDF) clearly favours all-cause and cardiovascular mortality when compared to high-flux haemodialysis (HD) especially when convective volumes surpass 23 liters per session (L/S). Data from several randomized controlled trials and real-world cohort

studies, including the CONVINCE trial, were used to carry out this analysis, which demonstrated that compared to high-flux HD, high-dose HDF contributed to all-cause mortality reduction of about 23% (HR = 0.77; 95% CI: 0.65–0.93) and further to cardiovascular-specific mortality. The benefits of mechanistic were attributed with the clearance of middle molecule toxins, improved hemodynamic stability, and reduced systemic inflammation, compared to low-flux and standard high-flux haemodialysis. The study concluded that although a high volume HDF method is now evidenced based standard treatment, high-flux dialysis continues to be an important technology that is not available in the HDF method (23).

In 2025 B. Korucu, et al., carried out a study titled "Improvement of Serum Calcification Propensity in Dialysis Patients: Comparison Between Low-Flux and Medium Cut-Off Dialyzers" that reported that both, both low-flux and medium cut-off (MCO) dialyzers, significantly improved T50, a validated marker of serum calcification propensity and vascular calcification risk, after six months of treatment. In this crossover study, 15 haemodialysis patients were studied, with MCO membranes achieving better middle-molecule toxin clearance, but neither dialyzer type was found to have a significant difference in T50 reduction after the study. The authors commented that the "calcification risk reduction seemed to level off and was not strictly membrane flux dependent. Given that both of these membranes can help improve the calcification propensity, the selection of membranes for this effect should consider patient's individual characteristics, the study concluded (24).

MATERIAL AND METHODS

This observational analytical study was conducted at Muhammad Sulman Khalid Hospital over a period of four months following synopsis approval. A total sample size of 27 patients was determined using a 95% confidence level and 5% margin of error and selected through purposive sampling. Patients included were adults aged 18 years or older with end-stage renal disease on maintenance haemodialysis for at least three months using either high-flux or low-flux dialyzers, and only clinically stable individuals who provided informed consent were enrolled, while patients with active infections, recent hospitalizations, malignancy, severe liver disease, temporary dialysis, or those refusing consent were excluded.

Data were collected using a researcher-developed semi-structured questionnaire based on literature review and expert input, extracting relevant information from patient medical records and dialysis unit charts. The dependent variables included dialysis adequacy (Kt/V), hemoglobin, urea, creatinine, dialysis-related complications, hospitalizations, and survival, while the independent variable was the type of dialysis membrane. At the end of the study period, patient survival outcomes were also recorded to evaluate clinical differences between high-flux and low-flux dialysis groups.

Ethical approval was obtained from the Ethical Review Committee of Superior University, and all participants provided written informed consent after receiving a clear explanation of the study purpose and procedures. Confidentiality, anonymity, and patient dignity were strictly maintained, and participation was voluntary with the right to withdraw at any time without affecting clinical care. No additional risks beyond routine haemodialysis were involved, as the study was purely observational and based on existing clinical data.

Data analysis was performed using IBM SPSS Statistics, where continuous variables were summarized using descriptive statistics including mean, median, standard deviation, and range, while categorical variables were presented as frequencies and percentages. Inferential analysis was conducted using Pearson Chi-square and Fisher's Exact Test to assess associations between dialyzer type and clinical outcomes, with statistical significance set at a p-value of less than 0.05.

RESULTS

Overall, 27 haemodialysis patients participated in this study, and they were nearly equally gendered with a 0.48 coefficient of determination. There was no variance in the patients in terms of hypertension as all patients in this study showed the symptom. Almost half of the sample (n = 14, 51.9%) were low-flux dialyzers, while the remaining patients used high flux (n = 13, 48.1%)

and most of them were undergoing dialysis through an AV fistula (77.8%) and the rest through a permanent dialysis catheter. Approximately 81.5% of the total sample had diabetes mellitus and about 48% had cardiovascular disease. Pre-dialysis biochemical markers showed a fairly even distribution across urea and creatinine categories, albumin levels were *consistently normal* across nearly all patients (96.3%), and potassium levels leaned slightly toward the elevated range overall. Then associations between dialyzer type and eleven clinical variables were analyzed using the Chi-square and Fisher's Exact tests, and, truth be told, the results were astonishing! Seven variables were found to be statistically associated with dialyzer type ($p < .05$): dialysis adequacy (Kt/V), CVD, session time, blood flow rate, urea, creatinine and potassium with the highest association for blood flow rate $\chi(2, N = 27) = 27.00$, at $p < .001$. The remaining four variables, diabetes mellitus, access type, sessions per week, and albumin, showed *no significant association* with dialyzer type, suggesting these were comparably distributed across both groups. Overall, there is a fairly consistent association towards higher flux dialysis surviving solute clearance and adequacy in this cohort.

Table No. 1 Descriptive Statistics

The sample consisted of 27 haemodialysis patients, with complete data across most variables and only one missing value recorded for serum albumin category. Gender distribution was nearly even, with a mean of 0.48, meaning roughly half the patients were male. Honestly, one of the more striking findings here is that *all* 27 patients had hypertension, as shown by the constant value of
1.00 with zero standard deviation.

Statistics												
		)ialyze type	adequacy (Kt/V achieved)	lyp er	DM	CVD	ccess Type	BFR	Urea Cat	Creat	ɔum in	ɔtassi um
N	Vali d	27	27	27	27	27	27	27	27	26	27	27
	Miss ing	0	0	0	0	0	0	0	0	1	0	0
Mean		.48	.52	1.00 00	.814 8	.481 5	1.2222	277. 78	1.44 44	1.50 00	1.0370	1.4444
Median		.00	1.00	1.00 00	1.00 00	.000 0	1.0000	250. 00	1.00 00	1.50 00	1.0000	1.0000
Mode		0	1	1.00	1.00	.00	1.00	250	1.00	1.00[a]	1.00	1.00
Std. Deviatio n		.509	.509	.000 00	.395 85	.509 18	.42366	32.0 26	.506 37	.509 90	.19245	.50637
Minimu m		0	0	1.00	.00	.00	1.00	250	1.00	1.00	1.00	1.00
Maximu m		1	1	1.00	1.00	1.00	2.00	350	2.00	2.00	2.00	2.00

Table No. 2 Gender

The following table represents a distribution of participants on a certain topic by gender. Among them, 14 are female (51.9%), and 13 are male (48.1%).

		Frequency	Percent
	Female	14	51.9
	Male	13	48.1
	Total	27	100.0

Graph No. 1 Gender

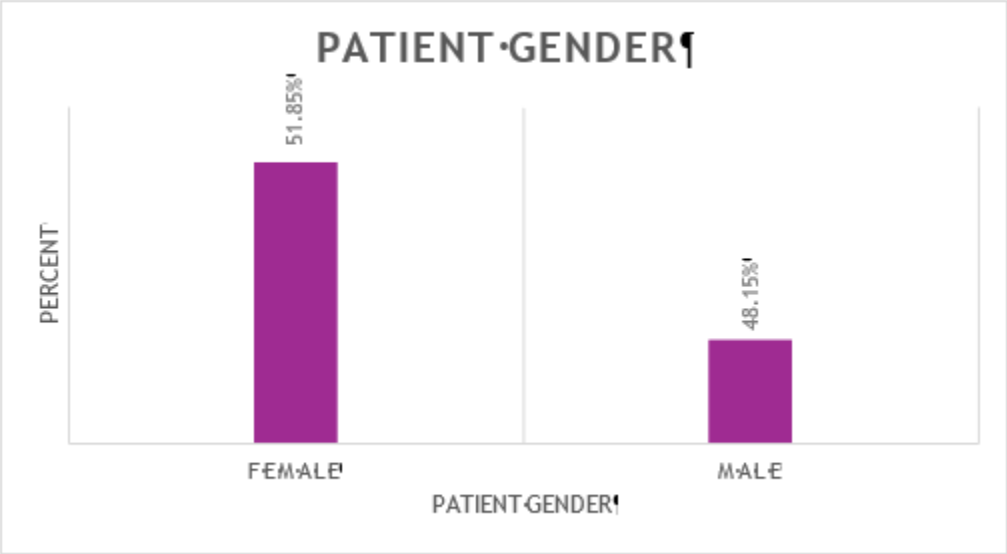

Table No. 3 Dialyzer Group Dialyzer type (1=High flux, 0=Low flux)

The present set of 27 patients studied consisted of approximately 52% low flux dialyzers. About forty-eight percent or the remaining 13 patients were using high-flux dialyzers.

	Frequency	Percent
Low flux	14	51.9
High flux	13	48.1
Total	27	100.0

Graph No. 2 Vascular Access Type

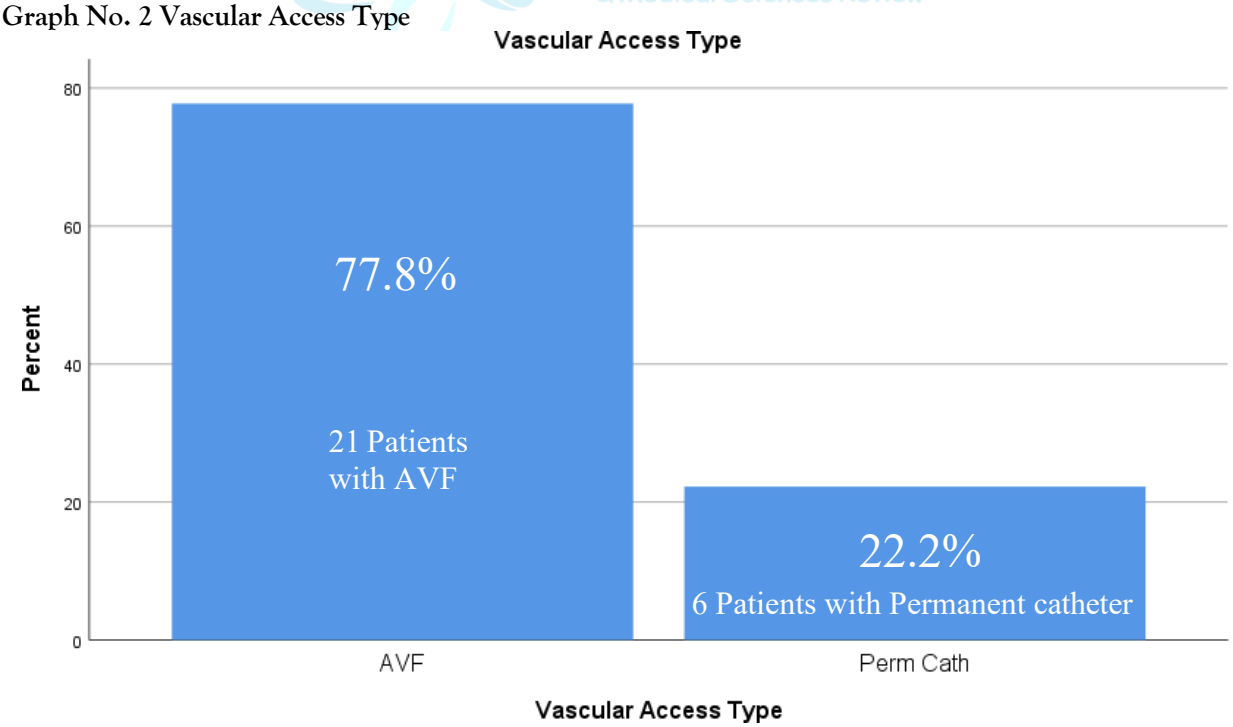

Table No. 4 AccessType

When it came to vascular access, the majority of patients, 21 out of 27, were using an arteriovenous fistula (AVF), accounting for 77.8% of the sample. The remaining 6 patients (22.2%) had a permanent catheter as their access type

AccessType	Frequency	Percent
AVF	21	77.8
Permanent catheter	6	22.2
Total	27	100.0

Table No. 5 Urea

Pre-dialysis urea levels in 15 patients (55.6%) were between 30 and 40mg/dL and 12 (44.4%) had urea levels above 50mg/dL.

Urea	Frequency	Percent
30-40 mg/dL	15	55.6
>50 mg/dL	12	44.4
Total	27	100.0

Graph No. 3 shows the percentage of diabetes mellitus

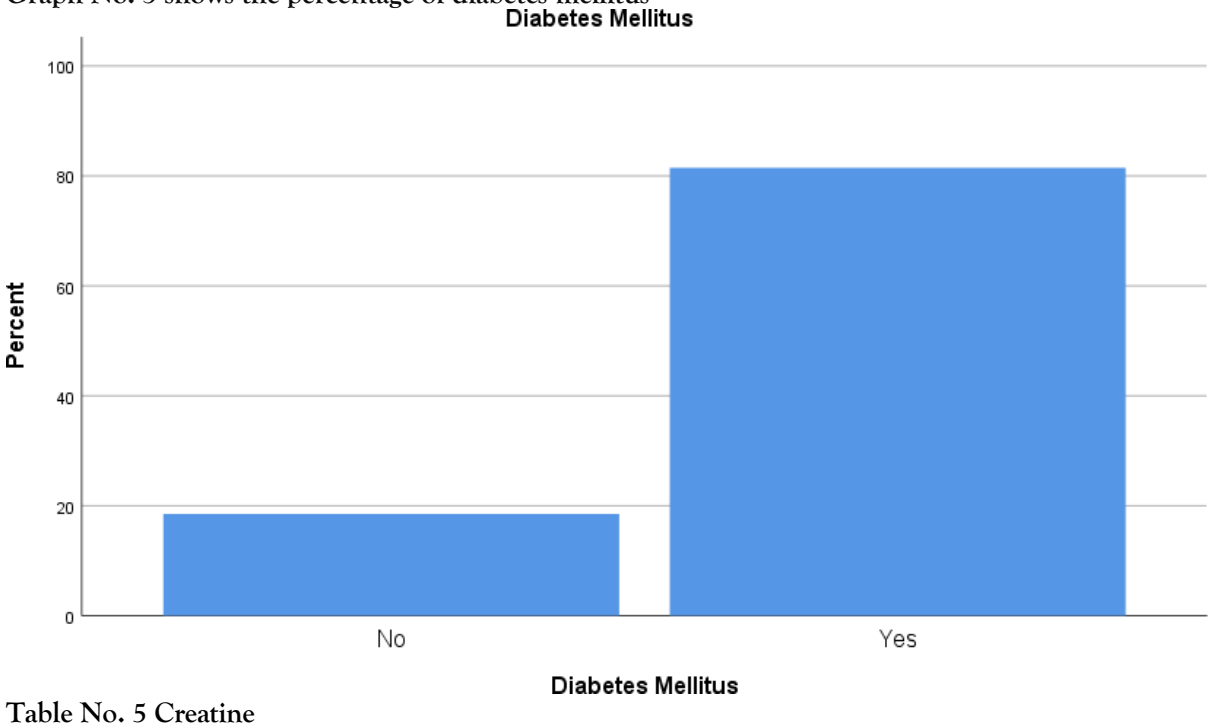

Table No. 5 Creatine

Twenty-seven patients had a value of creatinine, of which one was missing. The split was *perfectly even*, 13 patients (50.0%) fell in the 3–5 mg/dL range, and the other 13 (50.0%) had creatinine levels above 5 mg/dL.

		Frequency	Percent
	1.00 3-5 mg/dL	13	48.1
	2.00 >5 mg/dL	13	48.1
	Total	26	96.3

Missing	System	1	3.7
Total		27	100.0

Graph No. 4 Kt/V Adequacy Achieved vs Dialyzer Type

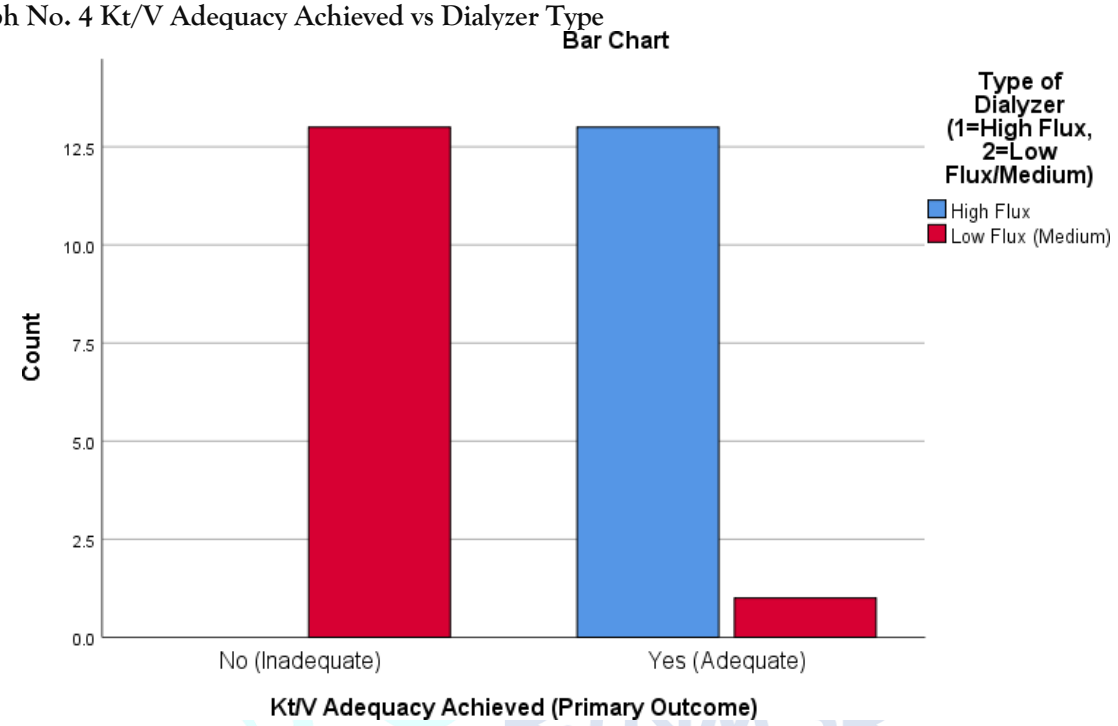

Table No. 6 Albumin

Serum albumin levels were well within the normal range for almost the entire sample. The majority of the patients who participated in this study (26 patients, 96.3%) had an albumin level between 3.4 and 5.4 g/dL, a widely accepted range for dialysis patients.

	Frequency	Percent
1.00 3.4-5.4 g/dL	26	96.3
2.00 5.5-10 g/dL	1	3.7
Total	27	100.0

Table No. 7: Association Between Dialyzer Type and Clinical Variables (Crosstabs and Chi-Square tests)

Variable	Test Used	χ^2 Value	df	p-Value	Significant
Dialysis Adequacy (Kt/V)	Pearson χ^2	23.28	1	< .001	Yes
Cardiovascular Disease (CVD)	Pearson χ^2	16.44	1	< .001	Yes
Session Time	Pearson χ^2	20.06	1	< .001	Yes
Blood Flow Rate (BFR)	Pearson χ^2	27.00	2	< .001	Yes

Urea Category	Pearson χ^2	20.06	1	< .001	Yes
Creatinine Category	Pearson χ^2	22.29	1	< .001	Yes
Potassium Category	Pearson χ^2	8.58	1	.003	Yes
Diabetes Mellitus (DM)	Fisher's Exact	—	1	.165	No
Access Type	Fisher's Exact	—	1	.165	No
Sessions per Week	Fisher's Exact	—	1	.678	No
Albumin Category	Fisher's Exact	—	1	1.000	No

The associations between dialyzer type and 11 clinical variables were explored in 27 haemodialysis patients by either chi-square or Fisher's Exact test. Seven variables (dialysis adequacy, CVD, session time, blood flow rate, urea, creatinine, and potassium) were significantly associated with dialyzer type at $p < .05$. Honestly, the pattern is pretty consistent. The remaining four variables, diabetes mellitus, access type, sessions per week, and albumin, showed *no significant association because of an insignificant p-value*, suggesting these were distributed similarly across both dialyzer groups. Where cell counts were < 5, Fisher's Exact Test was used as this was deemed to be more appropriate and reliable in these situations.

DISCUSSION

In a current study, the authors were interested in comparing dialysis adequacy and clinical outcomes between high-flux and low-flux dialyzers in a sample of 27 maintenance haemodialysis patients. The results were found to be statistically significant ($p < .05$) as displayed in Table 1 for dialyzer types in association with seven clinical variables namely, Kt/V adequacy, cardiovascular disease, session time, blood flow rate, urea, creatinine and potassium, with blood flow rate having the most significant association as ($N = 27$), $p < .001$. Results are grossly similar to other recently published studies that have reported better clearance of certain solutes and dialysis clearance (21).

After what is arguably the most important outcome, dialysis adequacy (measured as Kt/V), the study found that there was a clear association between the dialyzer type and Kt/V, with high-flux dialysis being associated with good Kt/V. The study results are similar to those of Nezami Ghale Noee et al. (2020), who assessed 185 haematodialysis (HD) patients, and observed that the Kt/V achieved dialysis adequacy was favorable in 79% of haemodialysis patients receiving a high-flux filter versus 1.5% in the haemodialysis patients having a low-flow filter ($p < .001$) between low-flux and high-flux filters. In a similar, multicenter 2026 dialysis that included 187 high-flux dialysis sessions and 189 low-flux dialysis sessions, Li et al. also reported higher Kt/V in the high-flux group ($p < .01$), higher urea reduction ratio (URR), and higher creatinine reduction ratio (CRR) that confirmed the superior clearance performance of highflux dialysis even with both groups of high and low flux still exceeding the Kt/V minimum adequacy criterion (K/DOQI), which is 1.2. Basically, the direction of this results concurs with the above mentioned recent studies, but the sample size in this particular study doesn't go far enough to push it quite so far into comparison(47).

The correlation between dialyzer type and the blood flow rate is of special interest and significance in this study. From this analysis, the blood flow

rate emerged as being most highly associated, which was consistent with literature regarding the relationship between these two variables. High blood flow rates resulted in higher mean Kt/V, ranging from 0.98 at the lowest blood flow rate of 100-200 ml/min to 1.72 at the highest blood flow rate >250 ml/min, and the best dialysis quality was obtained with high flux filters and high blood flow rates, reported by Nezami Ghale Noee et al. (2020). This is physiologically correct, as the flow rate more creates a higher membrane to blood gradient, and the high-flux membranes have greater pore size and surface area for the high flow to make besser, than the low flux have. Similar findings were observed in a systematic review published in Clinical Kidney J In 2024 that concluded that improved dialysis flow parameters are an important determinant of urea clearance and overall Kt/V delivery. Replication of this trend is significant in real world clinical practice contributing yet another little piece to the growing evidence base (48).

In this study, the type of dialyzer was also significantly associated with urea and creatinine clearance values, which also correlates well with the previously published data. Li et al., (2026) reported that relative mean (RM) URR and CRR were significantly higher for the high-flux group ($p < .05$) and attributed the statistically significant difference in absolute Kt/V values between the groups despite being only modest (0.05), to a consistently improved contribution of small-molecule clearance by the high-flux group. In a study published in 2022, researchers found that 110 patients with haemodialysis who were treated with high-flux dialysis showed significantly better levels of biochemical parameters compared with low-flux dialysis group (60 and 50 patients, respectively), these parameters include the urea and creatinine related ones. Collectively, these findings support the present study finding that the distribution of urea and creatinine categories is not random among the different types of dialyzers, but is appropriately linked to the dialysis modality. A higher level of pre-dialysis urea, indicative of accumulation due to less efficient clearance, was more common in the low-flux group, and this is a clinically relevant pattern even in this relatively small group of patients (49).

CONCLUSION

This study demonstrated a significant relationship between high-flux dialysis and better dialysis adequacy (Kt/V) and better urea and creatinine clearance across the entire dialysis duration, better blood flow parameters and differential burden of cardiovascular disease to low-flux dialysis in 27 maintenance haemodialysis patients. The results are also in line with the large and evolving literature from around the world that has been largely supportive of the use of a high-flux dialyzer to improve dialysis adequacy and cardiovascular mortality, thereby supporting its routine use in nephrology practice.

Several shortcomings of this study must be noted. The number of patients involved in this study (27) was small, compromising the statistical power and generalizability of the results. Because of its cross sectional design, causal inference is not possible for the study; only a few variables were not ceilinged due to high prevalence, but they were not discriminatory, such as diabetes mellitus. Lack of survival data is a significant absence, as is longitudinal follow-up, and beta-2 microglobulin, a middle-molecule clearance marker is not represented. Further, differences in the settings of the dialysis machines, composition of the dialysate and the presence or absence of medications between the two groups were not completely eliminated.

Further large, multicenter, randomized studies of high-flux vs low-flux haemodialysis should be performed to include more extensive panels of cytokines (beta-2 microglobulin, C-reactive protein, and parathyroid hormone) and have longer follow-up periods to collect the survival data. From a clinical standpoint, high-flux dialyzers should be the recommended treatment of choice for the maintenance hemodialysis patient with diabetes, cardiovascular disease, or low serum albumin as there is consistent evidence from several international studies of enhanced adequacy and mortality benefit from using high-flux as a standard of care when possible.

CHAPTER 8
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