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ORIGINAL ARTICLE

Comparison of the Efficacy of High Flux versus Low Flux membranes in Chronic Hemodialysis children

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ABSTRACT

Background: adequacy of dialysis is very important and has a major impact on morbidity as well as mortality among hemodialysis (HD) children. Many researchers have reported that high flux membrane (HFM) enhances the medium-sized molecules removal while other reports revealed no remarkable effect on them. This study aimed to compare the efficacy of high-flux hemodialysis (HFHD) versus low-flux hemodialysis (LFHD) in HD children.

Patients and methods: In the period from June to December 2023,50 caseson regular HD for end-stage renal disease included in this retrospective cohort study at the Pediatric nephrology unit, Zagazig University Children's Hospital. Blood samples were collected pre- and post-dialysis and forwarded to the lab for analysis. To evaluate dialysis effectiveness, we employed KT/V, blood urea nitrogen (BUN), as well as urea reduction ratio (URR) parameters.

Results: Post dialysis, a significant difference between the groups concerning the adequacy of HD was found according to URR and KT/V($p<0.001$, $p=0.008$ respectively). According to having URR (≥65%), 56% within HF group versus 24% had adequate HD. While according to KT/V (≥1.2), 72% versus 20% within HFHD and LFHD groups respectively had adequate HD.There was a notable variation between the tested groups in terms of HD sufficiency according to URR and KT/V ($p=0.041$, $p<0.001$ respectively).

Conclusion: High-flux hemodialysis demonstrates more successful efficacy in improving biochemical parameters, including URR and KT/V, compared to low-flux hemodialysis in pediatric patients.

Keywords: High flux, low flux, hemodialysis, URR, KT/V.

INTRODUCTION

CKD is referred to as the presence of either functional or structural kidney impairment lasting at least three months. Functional impairment is often defined by a continuous reduce in estimated glomerular filtration rate (eGFR), an ongoing rise in urine protein excretion, or both **[1]**.

Several factors should be considered when selecting a dialysis membrane: the material's biological compatibility with leukocytes and complement activation; the requirement for blood volume priming, which is associated with membrane area; and permeability, which is essentially identified by two characteristics: hydraulic permeability and molecular permeability, which are at least estimated by the molecular weight of the molecule under consideration **[2].**

HD works on the basis of solute clearance by ultrafiltration and diffusion across a semi-permeable membrane. The utilized membranes can be allocated into two primary categories: low-flux (LF), which is based on using low-permeability water dialyzers **[3]**; and high-flux (HF), a non-cellulose membrane with increased permeability that can eleminate moderate size molecules, ranging from 10,000 to 15,000 Dalton, such as lipoproteins and ß2 macroglobulin **[4].**

The efficacy of the HD process is one of the main worries in pediatric HD. HD clinics should conduct routine reviews of the efficacy of dialysis. **[2]**.

HF dialyzers are formed of cellulose membranes with an increased permeability than LF dialyzers. In comparison to LF dialyzers, HF dialyzers have a greater clearance rate of phosphorus and toxins with both medium and high molecular weights that accumulate during CKD **[5, 6]**. It is believed that the hydrophobic properties of HF dialyzers enable them to collect toxins correlated with uremia, decrease complement activators and cytokines, and ultimately reduce inflammatory reactions. Furthermore, it can delay the long-term effects of HD **[7]**.

This study aims to compare between the efficacy of HFHD versus LFHD patients who referred to pediatric dialysis unit of the Zagazig University Hospitals.

PATIENTS AND METHODS

Patients:

This retrospective cohort study was performed among 50 children on regular HD for end-stage renal disease (ESRD) at the pediatrics nephrology unit at Zagazig University Children's Hospital in the period from July to December 2023. 50 children (24 males and 26 females) on regular HD (3 times/ week, 3-4 hours /session) were subjected in the study. The cases were allocated into Group (A): ESRD patients on LFHD. Group (B): ESRD patients on HFHD. All cases underwent screening to ascertain their eligibility for the study based on the predetermined inclusion and exclusion criteria. Written informed consent was obtained from all patients' parents and the study was approved by the research ethical committee (International Review Board) ZU-IRB (IRB#10723). The research was conducted under the World Medical Association's Code of Ethics (Helsinki Declaration) for human research.

Cases with the following characteristics were included; ages between 3 to 16 years old, at least 6 months on regular HD (3 times/ week, 3-4 hrs. /session), and arterio-venous fistula was created for HD.

Cases with the following characteristics were excluded; refusal to participate in the study, severe infections in the past 3 months, cases with hepatic disease, previous peritoneal dialysis treatment.

Methods*:*

All study populations were subjected to; complete history taking (age, sex, height, weight, and anthropometric measurements), history of any associated diseases, and frequency of HD per week and duration of hemodialysis.

The general and local examination was done on all cases including evaluation of general condition, vital signs, and systematic examinations.

Laboratory investigations included liver function tests (serum albumin in addition to total protein; kidney function tests including urea and creatinine,A complete blood count (CBC) was performed using automated cell counter (XN330-Sysmex, Japan), total iron binding capacity (TIBC), serum iron in addition to serum calcium (Ca), phosphorus, magnesium, and uric acid; using Cobas 8000 Rochdiagnostic. C-reactive protein (CRP) was measured using turbidimetry on the Roche Cobas C 501; potassium (k) as well as sodium (Na) were measured on the Sensacore ST200 Plus. Serum ferritin and PTH were measured on the Cobas 6000, Rochdiagnostic, bleeding profile (PT, PTT, and INR using automated -1600 sysmexfully Roch-diagnostic.

Blood sampling: 10 ml of venous blood sample was gathered from each case under a septic condition by antecubital venipuncture and collected into 3.2% sodium citrate except for CBC samples which were drawn into EDTA tubes.

Serum preparation: The specimens were then processed using twofold centrifugation. Centrifuged at 2500 g for 15 minutes at room temperature, all blood samples were separated to obtain 3 mL of platelet-poor plasma. This process removed any platelets from the upper layer and buffy coat. The obtained plasma was centrifuged at 2500g for 15 min at room temperature, and 2.6 mL of supernatant was recovered. The resultant was kept in aliquots at -80°C for testing.

Special investigation

URR and the KT/V were employed to assess the effectiveness of HD. Two blood samples were collected from each patient pre and post the same session of HD, a blood sample before hemodialysis was taken from the needle arteries, and a blood sample after HD was collected from the arterial line around 2 min after lowering the blood flow rate to 80 mL/min.

In the KT/V test, the dialyzer clearance is represented by K in milliliters per minute, the dialysis time by T in minutes, and the urea distribution, which is equivalent to total body water, is represented by V, the bottom component of the percentage. In order to determine if HD was sufficient based on KT/V, the Daugirdas formula was used, which is SPkt/v = -Ln(R- 0.008Ït) + (4+3.5R) UF. The natural logarithm (Ln), the pre- to post-HD blood urea nitrogen (BUN) ratio (R), and ultrafiltration/liter (UF) are the variables in this equation. The URR is determined using the following formula:

$$URR = \frac{(\mathbf{Urea\ pre - HD}) - (Urea\ post - HD)}{(\mathbf{Urea\ post - HD})\ x\ \mathbf{100}}$$

The optimum URR dosage varies between >65% to >75%. The KDOQI recommendations suggest a target spKt/V of 1.4 per HD session for cases treated 3 times/week, with a minimum delivered spKt/V of 1.2.

STATISTICAL ANALYSIS

Information collected from a case's history, physical examination, laboratory tests. Data were analyzed utilizing SPSS version 20. Numbers and percentages were used to represent data for qualitative factors, while mean and standard deviation were used for quantitative ones. The Student t-test was used to compare multiple quantitative variables independently, while the Chi-square (χ 2) test was used to evaluate categorical data. The Mann Whitney test (Z) was utilized to calculate the difference between two groups of not regularly distributed quantitative variables. P < 0.05 was considered significant.

RESULTS

In the HF group, the mean age was 12.02 ± 3.78 years, 56% were males and 44% were females. For the LF group, the mean age was 11.59 ± 3.81 years, 44% were males and 56% were females (Table 1).

There was non-substantial variance between the groups concerning dry weight, height, and body mass index (BMI), systolic or diastolic blood pressure (SBP and DBP) (Table 1).

Post-dialysis, there was **significant** variation between the groups respecting BUN (**significantly** lower in HF group). Within each group, there was **significant** reduction in BUN post-HD (p<0.001). There was **remarkable** variation between the groups concerning % of change in BUN (62.16% within HF group versus 53.58% within LF group) (p<0.001) (Table 2).

Post-dialysis, there was a substantial variation between the groups respecting the adequacy of HD according to URR (p<0.001) and KT/V (p=0.008) (**significantly** higher in HF group) (Table 3).

There was a notable variation between the tested groups in terms of HD sufficiency according to URR and KT/V (p=0.041, p<0.001 respectively). High-Flux HD (HFHD) was adequate in 56% of instances and insufficient in 44% of cases based on URR (≥65%). However, the use of low-flux membrane (LFM) is resulted in acceptable dialysis in just 24% of cases, while it was unsatisfactory in the remaining 76%. In HFHD, 72% of patients had adequate dialysis (KT/V values ≥1.2), while 28% had inadequate HD. In low-flux HD (LFHD), only 20% of cases received adequate dialysis, whilst 80% had inadequate dialysis. (Table 4).

Table (1) Comparison between the studied groups regarding clinicodemographic data

	HF group N=25 (%)	**LF group N=25 (%)**	χ^2	**p**
Gender Male Female	 13 (56%) 12 (44%)	 11 (44%) 14 (56%)	0.321	0.571
	Mean ± SD	**Mean ± SD**	**t**	**p**
Age (year)	12.02 ± 3.78	11.59 ± 3.81	0.399	0.692
Height (cm)	127.88 ± 18.06	121.64 ± 20.28	1.149	0.256
BMI (kg/m2)	19.3 ± 4.68	17.99 ± 3.87	1.08	0.285
Systolic blood pressure (mmHg)	117.6 ± 16.9	120.0 ± 16.58	-0.507	0.615
Diastolic blood pressure (mmHg)	77.2 ± 13.39	80.8 ± 13.2	-0.957	0.343
	Median (IQR)	**Median (IQR)**	**Z**	**p**
Dry weight (kg)	29(22.25 – 41.5)	23(19.25 – 35.5)	-1.398	0.162

χ^2Chi square test t independent sample t test Z Mann Whitney test IQR interquartile range BMI: Body mass index.

Table (2) Comparison between the studied groups regarding blood urea nitrogen before and after dialysis

	HF group (n=25)	LF group (n=25)	Z	p
	Median (IQR)	**Median (IQR)**		
Pre BUN (mg/dl)	43(37 – 55)	53(43.5 – 65)	-1.816	0.069
	Mean ± SD	**Mean ± SD**	t	p
Post-dialysis BUN	17.11 ± 5.72	24.92 ± 7.24	-4.232	<0.001**
p (Wx)	<0.001**	<0.001**		
	Median (IQR)	**Median (IQR)**	Z	p
% decrease	62.16(57.84 – 65.17%)	53.58(48.83 – 57.74%)	-4.819	<0.001**

IQR interquartile range Z Mann Whitney test **p≤0.001 is statistically highly significant t independent sample t-test *p<0.05 is statistically significant Wx Wilcoxon signed rank test BUN: Blood urea nitrogen.

Table (3): Comparison between the studied groups regarding dialysis-related data

	HF group (n=25)	**LF group (n=25)**	**t**	**p**
	Mean ± SD	**Mean ± SD**		
URR (%)	62.95 ± 7.66	50.83 ± 12.63	4.102	<0.001**
KT/V	1.39 ± 0.39	1.14 ± 0.22	2.782	0.008*

****p**≤0.001 is statistically highly significantt independent sample t test ***p**<0.05 is statistically significant, **URR**: urea reduction ratio.

Table (4): Comparison between the studied groups regarding adequacy of dialysis:

	HF group N=25(%)	LF group N=25(%)	χ^2	p
URR **Adequate (≥65%)** **Inadequate (<65%)**	 13 (56%) 12 (44%)	 6 (24%) 19 (76%)	4.16	0.041*
KT/V **Adequate (≥1.2)** **Inadequate (<1.2)**	 18 (72%) 7 (28%)	 5 (20%) 20 (80%)	13.607	<0.001**

χ^2 :Chi square test ****p**≤0.001 is statistically highly significant ***p**<0.05 is statistically significant, **URR** :urea reduction ratio.

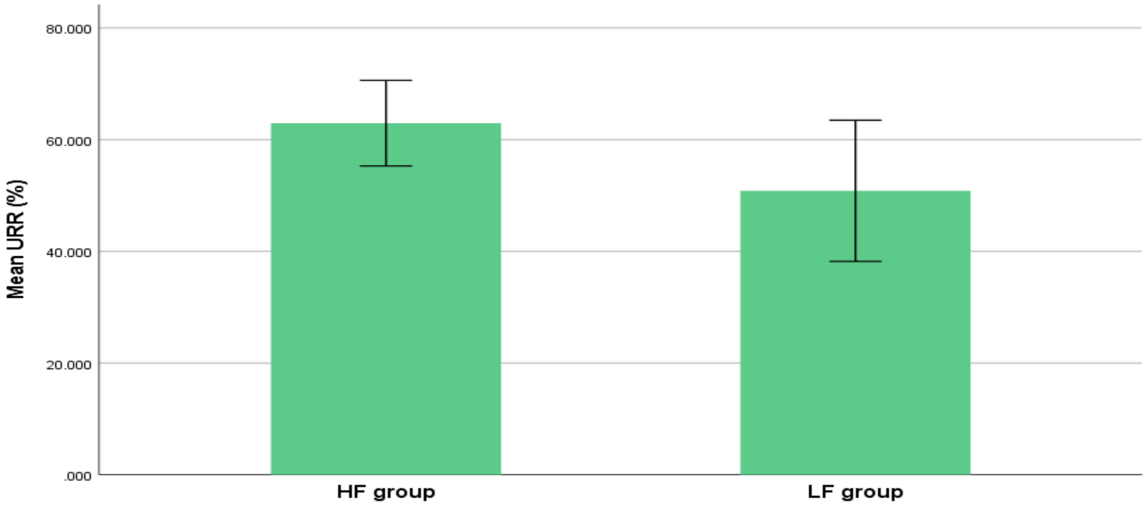

Figure (1): A Simple bar chart showing a comparison between groups regarding urea reduction ratio.

DISCUSSION

HD is the process of eliminating solutes by diffusion and ultrafiltration through a semi-permeable membrane. Dialyzers with low permeability (LF) and high permeability (HF) are the two types of membranes utilized in this process. HF dialyzers can remove moderate-sized molecules such as $ß_2$ macroglobulinandsome inflammatory proteins **[8]**.

The HD and Membrane Outcome Permeability (MPO) studies indicate that larger molecules can be eliminated by HF membranes (HFM) more effectively than by LF ones. However, the eventual impact of HFM on clinical outcomes remains uncertain **[9]**.

This study aimed to assess the effect of HFHD compared to LFHD on biochemical indices in pediatric cases undergoing HD.

Our study included 50 children allocated into two groups, 25 children in the HF group and 25 children in the LF group. Demographic data were comparable between the studied groups in terms of sex, age, dry weigh, height, BMI, SBP, and DBP.

The current findings exhibited that there was a substantial variation between the groups respecting the post-dialysis BUN (significantly reduced in the HF group). There was a substantial variation between the groups concerning the present change in BUN. While **Tawfik et al. [10]** showed that pre and post-HD BUN values elevated in the LFHD group compared to the HFHD group.

Our study showed that HD adequacy measures (Kt/V and URR) were significantly elevated in the HF compared to the LF. In line with our results, studies by **Tawfik et al**. **[10], Moslem et al. [12],and Iseni et al**. **[11]** reported similar results.

Moslem et al. [12] conducted research on the efficacy of HD in two groups, with fifteen participants in each, and found that in the HF group, the average Kt/V was 1.44 ± 0.32, and in 80% of instances, HD adequacy was greater than 1.2. Our study found that the HF group had significantly greater adequacy, even though the HF group had a higher KT/V (Kt/V was 1.39 ± 0.39 in 72% of cases with HD adequacy ⩾ 1.2) and was not significantly different from the LF group.**Moslem et al.[12]** reported that No information was provided regarding the blood flow rate, vascular access, or types of membranes used. Furthermore, when contrasted with our research, the sample size is quite small.

Ponikvar et al. **[13]** evaluated the efficacy of HFM versus LFM in cases with acute kidney failure in ICUs. The findings revealed no significant variations between the two membranes, indicating that the HFM is inadequate for these individuals. The result could be related to either the chronic or acute phases of the condition. In the chronic stage of renal failure caused by waste material accumulation, the productivity of HFMs would be noticeable when compared to LFMs.

Oates et al.[14] examined the impact of flux on phosphorous levels and erythropoietin responses. They also evaluated the effects of HFMs and LFMs on HD adequacy. The findings revealed no significant variations across the membranes. But, **Eknoyan et al. [15]** determined that HFM increases the efficacy of HD in chronic kidney failure. The results of the current investigation are compatible with our results.

Makar et al. [16] compared the efficacy of HFM and LFM on children undergoing HD. They found no significant differences in the effectiveness of HFM and LFM. **Makar et al. [16]** study was carried out on children who need specific features such as reduced blood flow rate, reduced dialysate flow rate, and membranes with smaller diameters to augment the comfort. These variables may have impacts on dialysis adequacy.

Oshvandi et al. **[17]** reported that KT/V in HFHD, 58.4% of cases had a mean KT/V ≥ 1.2, which was not substantially different from LFHD. However, adequacy was significantly greater in HFHD.

Malekmakan et al. **[18]** revealed that only 32.1% of kidney failure cases attained the ideal KT/V ratio and suggested employing sophisticated dialyzers (30). In the present research, the LF group had effective HD with KT/V ≥ 1.2, while the HF group had over 72%. These results indicate the vital necessity of HFMs in attaining the need for optimum dialysis.

Using HFMs improves dialysis efficiency and effectiveness. Furthermore, because of the capabilities of HFM in eliminating middle and large-size molecules, employing HFMs enables better elimination of a broader spectrum of toxins, potentially improving the quality of life of cases on chronic HD. Based on our findings, employing these HFMs in additional HD centers is advised.

Limitations

There are limitations in our study; the sample size might be quietly small, a totalof 50 cases only. This may restrict the capability for generalizing the results.Secondly, the investigation was carried out at a single dialysis unit at a specific hospital, This can limit the extent to which the findings can be employed to other groups or situations. Thirdly, short-term follow-up. It is advised that additional research on the comparison of HFMs and LFMs should be conducted over a longer duration.

We highly recommend conducting larger-scale multicenter studies to validate the findings of this study and enhance the generalizability of the results across diverse populations and settings. Implement long-term follow-up assessments to evaluate the sustained impact of high-flux hemodialysis on clinical outcomes, including mortality, hospitalization rates, and quality of life measures. Explore the comparative effectiveness of high-flux hemodialysis with other dialysis modalities, such as peritoneal dialysis or hemodiafiltration, to determine the most optimal treatment approach for pediatric cases with ESRD.

CONCLUSION

High-flux hemodialysis demonstrates more successful efficacy in improving biochemical parameters, including URR and KT/V, compared to low-flux hemodialysis in pediatric patients. These results highlight how HF membranes significantly improve dialysis outcomes and recommend more research in more extensive, multicenter studies.

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