

## Incremental Versus Conventional Hemodialysis for Preservation of Residual Kidney Function in Patients on Regular Hemodialysis

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### ABSTRACT

**Background:** Incremental hemodialysis (HD) has several potential advantages for patients, physicians and health care systems. In incident HD patients, conservation of residual kidney function "RKF" is significant and is correlated with several advantages, including survival of patient, improved quality of life, improved overall nutritional status and less anemia. The aim of this work was to evaluate incremental hemodialysis (twice/week) compared with conventional dialysis (thrice/week) for the conservation of the residual kidneyfunction among patients initiating regular hemodialysis.

**Aim of work:** The primary outcome of the study was an evaluation of incremental hemodialysis (twice/week) compared with conventional dialysis (thrice/week) for the conservation of the residual kidney function among patients initiating regular hemodialysis.

**Patient and Methods:** We assigned 40 patients with chronic kidney disease stage V D who early started hemodialysis into 2 groups: Group 1: 20 patients underwent incremental hemodialysis (twice/week), and Group 2: 20 patients underwent conventional hemodialysis (thrice/week). All patients followed for laboratory findings of (complete blood picture, creatinine, urea, calcium, albumin, phosphorus, parathyroid hormone, alkaline phosphatase, glomerular filtration rate). Also, Kt/v at start and every month was done. Clinical outcome measures included; mortality, cardiovascular outcome, hospital admission and dialysis complications.

**Results:** In the studied population, the mean age was (45.95 ± 2.97) years. Regarding sex 60% were males and 40% were females. Regarding outcome data, (20%) of patients had hypotension, (15%) had hospital admission, while nobody suffered mortality. Comparative study among the two groups showed a substantial decrease in the incidence of hypotension in the incremental group (40 %) relative to the conventional group (10%) (p = 0.03).

**Conclusion:** To conclude, our research investigates the correlation among the frequency of HD treatment and survival of patient. In line with recent literature, our results show that some selected patients with acceptable RKF, sufficient control of interdialytic gaining weight, and low or moderate burden of comorbid disease (CCI < 5) in an incident HD population, an HD incremental approach may be deemed as an appropriate alternative to conventional thrice-weekly HD.

**Keywords:** Incremental dialysis; Conventional dialysis; Residual Kidney Function.

### INTRODUCTION

There is substantial residual kidney function (RKF) for many HD-initiated patients. More than 90% of new ESRD hemodialysis patients start a standardized HD prescription 3 times a week in the United States<sup>1</sup>.

Incremental HD twice-weekly regimens are deemed suboptimal, whereas in some, with restricted resources, this is the only choice. In peritoneal dialysis, maintaining residual urine production is a significant goal, but this issue is not typical in hemodialysis. Vilar et al. and Fernández-Lucas et al. both found that patients beginning with twice-weekly incremental HD had better survival and greater residual urine production than patients beginning with a thrice-weekly regimen<sup>2</sup>.

Incremental dialysis uses the principle of changing the dialysis dose as per to RRF so that the dialysis dose is individualized. The basis is to provide adequate dialysis to achieve supra-minimum elimination of uremic solutes and the control of hypervolemia and then to increase the dialysis dose as the RRF decreases. In order to provide complete composite clearance, the general idea is to measure the total amount of urea extraction during dialysis and add it to the residual renal urea clearance (KRU)<sup>3,4</sup>.

Incremental HD offers patients, physicians, and health systems several possible advantages. In incident HD patients, 'preservation of RKF' is

significant and is correlated with many advantages, like patient longevity, improved quality of life, enhanced overall dietary status and decreased anemia (The Importance of Residual Kidney Function, see above). The "longevity of vascular access" associated with less regular arteriovenous fistula or graft cannulations are another advantage of incremental HD. In an examination from the FHN study, more frequent HD decreased the composite endpoint of vascular access loss, repair or access-related hospitalization. The chance of a first access event was 76 % higher with regular HD than with conventional HD<sup>5</sup>.

For less frequent HD therapy regimens, economic advantages also need to be considered. Conventional thrice-weekly HD treatments cost around \$89,000 per person per year in the United States, with a gross annual cost of \$42 billion (\$34 billion covered by Medicare, the rest by private insurance, Medicaid or out-of-pocket payments)<sup>6</sup>.

### PATIENTS AND MATERIALS

We assigned 40 patients with chronic kidney disease stage V D who early started hemodialysis into 2 groups: Group 1: 20 patients underwent incremental hemodialysis (twice/week). and Group 2: 20 patients underwent conventional hemodialysis (thrice/week).

During 6 months in Nephrology department, Military Hospitals (AL-maadi, kobry AL-koba and air force military hospital).

All patients will be subjected to: History & complete physical examination, Routine laboratory investigations: CBC, liver and kidney function Calcium, phosphorus, intact parathyroid hormone GFR and KT/V. Clinical outcome

Measures: Mortality, Cardiovascular outcome, Hospital admission and Dialysis complications,

Statistical analysis:

Using MedCalc ver. 18.2.1 (MedCalc, Ostend, Belgium), data input, processing and statistical analysis have been conducted out. Significance tests were used (Mann-Whitney's, Chi square, tests, factorial ANOVA, logistic regression analysis, and analysis of the ROC Curve). Data were supplied and appropriate analysis was carried out as per type of data obtained for each variable (parametric and non-parametric). P-values of lower than 0.05 (5%) were deemed statistically important.

### RESULTS

In the studied population, the mean age of all patients was  $(45.95 \pm 2.97)$  years, and the average UOP was  $(1124.3 \pm 337.2)$  ml/day. Regarding gender of the patients, the majority (60%) of patients were males; while (40%) were females, with (65%) had DM, and (75%) had HTN.

Regarding outcome data, (20%) of patients had hypotension, (15%) had hospital admission, while nobody suffered mortality.

Comparative studies: The 40 CKD patients were split into two separate groups accordingly to the dialysis

technique: Conventional group (20 patients) and Incremental group (20 patients).

Non-significant differences in all basic clinical data were observed in a comparative analysis among the two groups ( $p > 0.05$ ).

Non-significant differences in all baseline laboratory data were observed in the comparative analysis among the two groups ( $p > 0.05$ ).

ROC curve analysis to predict patients (6-months) improvement (Table 1, Fig. 1 - 4): By using ROC-curve analysis, Incremental dialysis technique expected patients with hemoglobin improvement, with excellent (93%) accuracy, sensitivity= 75% and specificity= 100% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique predicted patients with platelets improvement, with fair (70%) accuracy, sensitivity= 55% and specificity= 100% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique predicted patients with GFR improvement, with perfect (100%) accuracy, sensitivity= 100% and specificity= 100% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique predicted patients with uric acid improvement, with fair (70%) accuracy, sensitivity= 50% and specificity= 90% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique expected patients with Ca improvement, with excellent (96%) accuracy, sensitivity= 100% and specificity= 80% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique expected patients with Ph improvement, with excellent (94%) accuracy, sensitivity= 85% and specificity= 90% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique expected patients with PTH improvement, with excellent (91%) accuracy, sensitivity= 80% and specificity= 90% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique predicted patients with albumin improvement, with fair (79%) accuracy, sensitivity= 55% and specificity= 90% ( $p < 0.05$ ).

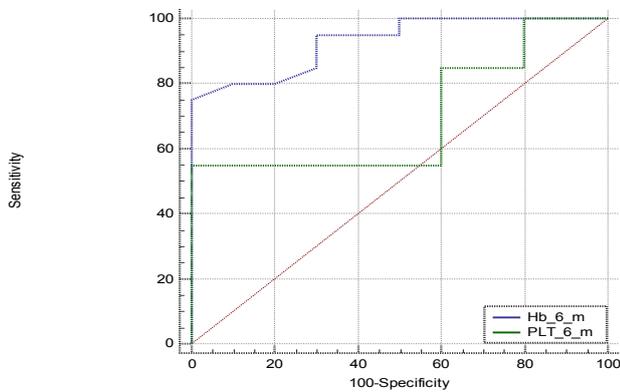
By using ROC-curve analysis, Incremental dialysis technique predicted patients with Kt/V improvement, with good (89%) accuracy, sensitivity= 60% and specificity= 100% ( $p < 0.05$ ).

By using ROC-curve analysis, Incremental dialysis technique showed non-significant predictive values regarding TLC, creatinine, urea, Na and K improvements ( $p > 0.05$ ).

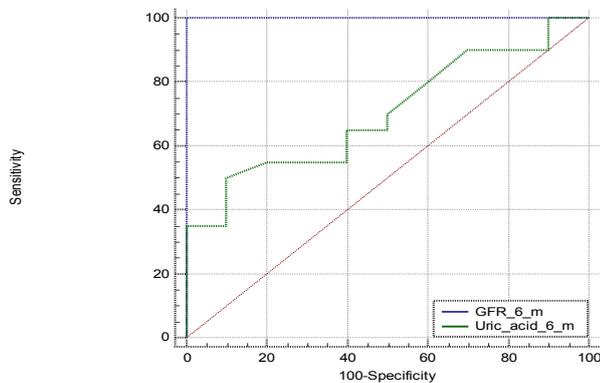
| Variable               | AUC   | SE    | Sensitivity (%) | Specificity (%) | P value   |
|------------------------|-------|-------|-----------------|-----------------|-----------|
| Hb                     | 0.930 | 0.038 | 75              | 100             | <0.0001** |
| PLT                    | 0.700 | 0.087 | 55              | 100             | 0.022*    |
| TLC                    | 0.585 | 0.093 | 65              | 60              | 0.3652    |
| Creat. (post-dialysis) | 0.660 | 0.090 | 90              | 60              | 0.0781    |
| Urea (post-dialysis)   | 0.600 | 0.094 | 100             | 40              | 0.2882    |
| GFR                    | 1.000 | 0     | 100             | 100             | <0.0001** |
| Uric acid              | 0.703 | 0.083 | 50              | 90              | 0.015*    |
| Na                     | 0.623 | 0.096 | 40              | 100             | 0.2053    |
| K                      | 0.588 | 0.091 | 90              | 30              | 0.3399    |
| Ca                     | 0.968 | 0.023 | 100             | 80              | <0.0001** |
| Ph                     | 0.941 | 0.033 | 85              | 90              | <0.0001** |
| PTH                    | 0.915 | 0.043 | 80              | 90              | <0.0001** |
| Alb.                   | 0.790 | 0.072 | 55              | 90              | 0.0001**  |
| Kt/V                   | 0.895 | 0.048 | 60              | 100             | <0.0001** |

ROC (Receiver operating characteristic), AUC= Area under curve, SE= Standard Error.

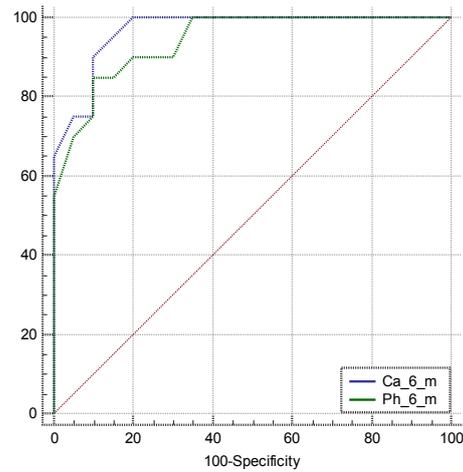
**Table 1:** Roc-curve of Incremental dialysis technique to predict patients (6-months) improvement:



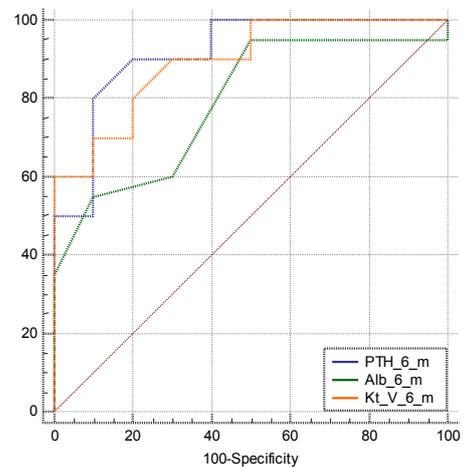
**Fig.1:** ROC curve of hemoglobin and platelets (Incremental dialysis technique).



**Fig.2:** ROC curve of GFR and uric acid (Incremental dialysis technique).



**Fig.3:** ROC curve of Ca and Ph (Incremental dialysis technique).



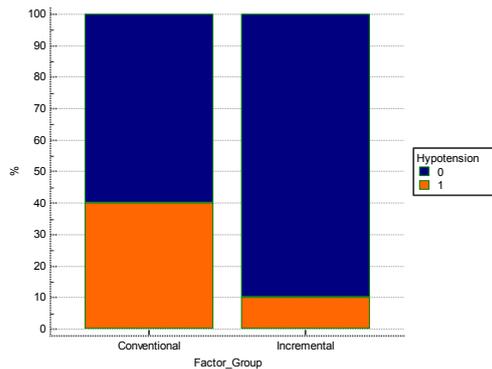
**Fig.4:** ROC curve of PTH, albumin and Kt/V (Incremental dialysis technique).

| Variable           |     | Conventional group (20) | Incremental group (20) | Chi square test |
|--------------------|-----|-------------------------|------------------------|-----------------|
|                    |     |                         |                        | P value         |
| Hypotension        | +ve | 8 (40%)                 | 2 (10%)                | = 0.03*         |
| Hospital admission | +ve | 6 (30%)                 | 2 (10%)                | = 0.1185        |

**Table 2:** Comparison between the two groups with respect to the results data using the Chi square test:

Comparative among the two groups identified; substantial decrease in the incidence of hypotension in incremental groups (40 %); relative to conventional groups (10%); with a very significant statistical difference (p = 0.03) (Table 2, Fig. 5).

Non-significant differences in hospital admission were observed in the comparative analysis among the 2 groups (p>0.05).



**Fig.5:** Comparison between the 2 groups of patients regarding hypotension.

## DISCUSSION

This was a prospective comparative research performed in 40 patients with chronic kidney disease (CKD); to assess incremental hemodialysis (twice/week) compared with conventional dialysis (thrice/week) for the conservation of residual kidney function among patients initiating regular hemodialysis.

The study will be conducted in patients with chronic end stage kidney disease through 2018 and 2019 in Military hospitals (Maadi Military Hospital, kobriekoba military hospital and air force military hospital). We assigned 40 patients with chronic kidney disease stage V D who early started hemodialysis.

Group1: 20 patients underwent incremental hemodialysis (twice/week) and Group 2: 20 patients underwent conventional hemodialysis (thrice/week).

Patients have been followed for laboratory findings of (complete blood picture, serum creatinine, urea, calcium, albumin, phosphorus, parathyroid hormone, alkaline phosphatase, glomerular filtration rate).

Regarding Baseline data, we found that; the mean age of all patients was ( $45.95 \pm 2.97$ ) years, and the average UOP was ( $1124.3 \pm 337.2$ ) ml/day. Regarding gender of the patients, the majority (60%) of patients were males; while (40%) were females, with (65%) had DM, and (75%) had HTN, which came in agreement with A. Mathew et al. <sup>7</sup> and Lucas et al. <sup>8</sup>.

Regarding Outcome data, (20%) of patients had hypotension, (15%) had hospital admission, while nobody suffered mortality, which came in agreement with Lucas et al. <sup>8</sup>

Lucas et al reported that in the 2- and 3-HD / week groups, hospitalization period was 4 (0-15) and 11 (2-14) days/patient-years, respectively (median and IQR,  $P = 0, 068$ ). <sup>8</sup>

No substantial difference in the comparative study between the 2 groups with respect to all basic clinical data ( $p > 0.05$ ), which came in agreement with A. Mathew et al. <sup>7</sup>, Lucas et al. <sup>8</sup> and Liu et al. <sup>9</sup>

A. Mathew et al. reported that, no statistical disparity with all-cause mortality in subgroups of age, gender

, ethnicity, central venous catheter use or diabetes condition in preset subgroup analyses of the matched cohort compared incremental HD to conventional HD. <sup>7</sup>

We found marked increase in UOP in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with Liu et al. <sup>9</sup>, A. Mathew et al. <sup>7</sup>, Lucas et al. <sup>8</sup>, A. T. Mathew et al. <sup>10</sup> and Merino et al. <sup>11</sup>

Liu et al reported that those on incremental HD appeared to be female and thinner relative to those on traditional HD. The amount of urine in the incremental HD group was higher relative to the conventional HD group <sup>9</sup>.

Lucas et al reported that the daily volume of urine and GFR (glomerular filtration rate) is higher throughout the 2 HD / week group. In patients who began 2- and 3 HD / week, the GFR range was 2–12, 6 mL / min and 0, 2–13, 6 mL / min, respectively. <sup>8</sup>

We found marked increase in hemoglobin in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with Merino et al. <sup>11</sup> and A. Mathew et al. <sup>7</sup>

Hemoglobin and hematocrit enhanced after 1 year and the mean dose of erythropoiesis stimulating factors (ESF) did not raise significantly, reported by Merino et al. 2017, which was darbepoetin (mcg / week),  $27 \pm 21$  and  $30 \pm 22$  mcg / week,  $p = 0.725$  in our case. <sup>11</sup>

Liu et al reported that those on incremental HD appeared to be female and thinner relative to patients on traditional HD. The calcium and hemoglobin levels between the groups were similar. <sup>9</sup>

Lucas et al reported that both groups had similar hemoglobin concentrations; however, the weekly erythropoietin dose was substantially lower in patients, who began 2 HD / week. <sup>8</sup>

We found marked increase in post-dialysis urea in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with A. Mathew et al. 2016. <sup>7</sup>

A. Mathew et al reported that patients with an incremental HD regimen and those with sufficient baseline RKF had substantially more conservation of renal clearance of urea in that study. <sup>7</sup>

We found marked increase in GFR in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with Kalantar-Zadeh et al. <sup>12</sup>, Bolasco et al. <sup>13</sup>, Rhee et al. <sup>14</sup>, Liu et al. <sup>9</sup>, A. Mathew et al. <sup>7</sup>, Lucas et al. <sup>8</sup> and Obi et al. <sup>14</sup>

In reality, Bolasco et al recorded faster loss of RKF by twice-weekly or more regular hemodialysis as a negative predictive factor for both mortality and morbidity; however, nephrologists have long undervalued the clinical significance of RKF. <sup>13</sup>

A. Mathew et al reported that, a prospective study of 168 patients with HD incidence showed that in twice-weekly HD-initiated patients, the proportion of

patients with RKF loss was substantially lower in twice-weekly HD-initiated patients relative to conventional thrice-week HD-initiated patients<sup>7</sup>.

Obi et al reported that both the clearance of renal urea and the amount of urine in incremental vs conventional regimens (P, 0.001 for both) displayed considerably slower decreases over time in this matched cohort.<sup>14</sup>

We found marked increase in calcium in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with A. Mathew et al.<sup>7</sup> and Obi et al.<sup>14</sup>

A. Mathew et al reported that, the final cohort of the study consisted of 87,718 patients from 1737 facilities, comprising 201 frequent (\$4 times weekly) HD patients from 158 facilities and 682 incremental (twice weekly or less) HD patients from 444 facilities, with increased calcium level in incremental group  $9.1 \pm 0.5$ .<sup>7</sup>

Obi et al reported that, Trends in the selected parameters indicated lower dialysis frequency, shorter dialysis period, lower hemoglobin and corrected serum calcium concentrations in patients treated with an incremental regimen.<sup>14</sup>

Liu et al reported that, there are no statistically substantial variations in serum levels of calcium, phosphate, albumin, hemoglobin or hospitalization rates among groups. Serum calcium (SMD=-0.397, 95% CI: -0.523 to -0.272,  $P < 0.001$ ; I<sup>2</sup> = 0 %) relative to laboratory values at the end of follow-up (subgroup 1).<sup>9</sup>

We found marked decrease in phosphorus in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with A. Mathew et al.<sup>7</sup>, Merino et al.<sup>11</sup> and Liu et al.<sup>9</sup>

A. Mathew et al reported that, the final cohort of the study consisted of 87,718 patients from 1737 facilities, comprising 201 frequent (\$4 times weekly) HD patients from 158 facilities and 682 incremental (twice weekly or less) HD patients from 444 facilities, with decreased phosphorus in incremental group  $4.3 \pm 1.0$ .<sup>7</sup>

Merino et al reported that after 1 year, serum phosphate level control had improved, but the variations were not statistically relevant.<sup>11</sup>

Liu et al reported that, Serum phosphate levels in the incremental HD group were lower, and serum albumin levels were higher.<sup>9</sup>

We found marked decrease in PTH in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with Merino et al.<sup>11</sup>

Merino et al reported that after 1 year, control of PTH levels improved, but the variations were not statistically relevant.<sup>11</sup>

We found marked decrease in albumin in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in disagreement with Liu et al.<sup>9</sup>.

Liu et al reported that, Serum phosphate levels in the incremental HD group were lower, and serum albumin levels were higher.<sup>9</sup>

We found marked decrease in Kt/V in incremental group; compared to conventional group; during the serial measurements ( $p < 0.05$ ), which came in agreement with Lucas et al.<sup>8</sup>

A comparative study among the 2 groups demonstrated; a substantial decrease in the incidence of hypotension in the incremental group (40%); a highly substantial statistical difference ( $p = 0.03$ ), relative to the conventional group (10%); which came in agreement with A. Mathew et al.<sup>7</sup>, Merino et al.<sup>11</sup>, Kalantar-Zadeh et al.<sup>12</sup> and A. T. Mathew et al.<sup>10</sup>

Merino et al reported that, the average baseline systolic blood pressure (mmHg) was  $145 \pm 12$  mmHg versus  $151 \pm 14$  after 12 months ( $p = 0.165$ ) and the average baseline diastolic blood pressure was  $72 \pm 13$  versus  $67 \pm 20$  at baseline and 1 year ( $p = 0.243$ ). Blood pressure was similar at baseline relative to 12 months.<sup>11</sup>

Comparative study among the two groups showed no substantial difference in hospital admission ( $p > 0.05$ ), which came in agreement with A.T. Mathew et al.<sup>10</sup>, Liu et al.<sup>9</sup> and Lucas et al.<sup>8</sup>

A. T. Mathew et al reported that, more frequent HD decreased the composite endpoint of vascular access loss, repair, or access-related hospitalization in the analysis of the FHN study.<sup>10</sup>

Kalantar-Zadeh et al reported that, this incremental approach to hemodialysis offers a more gradual and tolerable transition to renal replacement treatment, possibly resulting in improved quality of life linked to health, longer conservation of residual kidney function, reduction of inflammatory and oxidative stress caused by hemodialysis, reduced rate of intradialytic hypotension, decreased stimulating agent dose of erythropoiesis and decreased mortality and morbidity.<sup>12</sup>

## CONCLUSION

To conclude, our research investigates the correlation among the frequency of HD treatment and survival of patient. In line with recent literature, our results show that some selected patients with acceptable RKF, sufficient control of interdialytic gaining weight, and low or moderate burden of comorbid disease (CCI < 5) in an incident HD population, an HD incremental approach may be deemed as an appropriate alternative to conventional thrice-weekly HD.

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