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# BANGLADESH RENAL JOURNAL

(A Journal of continuing education in kidney diseases)

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## GENERAL INFORMATION

Bangladesh Renal Journal is the official organ of the Bangladesh Renal Association. The Journal publishes two issue in a year i.e. June and December. The Journal is devoted to continuing education in kidney diseases.

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## Quality of life in patients of end stage renal disease on different modalities of treatment

In Bangladesh, nearly 35,000 patients with chronic kidney disease report to Government hospitals with features of ESRD who require renal replacement therapy. Most of the patients cannot afford any form of RRT and have no option other than conservative management. Only few fortunate patients can start HD, fewer than 10% of patients choose PD as their initial therapy<sup>1</sup>.

Comparisons of KDQOL on HD and PD have produced conflicting results. A review of this literature that focused on the relationship of dialysis modality to mental health domains suggested that patients experience less distress and better psychologic well-being on PD<sup>2</sup>. However, interpretation of this literature was limited because of small and convenient samples of patients, use of new instruments or instruments not tested in ESRD, inadequate control of case-mix, and a lack of repeated measures.

There have been just a few studies on quality of life in ESRD who are on conservative, HD and CAPD. It is expected that quality of life cannot be maintained without RRT, it is only to calculate the days of life without dialysis. Mejbah Uddin Noman and others in their paper in this issue of BRJ has shown that conservative management has no role in the ESRD management. At the same time it also evident that an eight hour dialysis is inadequate.

The only longitudinal comparison of modalities was a study of consecutive patients who began dialysis in 13 Dutch dialysis centers. The results suggested that HD was associated with a relative benefit in physical aspects of patient-reported health<sup>3</sup>. Patients on both HD and PD reported improvements in nearly all aspects of general functioning and psychologic well-being. The surprising finding was that patients on HD improved more on aspects of general parameters of quality of life than patients on PD, with greater improvements. Despite lower scores at baseline, at 1 yr, patients on HD actually reported better scores in some domains, such as better physical role

functioning. These findings remained after adjustment for baseline patient characteristics, although the differences were no longer statistically significant.

Changes in dialysis-specific aspects of life were more mixed, and there were more differences between the two modalities. HD patients improved more in some aspects, such as sleep (which for PD patients actually became worse over time) and body image. At the end of 1 yr, patients on HD reported significantly better sexual functioning than those on PD. PD patients improved more on other dialysis-spectrum. The good news for patients on both modalities is that health and general well-being should improve during the first year of dialysis. In their paper of Mejbah uddin et al there is a clear benefit with CAPD in alleviating mental and physical parameters. This clear difference in the findings of Dutch study and Bangladesh study could be regional, socio-economic or due to factors yet to found out. More and more studies required in this field to solve these issues.

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*(Bang. Renal J. 2013; 32(1): 1)*

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3. Cameron JI, Whiteside C, Katz J, Devins GM: Differences in quality of life across renal replacement therapies: A meta-analytic comparison. *Am J Kidney Dis* 35: 629–637, 2000

## Quality of Life among the CKD Patients on Different Modalities of Treatment

Mesbah Uddin Noman<sup>1</sup>, Abu Saleh Ahmed<sup>2</sup>, Ratan Das Gupta<sup>3</sup>, Hedayetul Islam<sup>4</sup>, Syed Mahtab-Ul-Islam<sup>5</sup>, Fazla Alahi Khan<sup>6</sup>

### Abstract

*Quality of life is considered not only as parameter of efficacy of a treatment modality but also an indicator for morbidity and survival in chronic kidney disease. In Bangladesh, 8 hours dialysis per week has been adopted as renal replacement therapy in government hospitals and became a common practice even in non-government institutes mainly due to financial strain. This longitudinal study with purposive sampling was conducted in Dhaka Medical College and Dialysis Unit, BIRDEM, during the period from November 2010 to October, 2011 among 132 patients. The subjects were divided in four groups, patients only on conservative treatment (42 patients), patients on 8 hours dialysis per week (39 patients), patients on 12 hours dialysis per week (30 patients), patients on CAPD (23 patients). The patients were followed up at monthly interval using KDQOL survey. The result showed that physical and mental component of the patients on conservative and 8 hours dialysis per week did not show any difference and both groups were significantly worse than that of 12 hours dialysis and CAPD; CAPD patients were found to enjoy best physical and mental component. The 'burden of kidney disease' and 'effects of kidney disease' were also significantly lower among the patients with conservative treatment and 8 hours dialysis in comparison to 12 hours dialysis per week and CAPD patients, the CAPD patients were even better also in these two components. In the component which compared efficacy of a treatment modality to reduce the symptoms of kidney disease, 8 hours dialysis showed significant difference from conservative treatment, but 12 hours dialysis per week and CAPD were still better even in this segment. The study result concluded that 8 hours dialysis per week does not provide any benefit in comparison to conservative treatment except in symptom relief, whereas 12 hours dialysis per week and CAPD were found to be effective alleviating in all the components of quality of life among CKD patients.*

(Bang. Renal J. 2013; 32(2): 3-11 )

### Introduction

The protean physical manifestations of chronic kidney disease (CKD) span every organ system, range in severity from minute disturbance to life threatening, and negatively disrupt patients' lifestyles without exception.<sup>1-2</sup> Hemodialysis, peritoneal dialysis and kidney transplantation are miracles of medical technology, and the ability of these technologies to sustain lives is of unquestioned significance. Blake et al.<sup>3</sup> and Lin et al.<sup>4</sup> documented in two different population that hemodialysis, which is time-intensive, expensive, and requires fluid and dietary restrictions, in long term often results in a loss of freedom,

dependence on caregivers, disruption of marital, family, and social life, and reduced or loss of financial income.

Canadian Erythropoietin Study Group<sup>5</sup> and Moreno et al.<sup>6</sup> showed patients having dialysis have lower QOL score in comparison to normal person of same age and sex. Evans, Manninen and Garrison<sup>7</sup> and Simmons<sup>8</sup> compared hemodialysis against continuous peritoneal dialysis, which showed better result among continuous peritoneal dialysis group. A multicentre study in Italy showed more independence and positive attitude among continuous peritoneal dialysis patients but more anxiety and feeling

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of insecurity in the same group.<sup>9</sup> Impaired functioning and well-being in dialysis patients is linked to increased risk of death and hospitalization while improvement in scores has been associated with better outcomes.<sup>10</sup>

In Bangladesh, due to financial strain and inadequate health facility, almost all government hospitals and semi government organization that provide hemodialysis at low cost and contribute to major share of health care delivered to Chronic kidney disease patients allocate only 8 hours dialysis per week for each patient rather than recommended at least 12 hours dialysis per week. On the other hand, due to poverty, illiteracy and lack of health consciousness in majority people risk of infection is assumed to be very high among Continuous Ambulatory Peritoneal Dialysis patients and still it is not a widely prescribed method of renal replacement therapy in Bangladesh. The scenario is further complicated by lack of regular use of erythropoietin and very high incidence of malnutrition among the patients undergoing hemodialysis<sup>11</sup> which are independent predictors of Quality of life.

This study is intended to assess KDQOL among patients receiving hemodialysis for 8 hours and 12 hours per week, patients receiving CAPD, and patients of CKD stage V who decline any form of renal replacement therapy and remained on conservative treatment. For the purpose of measurement KDQOL SF-36 survey which was used in DOPPS study and proved to be validated in terms of reproducibility and internal consistency, translated in Bengali version, obtained from KDQOL Working group website has been adopted.

### Material and Methods

The patients who received dialysis at Department of Nephrology, Dhaka Medical College Hospital, Dialysis Unit, BIRDEM, and the patients who received consultation at Outdoor Department of Nephrology, Dhaka Medical College Hospital during the period of November, 2010 to October, 2011 were enrolled in the study. This longitudinal study was conducted by purposive sampling. All the patients diagnosed as chronic kidney disease stage V fulfilling the criteria to commence renal replacement therapy were included. The patients who received dialysis for less than 3 months, those who were compelled to choose one certain form of renal replacement therapy or those who were admitted due to acute illness were not included in the study. The patients who were not able to answer the questionnaire due to cognitive impairment were also not included. 134 patients were enrolled in this study, out of which 42 patients who were advised to commence renal replacement therapy and after counseling opted to remain in conservative treatment were enrolled in GROUP I, 39

patients who received hemodialysis 8 hours per week were enrolled in GROUP II, 30 patients who received hemodialysis 12 hours per week in one or more centers were enrolled in GROUP III and 23 patients who received Continuous Peritoneal Dialysis at least 3 exchanges per day were enrolled in GROUP IV.

Data was collected using Kidney Disease Quality Of Life-36 (KDQOL-36) survey. KDQOL-36 is 36 items health related quality of life survey which has a generic component consisting of 12 assessments adopted from SF12 for aspects of general health and another specific component for kidney disease consisting of 24 assessments. KDQOL-36 has five subscales: Physical component summary (PCS), Mental component score (MCS), Burden of kidney disease, Symptoms /Problem subscale and Effects of Kidney disease. However, while conducting the study it was noticed that some of the questions were not self-explanatory in our context which required assistance of the researcher. To overcome this short coming a number of questions have been elaborated with appropriate examples. A detailed history and examination according to designed preform was conducted which included demographic data like age, sex, employment, income level and monthly expenditure.

KDQOL-36 survey was administered in Bengali language during first 2 hours of hemodialysis and during first 2 hours of first exchange of the day among patients having CAPD and during outdoor visit among the patients of CKD stage V receiving conservative treatment, preferably by patient himself and if not possible in form of interview after obtaining written consent. The process was repeated for three times at approximately 30 days interval keeping all parameters uninterrupted. Biochemical variables are to be investigated include Hemoglobin level, Serum albumin. Statistical analyses of the results were obtained by using SPSS-16. For statistical analysis continuous variable was analyzed by unpaired t-test, ANOVA and categorical data was analyzed by  $\chi^2$  test (Chi-square test) and Pearson's correlation coefficient was used. A 'p' value of <0.05 was considered significant.

### Result

Socio demographic pattern of the study population is presented in table 1. Variation of age distribution were not different among the different groups. Male predominance was noted among the whole study population as well as among all groups of study population, however, the variance of distribution among different study groups were not statistically significantly different. The marital status was also not significantly different among the groups.



**Table I**  
*Socio-demographic characteristics of the study patients (n=134).*

Socio-demographic characteristics	Group I (n=42)		Group II (n=39)		Group III (n=30)		Group IV (n=23)		P value
	n	%	n	%	n	%	n	%	
Age (in year)									
<20	1	2.4	0	0.0	0	0.0	0	0.0	
21-30	7	16.7	7	17.9	3	10.0	0	0.0	
31-40	7	16.7	4	10.3	6	20.0	0	0.0	
41-50	8	19.0	15	38.5	9	30.0	8	34.8	
51-60	11	26.2	10	25.6	5	16.7	14	60.9	
61-70	5	11.9	2	5.1	6	20.0	0	0.0	
71-80	2	4.8	1	2.6	1	3.3	1	4.3	
>80	1	2.4	0	0.0	0	0.0	0	0.0	
Mean ± SD	48.14±16		46.28±12.11		48.07±12.43		53.57±7.16		0.130 <sup>ns</sup>
Range (min-max)	(18-82)		(23-75)		(25-71)		(43-75)		
Sex									
Male	27	64.3	30	76.9	20	66.7	14	60.9	0.521 <sup>ns</sup>
Female	15	35.7	9	23.1	10	33.3	9	39.1	
Marital status									
Married	37	88.1	34	87.2	29	96.7	23	100.0	0.182 <sup>ns</sup>
Unmarried	5	11.9	5	12.8	1	3.3	0	0.0	

s= significant; ns=not significant

P value reached from ANOVA test.

P value reached from Chi square test

The distribution of physical component summary of quality of life (table 2) were analyzed in three consecutive follow ups 1 month apart and it was found that in all the follow ups the patients belonging to 8 hours dialysis per week (Group 2) and the patients on conservative treatment (Group 1) did not show significant difference. On the contrary 12 hours dialysis per week Group 3) and the patients on CAPD (Group 4) were significantly better than Group 1 and Group 2. Moreover, the patients on CAPD were better than 12 hours dialysis per week in all the follow ups.

Table 3 showed the mental component summary among the study groups and it was found that group 1 and group 2 did not show any significant difference. Whereas in comparison between 8 hours dialysis/week and 12 hours dialysis/week, though mental component summary was better among the patients with 12 hours dialysis/week in all the follow ups but it was statistically significant in 1<sup>st</sup> and 3<sup>rd</sup> follow up but not in 2<sup>nd</sup> follow up. CAPD patients (group 4) showed better performance in terms of mental

component summary significantly in comparison to 8 hours dialysis/week in all follow ups. However, the results were not significantly different between CAPD patients and the patients with 12 hours/ week dialysis though CAPD patients enjoyed better mental component.

The distribution of the treatment modalities to reduce the burden of kidney disease is shown in table 4. The patients on conservative treatment only and 8 hours dialysis/week suffered almost same burden and the results were not significantly different in any follow up. 12 hours dialysis/week reduced the burden more efficiently in comparison to 8 hours dialysis/week, though the results were not significantly different in 1<sup>st</sup> follow up between these two groups, but they were significantly different in consecutive follow ups. Group 4 (CAPD patients) were better in terms of reducing the burden of kidney disease in all the follow ups in comparison to 8 hours dialysis/ week, but there was no statistical difference among the patients with 12 hours dialysis/ week and CAPD patients, although the latter group showed better performance.

**Table II***Mean distribution of the study patients according to physical component summary at different follow-ups (n=134)*

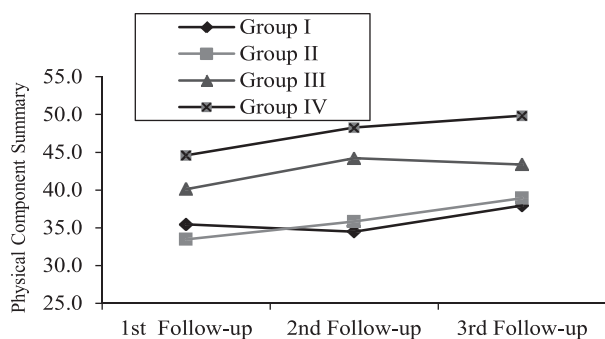
Physical componentsummary	Group I (n=42)	Group II (n=39)	Group III (n=30)	Group IV (n=23)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
1 <sup>st</sup> Follow-up	35.46±8.08	33.46±7.17	40.12±9.31	44.59±7.52
Range (min-max)	(21.6-56.8)	(20.2-45.7)	(25.7-58.1)	(25.1-57)
2 <sup>nd</sup> Follow-up	34.47±6.33	35.84±6.66	44.2±8.34	48.28±4.38
Range (min-max)	(25.7-45.6)	(21.1-46.2)	(27.9-54.9)	(39.3-56.2)
3 <sup>rd</sup> Follow-up	37.94±6.58	38.94±6.71	43.39±9.31	49.85±5.93
Range (min-max)	(28.7-51.7)	(21.7-46.3)	(30.3-58.9)	(28.4-55.7)
Comparison group	1 <sup>st</sup> follow up p value	2 <sup>nd</sup> follow up p value	3 <sup>rd</sup> follow up p value	
Group I vs. group II	0.243	0.345 <sup>ns</sup>	0.500 <sup>ns</sup>	
Group II vs. group III	0.001 <sup>s</sup>	0.000 <sup>s</sup>	0.000 <sup>s</sup>	
Group II vs. group IV	0.000 <sup>s</sup>	0.000 <sup>s</sup>	0.000 <sup>s</sup>	
Group III vs. group IV	0.025 <sup>s</sup>	0.049 <sup>s</sup>	0.009 <sup>s</sup>	

ns=not significant, s=significant  
P value reached from unpaired t-test.

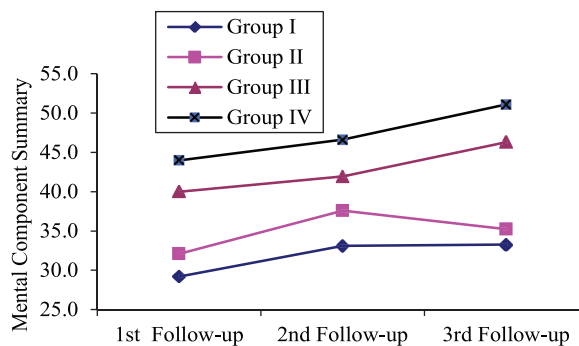
**Table III***Distribution of the study patients according to mean mental component summary at different follow-ups (n=134)*

Mental component summary	Group I(n=42)	Group II(n=39)	Group III(n=30)	Group IV(n=23)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
1 <sup>st</sup> Follow-up	29.21±7.7	32.11±9.05	40.01±8.12	43.99±8.48
Range (min-max)	(17.1-43.2)	(19.3-57.3)	(24.4-52.8)	(22.8-67.4)
2 <sup>nd</sup> Follow-up	33.11±8.62	37.61±9.56	41.93±10.59	46.62±5.62
Range (min-max)	(21.9-55.9)	(19.1-63.7)	(25.2-59.9)	(28.6-56.9)
3 <sup>rd</sup> Follow-up	33.27±9.75	35.25±8.04	46.31±8.15	51.1±4.4
Range (min-max)	(19.1-50.5)	(16.5-56.3)	(29.4-57.4)	(33.3-55.2)
Comparison group	1 <sup>st</sup> follow up p value	2 <sup>nd</sup> follow up p value	3 <sup>rd</sup> follow up p value	
Group I vs. group II	0.123 <sup>ns</sup>	0.056 <sup>ns</sup>	0.454 <sup>ns</sup>	
Group II vs. group III	0.001 <sup>s</sup>	0.080 <sup>ns</sup>	0.000 <sup>s</sup>	
Group II vs. group IV	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.000 <sup>s</sup>	
Group III vs. group IV	0.088 <sup>ns</sup>	0.060 <sup>ns</sup>	0.144 <sup>ns</sup>	

ns=not significant, s=significant  
P value reached from unpaired t-test.



**Fig 1:** Line graph showing distribution of the study patients according to physical component summary at different follow-ups (n=134).



**Fig 2:** Line diagram showing distribution of the study patients according to mean mental component summary at different follow-ups (n=134).

**Table IV**

Mean distribution of the study patients according to Burden of kidney disease at different follow-ups (n=134)

Burden of kidney disease	Group I(n=42)	Group II(n=39)	Group III(n=30)	Group IV(n=23)
	Mean±SD	Mean±SD	Mean±SD	Mean±SD
1 <sup>st</sup> Follow-up	20.42±15.1	21.22±15.39	28.08±29.97	38.86±18.65
Range (min-max)	(0.0-56.3)	(0.0-50.0)	(0.0-81.3)	(0.0-75)
2 <sup>nd</sup> Follow-up	25.18±20.37	27.99±18.21	43.03±22.8	48.81±11.63
Range (min-max)	(0.0-75.0)	(0.0-93.8)	(0.0-75.0)	(37.5-75.0)
3 <sup>rd</sup> Follow-up	24.69±20.81	21.06±24.51	42.25±22.12	57.74±9.66
Range (min-max)	(0.0-68.8)	(0.0-93.8)	(0.0-75.0)	(43.8-75.0)
Comparison group	1 <sup>st</sup> follow up	2 <sup>nd</sup> follow up	3 <sup>rd</sup> follow up	
	p value	p value	p value	
Group I vs. group II	0.814 <sup>ns</sup>	0.515 <sup>ns</sup>	0.473 <sup>ns</sup>	
Group II vs. group III	0.221 <sup>ns</sup>	0.003 <sup>s</sup>	0.001 <sup>s</sup>	
Group II vs. group IV	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.001 <sup>s</sup>	
Group III vs. group IV	0.136 <sup>ns</sup>	0.272 <sup>ns</sup>	0.002 <sup>s</sup>	

ns=not significant, s=significant  
P value reached from unpaired t-test.

The effects of kidney disease component was analyzed in table 5. The ability of treatment modality to alleviate the effects of kidney disease showed 8 hours dialysis/week did not show statistical significant performance in comparison to no renal replacement therapy. 12 hours dialysis/week and CAPD both showed statistically significant better performance in comparison to 8 hours dialysis/week in all follow ups. CAPD patients showed even significantly better achievement in terms of effect of

kidney disease in comparison to 12 hours dialysis/week in 2 follow ups among three.

The efficiency of a treatment modality to relief symptom of kidney disease is presented in table 6. It was noted unlike other components of Quality of life, symptoms were significantly reduced by 8 hours dialysis/week in comparison to no renal replacement therapy. However, 12 hours dialysis/week showed even better performance in comparison to 8 hours dialysis/week but there were no difference among the patients on CAPD and 12 hours dialysis.

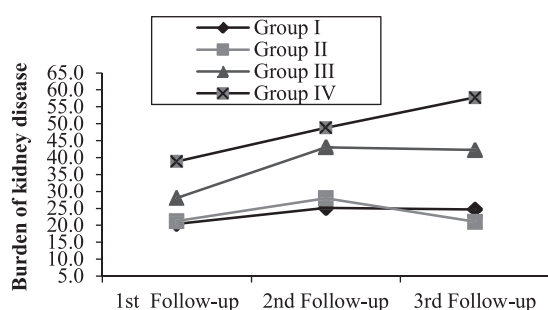


**Table V**

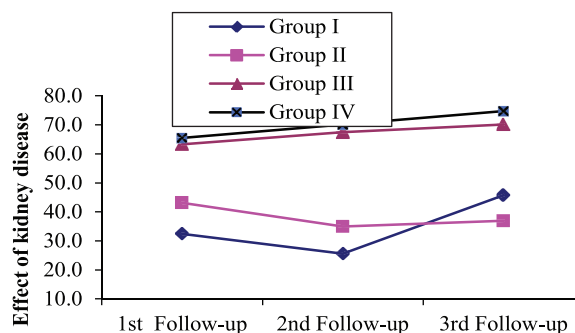
*Mean distribution of the study patients according to effects of kidney disease at different follow-ups (n=134).*

Effect of kidney disease	Group I (n=42) Mean ±SD	Group II (n=39) Mean±SD	Group III (n=30) Mean±SD	Group IV (n=23) Mean±SD
1 <sup>st</sup> Follow-up	32.44±25.2	43.11±18.71	63.33±26.64	76.49±13.93
Range (min-max)	(0.0-96.9)	(3.1-81.3)	(9.4-96.9)	(37.5-100)
2 <sup>nd</sup> Follow-up	25.59±19.18	34.98±18.88	67.43±15	70.09±8.48
Range (min-max)	(6.3-84.4)	(3.1-71.9)	(21.9-90.6)	(56.3-87.5)
3 <sup>rd</sup> Follow-up	25.78±16.89	36.9±20.19	70.13±12.27	76.7±6.24
Range (min-max)	(6.3-68.8)	(0.0-68.8)	(46.9-90.6)	(59.4-84.4)
Comparison group	1 <sup>st</sup> follow up P value	2 <sup>nd</sup> follow up p value	3 <sup>rd</sup> follow up P value	
Group I vs. group II	0.034 <sup>s</sup>	0.029 <sup>s</sup>	0.008 <sup>s</sup>	
Group II vs. group III	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.001 <sup>s</sup>	
Group II vs. group IV	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.001 <sup>s</sup>	
Group III vs. group IV	0.036 <sup>s</sup>	0.448 <sup>ns</sup>	0.023 <sup>s</sup>	

ns=not significant, s=significant P value reached from unpaired test.



**Fig 3:** Line graph showing distribution of the study patients according to Burden of kidney disease at different follow-up (n=134).



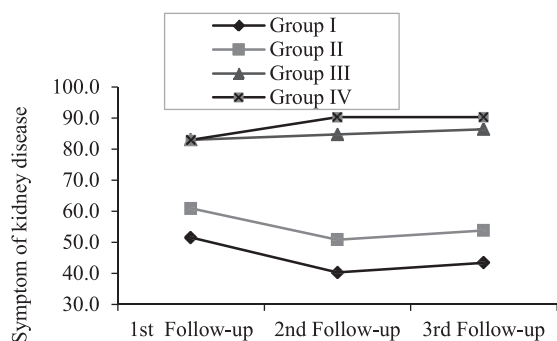
**Fig 4:** Line diagram showing distribution of the study patients according to effects of kidney disease at different follow-ups (n=134).

**Table VI**

*Mean distribution of the study patients according to symptoms of kidney disease at different follow-ups (n=134)*

Symptom of kidney disease	Group I (n=42) Mean±SD	Group II (n=39) Mean±SD	Group III (n=30) Mean±SD	Group IV (n=23) Mean±SD
1 <sup>st</sup> Follow-up	51.55±20.79	60.9±19.56	82.99±21.49	82.97±8.76
Range (min-max)	(9.1-86.4)	(2.1-100)	(6.3-97.9)	(64.6-100)
2 <sup>nd</sup> Follow-up	40.35±18.37	50.87±26.41	84.7±12.32	90.29±3.97
Range (min-max)	(22.7-90.9)	(0.0-93.8)	(47.9-100)	(81.3-95.8)
3 <sup>rd</sup> Follow-up	43.43±18.55	53.85±24.21	86.42±7.25	90.28±4.53
Range (min-max)	(4.5-79.5)	(4.2-93.8)	(72.9-100)	(77.1-95.8)
Comparison group	1 <sup>st</sup> follow up P value	2 <sup>nd</sup> follow up p value	3 <sup>rd</sup> follow up P value	
Group I vs. group II	0.040 <sup>s</sup>	0.039 <sup>s</sup>	0.032 <sup>s</sup>	
Group II vs. group III	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.001 <sup>s</sup>	
Group II vs. group IV	0.001 <sup>s</sup>	0.001 <sup>s</sup>	0.001 <sup>s</sup>	
Group III vs. group IV	0.996 <sup>ns</sup>	0.041 <sup>s</sup>	0.029 <sup>s</sup>	

ns=not significant, s=significant P value reached from unpaired test.



**Fig 5:** Line diagram showing distribution of the study patients according to symptoms of kidney disease at different follow-ups ( $n=134$ ).

### Discussion:

This longitudinal study was carried out in the department of Nephrology, Dhaka Medical College Hospital, Dialysis Unit, BIRDEM, and the patients who received consultation at Outdoor Department of Nephrology, Dhaka Medical College Hospital during the period of November, 2010 to October, 2011 were enrolled in the study.

In this present study it was observed that the mean  $\pm$  SD age was  $48.14 \pm 16$  years in group I,  $46.28 \pm 12.11$  years in group II,  $48.07 \pm 12.43$  years in group III and  $53.57 \pm 7.16$  years in group IV, which were almost similar in all modalities of treatment and majority of the patients were in 5<sup>th</sup> and 6<sup>th</sup> decade but under 5<sup>th</sup> decade patients were not observed in group IV patients. In a study, Jaar et al.<sup>12</sup> showed the mean age of patients on hemodialysis (HD) was  $53.7 \pm 14.8$  years and in Peritoneal dialysis (PD) was  $59.3 \pm 14.8$  years ( $P < 0.001$ ). Thaweethamcharoen et al.<sup>13</sup> worked on Quality of Life of hemodialysis patients and found the mean age was  $57.32 \pm 14.52$  years. Bloembergen et al.<sup>14</sup> have shown the mean age of Hemodialysis group was  $60.8 \pm 16.5$  years and  $56.1 \pm 7.3$  years in peritoneal dialysis group. Albert et al.<sup>15</sup> showed the mean age of HD group was 59 years and PD group 54 years at base line ( $p < 0.001$ ). Similarly, Han et al.<sup>16</sup> and Finkelstein et al.<sup>17</sup> found higher mean age in their study patients. This discrepancy may be due to, the etiological difference of CKD in our country in comparison to Western World; In Bangladesh a good proportion of CKD results from glomerulonephritis, though in this study DM was found to be the major cause of CKD in patients getting renal replacement therapy, a good number of patient suffered from glomerulonephritis in all groups except group IV.

In this present series it was observed that male female ratio was 2.1:1 in the whole study, which indicates that

chronic kidney disease stage V was more common in male subjects. However, 64.3% in group I, 76.9% in group II, 66.7% in group III and 60.9% in group IV patients were male. Sex difference was not statistically significant ( $p > 0.05$ ) among the groups, which closely resemble with Jaar et al.<sup>12</sup> study, where the authors showed male 55.5% and 53.7% in HD and PD group respectively. Similarly, male predominant showed by Albert et al.<sup>15</sup> and Finkelstein et al.<sup>17</sup> are consistent with the current study.

The above results revealed that physical component score increased significantly in Group III and Group IV at consecutive follow ups; however it was higher in Group IV. In a study, Zhang et al.<sup>18</sup> compare Physical component between Quality of life between patients on Hemodialysis and Peritoneal dialysis and observed  $45.07 \pm 30.86$  and  $49.88 \pm 30.63$  respectively, which support the current study. Gabbay et al.<sup>19</sup> studied temporal trends in Health-Related Quality of Life among Hemodialysis Patients and found Physical component improved "0.2 points/year from a baseline of 43.0. In this current study it was observed that patients in group II, the mean  $\pm$  SD physical component was  $33.46 \pm 7.17$  at first follow-up,  $35.84 \pm 6.66$  second follow-up and  $38.94 \pm 6.71$  third follow-up, which are significantly ( $p < 0.05$ ) lower than group III and group IV. Sathvik et al.<sup>20</sup> conducted a study on the patients getting hemodialysis for 8 hours per week which is equivalent to group II of present study found the physical component was  $38.81 + 18.36$ , which support the present study. On the other hand, the mean  $\pm$  SD physical component was  $35.46 \pm 8.08$ ,  $34.47 \pm 6.33$  and  $37.94 \pm 6.58$  in group I patients, at 1<sup>st</sup>, 2<sup>nd</sup> and 3<sup>rd</sup> follow-up respectively.

The mean  $\pm$  SD mental component score was  $40.01 \pm 8.12$  in group III and  $43.99 \pm 8.48$  in group IV during 1<sup>st</sup> follow-up, at second follow-up mean  $\pm$  SD mental component score were  $41.93 \pm 10.59$  and  $46.62 \pm 5.62$  in group III and group IV respectively and at third follow-up the mean  $\pm$  SD mental component was  $46.31 \pm 8.15$  in group III and  $51.1 \pm 4.4$  in group IV, thus were higher in group IV at all follow-ups, but two groups did not differ significantly. Albert et al.<sup>15</sup> showed the mean mental component were 46.8 and 47.3 in HD and PD patients respectively. Gabbay et al.<sup>19</sup> studied temporal trends in Health-Related Quality of Life among Hemodialysis Patients and found mental component superior +0.15 points/year from a baseline of 61.2. Lacson et al.<sup>21</sup> compared mental component summary (MCS) among hospitalized patients and non-hospitalized MCS score were  $46.1 \pm 10.8$  and  $47.8 \pm 10.4$  respectively ( $p < 0.05$ ). In group II the mean  $\pm$  SD mental component was  $32.11 \pm 9.05$

at first follow-up,  $37.61 \pm 9.56$  in 2<sup>nd</sup> follow-up and  $35.25 \pm 8.04$  in 3<sup>rd</sup> follow-up. In a study, Sathvik et al.<sup>20</sup> showed the mean mental component was  $40.92 + 18.66$ , which is comparable with the current study. In group I, the mean  $\pm$ SD mental component was  $29.21 \pm 7.7$  at first follow-up,  $33.11 \pm 8.62$  at second follow-up and  $33.27 \pm 9.75$  at 3<sup>rd</sup> follow-up.

The efficacy of a treatment modality to decrease the burden of kidney disease was noted significantly better in Group IV (mean  $\pm$ SD score  $38.86 \pm 18.65$  at 1<sup>st</sup> follow-up,  $48.81 \pm 11.63$  at 2<sup>nd</sup> follow-up and  $57.74 \pm 9.66$  at 3<sup>rd</sup> follow-up) followed by Group III ( $28.08 \pm 29.97$  at 1<sup>st</sup> follow-up,  $43.03 \pm 22.8$  at 2<sup>nd</sup> follow-up and  $42.25 \pm 22.12$  at 3<sup>rd</sup> follow-up), but it was poor in Group I and worse in Group II in which it declined at consecutive follow ups and at the end it was  $24.69 \pm 20.81$  in group I and  $21.06 \pm 24.51$  in group II, which was not significantly different. Fong, Bragman and Chan<sup>22</sup> found that in peritoneal dialysis patient the score of burden of kidney disease was  $47 \pm 3.8$  which was comparable to group IV of the present study population. Fukuhara et al.<sup>23</sup> conducted assessment of the same domain of quality of life among the patients on hemodialysis for 12 hours per week which is similar to group III of the current study. Gorodetskaya et al.<sup>24</sup> showed the mean  $\pm$ SD Burden of Kidney Disease was  $38.6 \pm 23.8$  in Dialysis patients. Fukuhara et al.<sup>23</sup> documented international differences in HRQOL among dialysis patients and found the mean  $\pm$ SD Burden of Kidney Disease were 35.4 in Europe, 28.6 in Japan and 40.8 in America. The above findings support the current study. These findings support the current study. However, this domain of quality of life was not widely studied in population comparable to other groups of current study.

The performance of a treatment modality in alleviating effect of kidney disease upon a patient's life were increased significantly in group IV ( $76.49 \pm 13.93$  at 1<sup>st</sup> follow-up,  $70.09 \pm 8.48$  at 2<sup>nd</sup> follow-up and  $76.7 \pm 6.24$  at 3<sup>rd</sup> follow-up) and group III ( $63.33 \pm 26.64$  at 1<sup>st</sup> follow-up,  $67.43 \pm 15$  at 2<sup>nd</sup> follow-up and  $70.13 \pm 12.27$  at 3<sup>rd</sup> follow-up) at all follow-up and remained higher in comparison to other two groups. In the study conducted in Toronto<sup>39</sup> found that in peritoneal dialysis patient the score of effect of kidney disease was  $60.7 \pm 2.7$  which was comparable to group IV of the present study population, on the other hand Fukuhara et al.<sup>23</sup> undertake a study to find out the international differences in HRQOL among hemodialysis patients who were comparable to group III of this current study and have shown the mean  $\pm$ SD effect of kidney

disease score was 57.3 in Europe, 67.7 in Japan and 62.5 in America. It is evident that in both hemodialysis for 12 hours per week and peritoneal dialysis group this score is found to be higher in current study in comparison to other studies conducted abroad, though all other studies were cross sectional study in contrast to longitudinal study design of present study the exact cause of these findings are not clear; however effect of kidney disease score depends on anticipation of adverse effects of a certain disease and ultimate perception of its effect on an individual, so a more positive perception of our population may be responsible for these optimistic findings. In group II, the mean  $\pm$ SD effect of kidney disease score was  $43.11 \pm 18.71$  at first follow-up,  $34.98 \pm 18.88$  at 2<sup>nd</sup> follow-up and  $36.9 \pm 20.19$  at third follow-up and in group I, the mean  $\pm$ SD effect of kidney disease score was  $32.44 \pm 25.2$  in first follow-up,  $25.59 \pm 19.18$  at second follow-up and  $25.78 \pm 16.89$  at third follow-up. But these two study population under group I and II, were not studied regarding this domain of quality of life hence comparison with the current study was not possible.

The efficacy of reducing symptoms of kidney disease was significantly higher in group IV ( $82.97 \pm 8.76$  at 1<sup>st</sup> follow-up,  $90.29 \pm 3.97$  at 2<sup>nd</sup> follow-up and  $90.28 \pm 4.53$  at 3<sup>rd</sup> follow-up), group III ( $82.99 \pm 21.49$  at 1<sup>st</sup> follow-up,  $84.7 \pm 12.32$  at 2<sup>nd</sup> follow-up and  $86.42 \pm 7.25$  at 3<sup>rd</sup> follow-up) and inclined in consecutive follow ups. Fong, Bragman and Chan<sup>22</sup> found that in peritoneal dialysis patient the score of symptoms of kidney disease was  $71.9 \pm 2.6$  which was comparable to group IV of the present study population. Fukuhara et al.<sup>23</sup> showed the international differences on symptom of kidney disease score in HRQOL among hemodialysis patients and observed that mean  $\pm$ SD symptom of kidney disease score was 69.9 in Europe, 75.8 Japan and 71.1 in America, which is consistent with the current study. In group II, the mean  $\pm$ SD symptom of kidney disease score was  $60.9 \pm 19.56$  at first follow-up,  $50.87 \pm 26.41$  at 2<sup>nd</sup> follow-up and  $53.85 \pm 24.21$  at third follow-up and in group I, the mean  $\pm$ SD symptom of kidney disease score was  $51.55 \pm 20.79$  in first follow-up,  $40.35 \pm 18.37$  at second follow-up and  $43.43 \pm 18.55$  at third follow-up. No study population comparable to these two groups were found in which this domain of QOL was evaluated.

#### **Conclusion:**

All the domains of quality of life scored by KDQOL 36 were highest among continuous ambulatory peritoneal dialysis patients, followed by patients receiving hemodialysis for 12 hours per week, patients receiving 8

hours per week hemodialysis and those on conservative treatment had worse quality of life score in comparison to other two groups and more importantly 8 hours per week hemodialysis failed to show any improvement in QOL in comparison to conservative treatment at most domains of quality of life.

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# Micro and Macrovascular Complications in Diabetic Nephropathy in Different Stages of Chronic Kidney Disease

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## Abstract :

*Diabetes mellitus, due to its effect on small and large blood vessels is known to cause various micro vascular and macro vascular complications. Diabetic nephropathy(DN) is found to be associated with diabetic retinopathy and coronary artery disease*

*This cross-sectional study was conducted among the patients of DN included both type-1 and type-2 diabetics in the Department of Nephrology, Dhaka Medical College Hospital in collaboration with the Department of Endocrinology, Dhaka Medical College Hospital and Department of Nephrology, BIRDEM Hospital, Dhaka between May 2010 to April 2011. A total 390 patients of DN were included in this study irrespective of the stages of CKD. Aim of this study was to find out the micro vascular (Diabetic retinopathy, peripheral neuropathy) and macro vascular (coronary artery disease, cerebrovascular disease and peripheral vascular disease) complications in different stages of CKD in patients with DN.*

*Patients of stage-5 CKD undergoing dialysis were not allowed to participate in the study. Staging of CKD was done using MDRD formula. Micro and macro vascular complications were then compared among the different stages of CKD.*

*The result obtained showed that stage-3 and stage-4 CKD were almost equal about 36.4% and 37.4% respectively. Stage-5 disease was 23.8%, stage-1 CKD and stage-2 consisted of only 7 (1.7%) and 2 (0.5%) patients. Regarding complications peripheral neuropathy and Non-proliferative diabetic retinopathy were frequently common than any other micro vascular complications where frequency of proliferative diabetic retinopathy progressively increases in higher stages of CKD. Also diabetic foot observed to be significantly common with the advancing CKD ( $p < 0.05$ ). The study concludes that patients of diabetic nephropathy are more often associated with a number of micro and macro vascular complications and their frequency increases with the progression of the disease.*

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## Introduction

Diabetic nephropathy (nephropatia diabetica), also known as Kimmelstiel-Wilson syndrome or nodular diabetic glomerulosclerosis now a days which is termed as diabetic kidney disease (DKD). The syndrome was discovered by British physician Clifford Wilson (1906–1997) and German-born American physician Paul Kimmelstiel (1900–1970) and was published for the first time in 1936<sup>1</sup>.

In diabetic patients diabetic nephropathy (DN) is clinically characterized by increasing rates of urinary albumin excretion, starting from normoalbuminuria, which progress to micro albuminuria, macro albuminuria and without

intervention these patients typically progress to overt proteinuria and eventually to end-stage renal disease (ESRD)<sup>2</sup>. This progression occurs in both type 1 and type 2 diabetes<sup>3</sup>.

Diabetes mellitus, due to its effect on small and large blood vessels is known to cause various microvascular and macrovascular complications. The incidence of microvascular complications, namely, nephropathy, retinopathy, autonomic neuropathy and peripheral neuropathy increase with the duration of diabetes<sup>3</sup>. Macrovascular complications associated with diabetes, namely, coronary artery disease, cerebrovascular disease

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and peripheral vascular disease are mainly due to accelerated atherosclerosis.

Diabetic nephropathy is the leading cause of end stage renal disease (ESRD)<sup>4</sup>, diabetic patients with nephropathy are at higher risk of fatal and non fatal cardiovascular and other complications<sup>5</sup>. Not only stroke and myocardial infarction but retinopathy and peripheral vascular disease have correlation with DN<sup>6,7</sup>.

Diabetic nephropathy is the leading cause of chronic renal failure in the United States today (ADA, 1999). It is also one of the most significant long-term complications in terms of morbidity and mortality for individual patients with diabetes. Both type 1 and type 2 diabetes mellitus (insulin-dependent diabetes mellitus [IDDM] and non – insulin-dependent diabetes mellitus [NIDDM], respectively) lead to ESRD. Approximately 40% of patients with type-1 diabetes and 5-15% of patients with type- 2 diabetes eventually develop ESRD, although the incidence is substantially higher in certain ethnic groups<sup>7</sup>.

This study was conducted to document association between diabetic nephropathy and other microvascular and macrovascular complications in diabetics presenting in Bangladesh. **Aims and Objectives**

To find out the micro vascular (Diabetic retinopathy, peripheral neuropathy) and macro vascular (coronary artery disease, cerebrovascular disease and peripheral vascular disease) complications in different stages of CKD in patients with Diabetic nephropathy (DN).

#### Patients & Methods

This was a cross sectional study carried out in the Department of Nephrology, Dhaka Medical College hospital (DMCH) in collaboration with Department of Endocrinology, DMCH and Department of Nephrology, BIRDEM Hospital, Dhaka conducted in the period of May 2010 to April 2011. Patients of diabetic nephropathy of all stages, except patients of stage V CKD who were already on dialysis, were the study population. Sampling done by Convenience sampling and sample size was 390. The study done after taking permission from the Ethical Committee of Dhaka Medical College (DMC), Dhaka, Bangladesh.

Patients who were included in this study are

- Patients with diabetic nephropathy irrespective of stages of CKD except those in stage V who have already underwent dialysis.
- Patients of DN of all ages and both sexes.

Patients who were excluded from this study are

- Patients of DN with CKD stage V who were already on dialysis.
- Patients of DN with valvular heart disease and collagen vascular diseases.

A structured questionnaire was developed containing all the variables of interest like demographic and anthropometric variables, risk factors, clinical characteristics and micro and macro vascular complications of diabetes and biochemical characteristics and data were collected by interview of the patients, clinical examination and laboratory investigations using the structured questionnaire.

#### Variables studied are defined as

**Micro-albuminuria** defined by Presence of 30 - 299 mg of albumin in a 24 hours urine sample or 30-300 mg albumin per gm of creatinine.

**Macroalbuminuria** diagnosed by the presence of more than 300 mg albumin in urine over 24 hours, or albumin creatinine ratio (ACR) more than 300 mg/gm.

**Nephropathy defined by** presence of microalbuminuria or macroalbuminuria with or without raised serum creatinine (>130 micro mole/liter or 1.5mg/dl). K/DOQI criteria for the definition of **CKD** used to estimate prevalence of chronic kidney disease stages 1 to 5. GFR estimation was done by MDRD formula

**Non-proliferative diabetic retinopathy (NPDR)** was diagnosed by the presence of, micro aneurysms exudates and blot hemorrhages on direct ophthalmoscopic examination in full dilated eye.

**Proliferative diabetic retinopathy (PDR)** was diagnosed by the presence of neovascularization in the retina.

**Peripheral sensory neuropathy (PN)** was assessed clinically by history of persistent paresthesia in the peripheral parts of the body or decreased pain by pinprick testing, or decreased touch by fine cotton wisp or decreased vibration sense by tuning fork of frequency 256Hz or absence of ankle reflexes.

**Cerebrovascular disease (CVD)** was assessed by history of previous transient ischemic attack or stroke which was also supported by focal neurological deficit like extensor planter reflex, absence or exaggeration of knee jerk, ankle jerk, bicep jerk, triceps jerk and or facial deviation.

**Coronary artery diseases (CAD)** were assessed by history of **angina**, acute coronary syndrome (ACS) and myocardial infarction (MI) and verified by previous hospital record, or ECG changes of Q waves, ST segment change, T wave



abnormality or poor progression of R waves in anterior leads with Echocardiography showing evidence of wall motion abnormalities, dilated left ventricle or ejection fraction of < 40%.

**Peripheral vascular disease (PVD)** was ascertained clinically by the absence of peripheral pulses.

**Data processing and statistical analysis:**

Data were processed using software SPSS (statistical Package for Social Sciences) version 11.5. The test statistics used to analyze the data were descriptive statistics and Chi-square ( $\chi^2$ ) Test. For all analytical tests, the level of significance was set at 0.05 and  $p < 0.05$  was considered significant.

**Results**

This study intended to find out the microvascular and macrovascular complications in patients of diabetic nephropathy included a total 390 patients. The non proliferative diabetic retinopathy, proliferative diabetic retinopathy, peripheral neuropathy and diabetic foot were the variables for studying microvascular complications, while the variables for macrovascular complications were coronary artery disease (CAD), angina, acute coronary syndrome. Myocardial infarction, peripheral vascular disease and cerebro vascular disease or stroke . The findings obtained presented below.

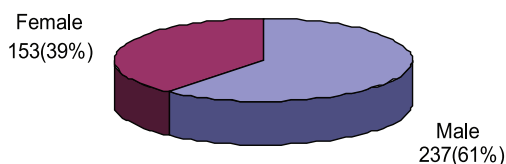
**Age distribution:**

Table I shows the age distribution of the patients.

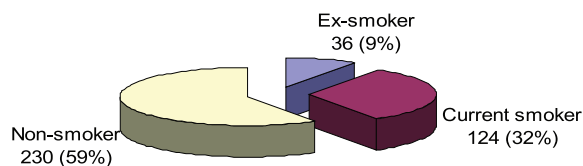
**Table I**  
*Age distribution of the participants*

Age (years)	Frequency	Percentage
≤40	18	4.6
41 – 50	109	28.0
51 – 60	147	37.7
>60	116	29.7
Total	390	100.0

# Mean age = (55.9 ± 9.9) years; range = ( 24 – 92 ) years



**Fig.1:** Distribution of patients by sex (n = 390)



**Fig.2:** Distribution of patients by smoking habit (n = 390)

**Family history of DM:**

**Table II**  
*Distribution of patients by family history of DM*

Family history of DM	Frequency	Percentage
Yes	182	46.7
No	208	53.3
Total	390	100.0

**Body Mass Index (BMI):**

**Table III**  
*Distribution of patients by BMI*

BMI (kg/m <sup>2</sup> )	Frequency	Percentage
<18.5 (under weight)	18	4.7
18.5 – 24.9 (normal)	263	67.4
≥25 (over weight & obese)	109	27.9
Total®	390	100.0

# Mean BMI = (25.3 ± 1.8) kg/m<sup>2</sup>; range: (15.2 – 40.4) kg/m<sup>2</sup>Clinical characteristics at presentation:

**Table IV**  
*Distribution of patients by Clinical characteristics (n = 390)*

Clinical presentation	Frequency (%)	Mean ± SD	Range
Systolic BP (Supine)	-	137 ± 21	85 - 210
Systolic BP (Standing)	-	132 ± 19	80 - 200
Diastolic BP (Supine)	-	82 ± 12	40 – 120
Diastolic BP (Standing)	-	80 ± 11	30 - 100
Age of onset of DM	-	45.5 ± 9.5	13 - 72
Duration of DM	-	10.6 ± 6.9	1 - 17
Type of DM			
Type-I	58(14.9)	-	-
Type-II	332(85.1)		
Hypertension	275(70.5)	-	-
Duration of HTN	-	5.9 ± 4.4	1-25

**Diabetic complications:**

**Table V**  
*Distribution of patients by diabetic complications (n = 390)*

Complications	Frequency	Percentage
<b>Micro vascular complications</b>		
Nonproliferative diabetic retinopathy	139	35.6
Proliferative diabetic retinopathy	72	18.5
Peripheral neuropathy	197	50.5
Diabetic foot	91	23.3
<b>Macro vascular complications</b>		
CAD	121	31.0
MI	84	21.5
ACS	22	5.6
Angina	52	13.3
Stroke	48	12.3
Peripheral vascular disease	45	11.5

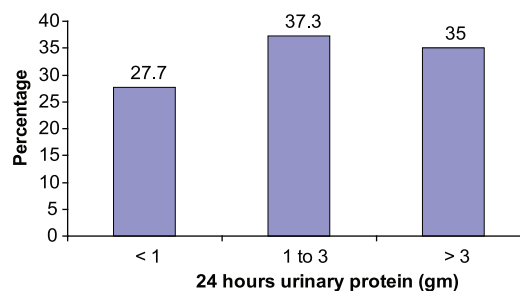
#Total will not correspond to 100% because of multiple responses.

**Biochemical investigations:**

**Table VI**  
*Distribution of patients by biochemical investigations (n = 390)*

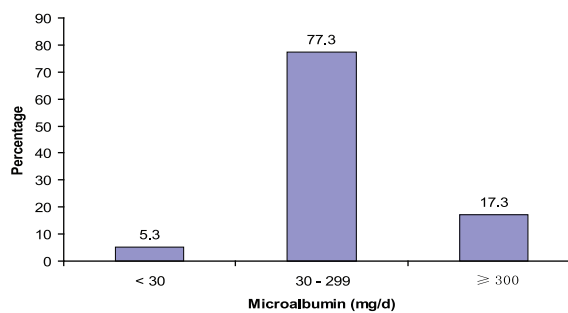
Biochemical investigations	Frequency	Mean ± SD (%)
<b>Urine for albumin (n = 390)</b>		
Nil/Trace	220 (56.5)	-
++	107 (27.4)	-
+++	50 (12.8)	-
++++	13 (3.3)	-
Total urinary protein (gm/24 hrs)	-	3.1 ± 0.2
Serum creatinine (mg/dl)	-	3.9 ± 0.5
Serum cholesterol (mg/dl)	-	169.8 ± 2.6
LDL (mg/dl)	-	112.5 ± 3.0
HDL (mg/dl)	-	41.9 ± 1.4
TG (mg/dl)	-	190.5 ± 6.7
FBS (mmol/l)	-	8.5 ± 0.3
HBA1c (%)	-	7.4 ± 0.1

**24-hours urinary protein:**



**Fig. 3:** 24-hours urinary protein in patients with overt proteinuria (n = 170)

**Microalbuminuria in study group :**



**Fig. 4:** Microalbuminuria in study group (n = 150)

**Distribution of patients in different stages of CKD:**

Table VII shows the prevalence of different stages of CKD by MDRD equations. Stage-3 and stage-4 CKD were found to be predominant (36.4% and 37.6% respectively). Nearly one-quarter (23.8%) of the patients were screened as having stage-5 disease (end stage renal disease).

**Table VII**  
*CKD staging by MDRD equations (n = 390)*

CKD staging	Frequency	Percentage
Stage 1	07	1.7
Stage 2	02	0.5
Stage 3	142	36.4
Stage 4	146	37.6
Stage 5	93	23.8
Total	390	100.0

**Comparison of micro and macro vascular complications:****Table VIII***Comparison of micro and macro vascular complications of DN patients in different stage of CKD (n = 390)*

Complications	Staging of CKD				p-value
	Stage 2(n= 2)	Stage 3(n= 142)	Stage 4(n= 146)	Stage 5(n=93)	
<b>Micro vascular</b>					
NPDR	1(50.0)	36(25.4)	58(39.7)	42(45.2)	0.010
PDR	00	17(12.0)	25(17.2)	30(32.3)	0.001
Peripheral neuropathy	1(50.0)	51(35.9)	90(61.6)	52(55.9)	<0.001
Diabetic foot	00	26(18.3)	42(28.8)	21(22.6)	0.167
<b>Macro vascular</b>					
CAD	00	30(21.1)	55(37.7)	35(37.6)	0.007
MI	1(50.0)	20(14.1)	35(24.0)	28(30.1)	0.018
ACS	00	2(1.4)	12(8.2)	8(8.6)	0.044
Angina	00	17(12.0)	23(15.8)	10(10.8)	0.611
Stroke	00	11(7.7)	21(14.4)	16(17.2)	0.135
Peripheral vascular disease	1 (50.0)	8(5.6)	17(11.6)	18(19.4)	0.004

\*Data were analyzed using Chi-squared ( $\chi^2$ ) Test.

Figures in the parentheses denote corresponding percentage

**Discussion**

The demographic characteristics of the patients showed that 70% of the patients were 50 or > 50 years old with mean age of the patients being 56 years. A male preponderance was observed among the study population. Housewife and service holders together formed half of the patients. About one-third (32%) of the patients was smoker. Risk factor study revealed that 70% were hypertensive 27.8% were overweight or obese. Of the 170 patients were tested for urinary excretion of 24 hours protein, 27.7 % had excreted < 1 gm of protein, 37.3 % 1 – 3 gm and 35% > 3 gm in 24 hours.

Stage-3 and stage-4 CKD were almost equal and together comprised more than 70% of the CKDs (36.4% and 37.6% respectively). Stage-5 disease was no less (23.8%). 7 patients had stage-1 CKD and stage-2 comprised of only 2 patients. So the present study will highlight the complications in stage-3, stage-4 and stage-5 CKDs. Peripheral neuropathy and non proliferative diabetic retinopathy were frequently common than any other microvascular complications. All the microvascular complications but diabetic foot were observed to be significantly common with the advancing CKD ( $p < 0.05$ ).

28 patients had cataract so ophthalmoscopic examination was not possible.

The risk of developing diabetic retinopathy or other microvascular complications of diabetes depends on both the duration and the severity of hyperglycemia. Development of diabetic retinopathy in patients with type 2 diabetes was found to be related to both severity of hyperglycemia and presence of hypertension in the U.K. Prospective Diabetes Study (UKPDS), and most patients with type-I diabetes develop evidence of retinopathy within 20 years of diagnosis [9]. Diabetic neuropathy is recognized by the American Diabetes Association (ADA) as “the presence of symptoms and/or signs of peripheral nerve dysfunction in people with diabetes after the exclusion of other causes.” As with other microvascular complications, risk of developing diabetic neuropathy is proportional to both the magnitude and duration of hyperglycemia.

In the present study more than 77% of patients exhibited 30 – 299 mg of albumin per 24 hours and hence were considered to have microalbuminuria.

As many as 7% of patients with type- 2 diabetes may already have microalbuminuria at the time they are

diagnosed with diabetes. In the European Diabetes Prospective Complications Study, the cumulative incidence of microalbuminuria in patients with type 1 diabetes was 12% during a period of 7 years<sup>10</sup>.

Like other microvascular complications of diabetes, there are strong associations between glucose control (as measured by hemoglobin A1c [HbA1c]) and the risk of developing diabetic nephropathy. Patients should be treated to the lowest safe glucose level that can be obtained to prevent or control diabetic nephropathy (The DCCT Research, 1993). Treatment with angiotensin-converting enzyme (ACE) inhibitors has not been shown to prevent the development of microalbuminuria in patients with type-1 diabetes but has been shown to decrease the risk of developing nephropathy and cardiovascular events in patients with type-2 diabetes<sup>11</sup>.

In the present study CAD, MI, ACS and peripheral vascular disease (macrovascular complications) demonstrated their increasing presence with advancing stage of CKD. Twenty one patients (5.3%) have already had amputation of either leg or toes because of gangrene resulting from peripheral vascular disease and/or peripheral neuropathy, 6 (1.5%) patients experienced coronary artery bypass graft (CABG) and 8 (2%) stenting. Among macrovascular diabetes complications, coronary artery disease has been associated with diabetes in numerous studies beginning with the Framingham study<sup>12</sup>. Diabetes is an independent predictor of risk of stroke or cerebrovascular disease. Patients with type-2 diabetes have a much higher risk of stroke, with an increased risk of 150-400%<sup>13</sup>. CVD is the primary cause of death in people with either type 1 or type-2 diabetes<sup>14</sup> but this study shows there is no significant association between DN and CVD.

Thus the study revealed that patients of diabetic kidney disease are frequently associated with a number of micro and macrovascular complications and their frequency increases with advance of the disease.

#### Limitation:

1. As this study was a clinical study and this study may not exclude other causes of vascular complications which might have confounded the study findings.
2. As no patient was not allowed to undergo investigations like Exercise Tolerance Test (ETE) or angiogram because of ethical ground and therefore in a substantial proportion of patients the diagnosis of coronary artery disease was based on clinical history, previous medical records, ECG and Echocardiogram.

3. As the main bulk of the study population taken from the department of Nephrology of DMCH and BIRDEM and as nephrology department is a department of specialty and patients come to this department after being referred from other departments after diagnosis. So early stages of CKD especially stage 1 and 2 were failed to be included in this study possibly due to late referral or late diagnosis.

#### Conclusion

From the data analysis and discussion thereof, it is concluded that patients of diabetic nephropathy are more often associated with micro and macrovascular complications. Of the microvascular complications, peripheral neuropathy and non-proliferative diabetic retinopathy are frequently associated with diabetic nephropathy than with any other microvascular complications. Of the macrovascular complications, coronary artery disease, MI and peripheral vascular disease are more often encountered than other macrovascular complications. Both micro and macrovascular complications appear with increasing frequency as the diabetic nephropathy advances.

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# Effects of Calcium Acetate Versus Calcium Carbonate as Oral Phosphate Binder in CKD Patients

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## Abstract

**Background:** Hyper-phosphatemia and secondary hyperparathyroidism are common complications of chronic kidney disease (CKD) leading to significant morbidity. Dietary restriction of phosphorus is limited by the need to provide adequate protein. Therefore most patients with CKD require an exogenous phosphate binder to prevent hyper-phosphatemia.

**Methods:** Sixty eight patients of CKD (III – V) not on renal replacement therapy were prospectively evaluated in the Department of Nephrology, SSMCH & MH and Dhaka from Jan 2010 – Dec 2011 to see the effect of calcium acetate and calcium carbonate as phosphate binder. Patients were subdivided into two equal groups, Group A (received calcium acetate, 67 mg BD), Group B (received calcium carbonate, 1250 mg BD). Both the groups were matched for age, sex, BMI and renal function. All patients were withdrawn from any phosphate binder and calcitriol for four weeks ago and restricted to protein (0.8 gm/day) and phosphate containing diet. After a wash out period, group A had taken calcium acetate and group B had taken calcium carbonate. All the biochemical parameters (S.PO<sub>4</sub>, S.Ca<sup>++</sup>, S.Creatinine & iPTH) were estimated at 0 month, 1st month, 2nd month and 3rd month.

**Results:** One month after intervention serum calcium and serum phosphate were significantly reduced in acetate group than those in calcium carbonate group ( $P=0.03$  &  $P=0.01$ ). 2nd month after intervention calcium acetate group showed significant reduction of calcium in comparison to calcium carbonate group ( $P<0.001$ ) & serum phosphate of calcium acetate group decreased further and its difference with calcium carbonate group was significant ( $P=0.001$ ). At the end of 3rd month calcium acetate group showed a considerable reduction of serum calcium as such there was significant difference between the groups with respect to the variables ( $P<0.001$ ). Serum phosphate of calcium acetate group also decreased faster causing a much wider difference with that of calcium carbonate group ( $P=0.005$ ). After end of the study iPTH decrease proportionately in both groups and serum creatinine did not significantly reduced in either group.

**Conclusion:** Reduction phosphate in CKD patient is important. Both acetate base and carbonate base phosphate binder have effect in reduction of phosphate. Calcium acetate has more effect than calcium bi-carbonate phosphate binder.

**Key words:** Phosphate binder, Calcium Acetate, calcium bicarbonate, CKD.

(Bang. Renal J. 2012; 32(1): 19-23)

## Introduction

Chronic kidney disease (CKD) is defined as either kidney damage or glomerular filtration rate (GFR)  $<60$  ml/min/1.73 m<sup>2</sup> for  $>3$  months. Kidney damage is defined as pathological abnormalities or markers of damage including abnormalities in blood or urine test or imaging studies. Hyper-phosphatemia and secondary hyperparathyroidism are common complication of CKD<sup>1</sup> which can lead to significant morbidity because of pain, bone loss, increased risk of fracture, anaemia, hypertension, atherosclerotic vascular disease, pruritus and sexual

dysfunction.<sup>2</sup> Dietary phosphate restriction is limited by the need to provide adequate daily protein intake to maintain neural nitrogen balance<sup>1</sup>. Therefore, most patients with advanced CKD or end stage renal disease (ESRD) require an exogenous phosphate binder to prevent hyper-phosphatemia. Calcium salts (usually calcium carbonate/ calcium acetate) have become the treatment of choice for hyper-phosphatemia, although provision of calcium can lead to hyper-calcaemia and increased risk of metastatic calcification, particularly among patients on Vit-D replacement.<sup>3</sup> Sheik et al first demonstrated the superior

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efficacy of calcium acetate over calcium carbonate as an intestinal phosphate binder; they also showed theoretical as well as experimental evidence of reduced calcium absorption with the acetate salt, offering hope for greatly improved phosphate control<sup>4</sup>.

### Methods

This clinical trial was performed in the Department of Nephrology, SSMCH, Dhaka and investigations were carried out in Laboratory Department of SSMC from Jan 2010 to Dec 2011. Total 68 patients were equally distributed into two groups using a random allocation procedure, one marked with A (for calcium acetate) and another with B (for calcium carbonate). The daily dose of calcium acetate was 667 mg tab (containing 169 mg of elemental calcium) twice daily after taking meal, while the dose of calcium carbonate was 1250 mg tab (containing 500 mg of elemental calcium) twice daily orally after taking meal. All patients were withdrawn from a phosphate binder and calcitriol for at least two weeks ago and restricted to protein (0.8 gm/kg) and phosphate containing drug. After a washout period of two weeks, baseline biochemical markers (S.PO<sub>4</sub>, S.Ca<sup>++</sup>, S.Creatinine and iPTH) were measured and then group "A" had taken calcium acetate and group "B" had taken calcium carbonate for 3 months. Biochemical markers (S.PO<sub>4</sub>, S.Ca<sup>++</sup>, S. Creatinine and iPTH) were measured at one month interval for 3 months.

### Statistical method

Data were processed and analyzed using SPSS version 11.5. The test statistics used to analyse the data were Chi-square (X<sup>2</sup>) or Fisher exact probability and Student's t test.

### Results

Mean age of the patients in calcium acetate group was 54.09 ± 9.66 years and in calcium carbonate group 53.37 ± 10.42 years, mean weight in kg 62.30 ± 3.55 in calcium acetate group and 58.20 ± 5.96 in calcium carbonate group, mean height (m.) was 1.69 ± 0.2 in calcium acetate group and 1.65 ± 0.25 in calcium carbonate, body mass index (BMI) in calcium acetate group was 21.78 ± 1.95 kg/m<sup>2</sup> and 21.32 ± 2.22 in calcium carbonate group. In the study patients, the baseline level of biochemical variables like S. Calcium, S. Phosphate, S. iPTH and S. Creatinine were almost identical between groups (8.7 ± 1.07 Vs 8.9 ± 0.92 mg/dl, P=0.27, 3.8 ± 1.1 Vs 4.3 ± 1.1 mg/dl, P=0.10, 234.50 ± 42.5 Vs 205 ± 36.2 pg/ml, P=0.65 and 3.6 ± 1.8 Vs 3.7 ± 2.0 mg/dl P=0.90 respectively). One month after intervention, changes in biochemical variables showed that calcium acetate group responded well than calcium carbonate group

with respect to S. Calcium and S. Phosphate (8.5 ± 1.2 Vs 8.9 ± 0.7 mg/dl, P=0.03; 3.5 ± 0.8 Vs 4.1 ± 0.9 mg/dl, P=0.01). iPTH and S. Creatinine also reduced in both groups but no significant intergroup difference was observed (188.1 ± 35.5 Vs 164 ± 28.9 pg/dl, P=0.41 and 3.49 ± 1.6 Vs 3.35 ± 1.6 mg/dl, P=0.52 respectively). Two months after intervention there was significant difference between the group with respect to S. Calcium (8.5 ± 0.97 Vs 9.10 ± 0.38 mg/dl, P=<0.01). S.PO<sub>4</sub> of calcium acetate group decreased further and its difference with calcium carbonate group was also significant (3.2 ± 0.69 Vs 4.21 ± 1.38 mg/dl, P=0.001). But there was no significant difference between groups with respect to S. iPTH and S. Calcium. Three months after intervention of the variable S. Ca<sup>++</sup> was significantly lower in calcium acetate group than calcium carbonate group (P=<0.05). No significant difference between calcium acetate and calcium carbonate group with respect to iPTH and S. Creatinine (P>0.05) was found.

**Table-I**

*Demographic characteristics of the study population*

Demographic Characteristics	Group		P Value
	Calcium Acetate (Group A) Mean ± SD	Calcium carbonate (Group B) Mean ± SD	
Age in yr*	54.09±9.66	53.37± 10.42	0.76
Weigh (kg)	62.30 (±3.55)	58.20 (±5.69)	0.005
Height (in.)	1.69 (±0.2)	1.65 (±0.25)	0.03
BMI (mean±SD)	21.78 (±1.95)	21.32 (±2.22)	0.39

Data were analyzed using Student's t-Test and were

**Table-II**

*Comparison of baseline values between groups*

Baseline variables	Group		P Value
	Calcium Acetate (Group A) (n=33)	Calcium carbonate (Group B) (n=35)	
Serum calcium (mg/dl)	8.7 ± 1.07	8.9 ± 0.92	0.27
Serum phosphate (mg/dl)	3.8 ± 1.1	4.3 ± 1.1	0.10
Intact serum PTH (pg iul)	234.5 ± 42.5	205 ± 36.2	0.65
Serum creatinine (mg/dl)	3.6 ± 1.8	3.7 ± 2.0	0.90

Data were analyzed using Student's t-Test and were presented as mean ± SD

**Table-III***Changes of biochemical variables 1 month after intervention*

Biochemical variables	Group		P Value
	Calcium Acetate (Group A) (n=33)	Calcium carbonate (Group B) (n=35)	
Serum calcium (mg/dl)	8.5±1.2	8.9±0.7	0.03
Serum phosphate (mg/dl)	3.5±0.8	4.1±0.9	0.01
Intact serum PTH (pg/ml)	188.1±35.5	164±28.4	0.41
Serum creatinine (mg/dl)	3.49±1.6	3.35±1.6	0.52

±Data were analyzed using Student's t-Test and were presented as mean ± SD

**Table-IV***Changes of biochemical variables 2 month after intervention*

Biochemical variables	Group		P Value
	Calcium Acetate (Group A) (n=33)	Calcium carbonate (Group B) (n=35)	
Serum calcium (mg dl)	8.5±0.97	9.38±0.7	0.001
Serum phosphate (mg/dl)	3.27±0.69	4.21±1.38	0.01
Intact serum PTH (pg nil)	158.1±30.9	153.9±27.7	0.62
Serum creatinine (mg dl)	3.69±1.57	3.34±1.70	0.25

±Data were analyzed using Student's t-Test and were presented as mean \* SD Group Statistics

**Table-V***Changes of biochemical variables 3 month after intervention*

Biochemical variables	Group		P Value
	Calcium Acetate (Group A) (n=33)	Calcium carbonate (Group B) (n=35)	
Serum calcium (mg/dl)	8.6± 1.06	9.45±0.44	<0.001
Serum phosphate (mg/dl)	3.13±1.31	3.98±0.67	0.005
Intact serum PTH (pg/ml)	128.1±17.8	148±36.2	0.64
Serum creatinine (mg/dl)	3.35±1.00	3.48±1.79	0.42

± Data were analyzed using Student's t-Test and were presented as mean ± SD

**Table-VI***Comparison of changes in serum calcium between the study groups*

Group	0 month	Mean serum calcium (mg/dl)			p value
		1 month	2 month	3 month	
Calcium Acetate	8.7± 1.07	8.5± 1.2	8.5±0.87	8.6± 1.06	0.003
Calcium Carbonate	8.9±0.92	8.5± 1.2	8.5±0.87	8.6± 1.06	

± Data were analyzed using Repeated measure ANOVA statistic and 'p' refers to the overall difference between the groups in terms of changes in serum calcium from baseline to end point of study.

**Table-VII***Comparison of changes in serum phosphate between the study groups*

Group	0 month	Mean serum phosphate (mg/dl)			p value
		1 month	2 month	3 month	
Calcium Acetate	3.5± 1.1	3.5±0.2	3.27±0.69	3.13± 1.31	0.003
Calcium Carbonate	4.3± 1.1	4.1±0.9	4.21± 1.38	3.98±0.67	

± Data were analyzed using Repeated measure ANOVA statistics and 'p' refers to the overall difference between the groups in terms of changes in serum phosphate from baseline to end point of study.

**Table-VIII**  
*Comparison of changes in serum intact PTH between the study groups*

Group	Mean serum PTH (mg/dl)				p value
	0 month	1 month	2 month	3 month	
Calcium Acetate	234±42.5	188.1±35.5	158.5±30.9	128±17.8	0.001
Calcium Carbonate	4.3±1.1	164±28.4	153.9±27.7	148±36.2	

± Data were analyzed using Repeated measure ANOVA statistics and 'p' refers to the overall difference between the groups in terms of changes in serum calcium from baseline to end point of study.

**Table-IX**  
*Comparison of changes in serum creatinine between the study groups*

Group	Mean serum creatinine				p value
	0 month	1 month	2 month	3 month	
Calcium Acetate	3.6±1.8	3.49±1.6	3.69±1.87	3.35±1.00	0.70
Calcium Carbonate	3.7±2.0	3.35±1.6	3.34±1.70	3.48±1.79	

± Data were analyzed using Repeated measure ANOVA statistics and 'p' refers to the overall difference between the groups in terms of changes in serum calcium from baseline to end point of study.

## Discussion

The present study was under taken to observe the effect of calcium acetate versus calcium carbonate on CKD patients as phosphate binder and also to see the effect of these two drugs on iPTH. It is generally believed that calcium acetate is better tolerated, binds phosphate efficiently and causes less incidence of hypocalcaemia as compared to calcium carbonate. In present study serum phosphate level was adequately controlled with both salts. The advantage we observed that this control was achieved using only less than half the amount of elemental calcium with the acetate formulation<sup>5</sup>. In our study, we used calcium acetate 1.3 gm/day and calcium carbonate 2.5 gm/day without calcitriol. There was significant reduction of serum phosphate (3.13 Vs 3.98) and S.Calcium (8.6 Vs 9.45) in acetate group and significant increases in serum calcium in calcium carbonate group than acetate group. One author<sup>6</sup> conducted a randomized cross-over study over 24 weeks, in 7 selected hemodialysis patients to compare calcium acetate with calcium carbonate. In acetate form, less elemental calcium was used but there was no difference in phosphate control and the incidence of hyperkalemia was also similar between the two treatments. At the end of present study, there was significantly higher decrease of Serum phosphate in calcium acetate group compared to calcium carbonate group (3.13 ± 1.06 Vs 9.45 ± 0.44) than that of calcium carbonate group and their difference was

significant. Borrego and Colleagues compared the efficacy of calcium acetate and calcium carbonate as phosphate binder in 28 patients with CKD<sup>7</sup>. The authors found that both drugs were similarly effective as phosphate binder in lowering phosphate level. Four fold greater dose elemental calcium was used in calcium carbonate than acetate group and exhibited more hypocalcaemia in carbonate group<sup>7</sup>. Pflanz et al (1994) performed a randomized cross-over study in 23 patients over 14 weeks<sup>8</sup>. Equimolar doses of calcium acetate and calcium carbonate and calcium carbonate were used<sup>9</sup>. Serum phosphate was significantly lower with calcium acetate (1.51 Vs 1.80 mmol/l) and iPTH was also lower with calcium acetate (17.8 Vs 25.4 ppmol/l). But Serum calcium was significantly higher in the calcium acetate (2.4 Vs 2.32 mmol/l) group than the calcium carbonate group. Our study also showed that the drugs effective as phosphate binder but acetate was more effective than calcium carbonate group<sup>10</sup>. At the end of third month's intervention, calcium carbonate group had significant higher calcium level (Table 7). This can be explained by the use of three fold higher eliminated calcium in calcium carbonate group than the acetate group.

## Conclusion:

Reduction phosphate in CKD patient is important. Both acetate base and carbonate base phosphate binder have effect in reduction of phosphate. Calcium acetate has more effect than calcium bi-carbonate phosphate binder.

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# Case Reports

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## A Middle Age Women with Amyloidosis and Nephrotic Syndrome – A Case Report

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### Abstract:

*Amyloidosis is a rare disease. It can affect various organs. Common and important presentation of renal amyloidosis is nephrotic syndrome. Proper history, clinical examination, laboratory investigations including renal biopsy and histopathological examination is mandatory to diagnose renal amyloidosis. We have experienced a middle aged lady who has developed nephrotic syndrome as part of renal amyloidosis.*

*Key Words: Amyloidosis, Nephrotic Syndrome, Renal Biopsy, Congo-Red stain.*

*(Bang. Renal J. 2013; 32(2): 24-27)*

### Introduction:

Amyloidosis refers to a variety of conditions where in normally soluble proteins become insoluble and are deposited in the extracellular space of various organs or tissues, disrupting normal function. It is a rare disease. The overall incidence in United States is 1 out of 10000 people. Common age group is 60-70 years and male affects twice than female. (Stephen J et al 2008) The spectrum of renal symptoms and sign in amyloidosis is variable such as isolated proteinuria, nephrotic syndrome, hypertension, hypotension and renal insufficiency. (Vanderhem & Van Rijswijk; Gertz MA 1992) Renal amyloidosis is confirmed by histopathological examination of renal tissue. (Laura 2006) Amyloidosis is a rare disease so we present here this case.

### Case Report:

Mrs. Beauty, 38 years old lady non diabetic, non hypertensive hailing from Rampal, Bagerhat admitted into Nephrology department, Dhaka Medical College Hospital on 12.03.2013 through outpatient department with the complaints of swelling of whole body for six months which first appeared on the face then legs and became generalized

During this period her urine volume & colour was normal. Patient gives no history of fever, cough, respiratory distress, chest pain, palpitation, joint pain, skin rash, morning stiffness, cold intolerance, bowel alteration, sore throat, jaundice, hematemesis, melaena or taking any NSAID prior to swelling of body.

She was diagnosed as a case of abdominal TB at initial period of her illness after admission in a tertiary level hospital and had taken anti TB drugs (category 1) for 6 months. Her previous hospital records on which basis anti TB had been started was not available during admission at nephrology department.

She has two sons and two daughters. All of them are in sound health. Both of her parents are alive and with good health.

On examination- she was puffy, mildly anaemic, moderately edematous, non icteric, pulse 96 beats/min, blood pressure 110/70 mm of Hg, JVP- not raised. Respiratory rate 14/min. Breath sound vesicular. Liver was palpable which was about 2 cm, firm in consistency, non tender, smooth surface, upper border of liver dullness was right 5<sup>th</sup> intercostal space. Conscious level was normal. All cranial

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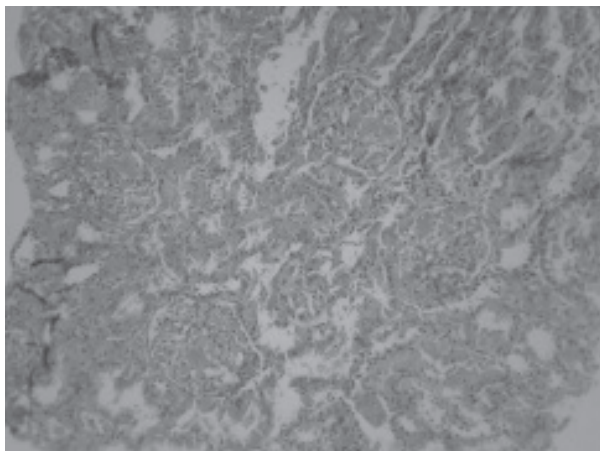
nerves were intact. Other neurological examination was normal. Bedside urine examination showed +++ proteinuria.

Laboratory investigations revealed- Total count of WBC-9700/cumm, Neutrophil-72%, Lymphocyte-22%, Eosinophil-06%, Monocyte-02%, Haemoglobin-12.7gm/dl, ESR-115 mm in 1<sup>st</sup> hour, Platelet count-400000/cumm. Urine R/E- Protein-+++ , Leucocyte-0-2/HPF, RBC-4-6/HPF, Granular cast-not found, Cellular cast-not found. Serum Bilirubin-0.51mg/dl, SGPT-38 U/L, SGOT-24 U/L, RBS-6.5 mmol/L, 24 hours urinary total protein-8.85 gm. Fasting lipid profile: Total cholesterol-170mg/dl, HDL cholesterol-42mg/dl, LDL cholesterol-83.40mg/dl, Triglyceride-223mg/dl. TSH- 3.64  $\mu$ IU/ml. ANA- Negative, AntidsDNA- Negative, RA test- Negative, cANCA- Negative, pANCA- Negative. CXR P/A view- Normal, ECG-Normal BT-3min. 30sec. CT-6min. 30sec.

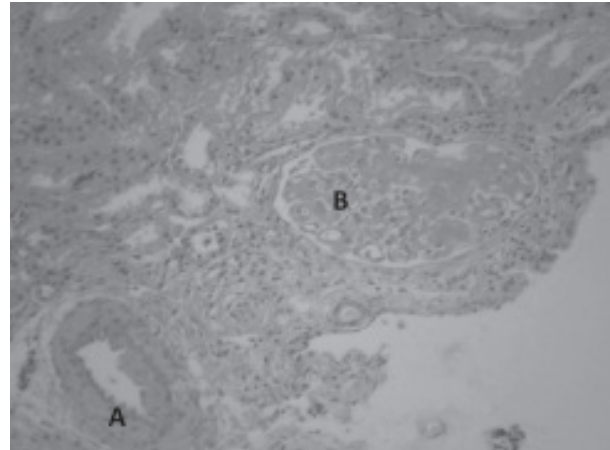
Liver: Mildly enlarged (14cm) echotexture was homogenous, Spleen: normal, KUB: Both kidneys appear swollen. Rt. kidney- 10.0 $\times$ 3.8cm, Lt. Kidney-13.3 $\times$ 5.6cm. CMD maintain, Urinary bladder: norml, Ascites-Present.

RENAL BIOPSY : Sections reveal single core renal tissue and contain 7 glomeruli. All glomeruli show deposit of homogenous amorphous congophilic material in the mesangium and basement membrane zone (Fig-1 and Fig-2). The same deposit is also present in the walls of blood vessels and some renal tubules. DIF: No deposit of IgA, IgG, IgM or C3 is present.

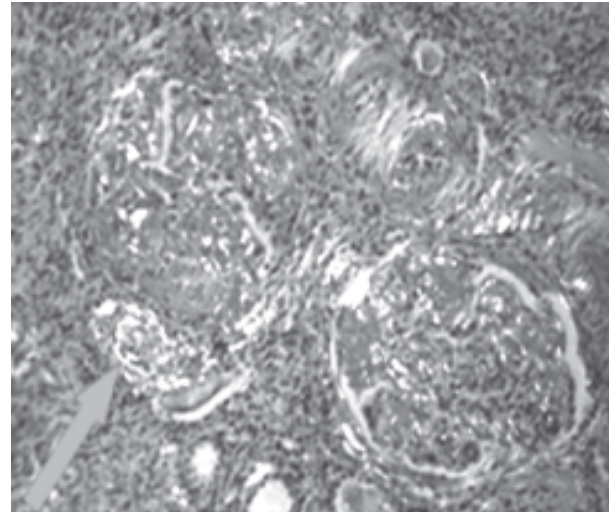
The patient was diagnosed as a case of renal amyloidosis.



**Fig.-1:** Glomeruli show amorphous homogenous deposit in mesangium and basement membrane zone.



**Fig.-2:** Congophilic material deposits in the wall of blood vessel (A) and in mesangium (B)



**Fig.-3:** Congophilic material shows Birefringence in polarized light.

#### Discussion:

In this case, before receiving renal histopathological report we had kept in mind this may be a case of primary glomerular disease. As history, clinical examination and relevant investigations did not favour any secondary cause of glomerulonephritis. Following getting renal histopathological report we had tried to identify whether it is primary, secondary or familial amyloidosis. For this goal we had gone through some additional investigations- (Xray skull lateral view- normal, urine for Bence-Jones protein- negative, serum protein electrophoresis- There is a faint band in the gamma region which may represent a monoclonal band. Serum immunoglobulin electrophoresis- No band is seen on serum capillary immune fixation



electrophoresis, suggestive of no abnormal (increased) accumulation of Ig molecule or free chain in the serum. Bone marrow study- Feature consistent with reactive bone marrow). But did not help to identify specific type of amyloidosis.

Amyloidosis is several types like- Primary: It is associated with Monoclonal light chains, Fragments of light chains alone, MM.

Secondary: Results from deposition of fragments of serum amyloid A proteins in patients with underlying inflammatory conditions. Familial: Due to defect of transthyretin lead to amyloid formation in middle age. (Paul J et al 2008)

Final diagnosis of amyloidosis requires histologic demonstration of amyloid deposits. This usually is accomplished by staining with Congo red dye. Congo red-stained amyloid has an orange-red appearance under light microscopy and produces apple-green birefringence under polarized light. Different types of amyloid are indistinguishable by light or electron microscopy. The most direct method for identifying the amyloidogenic protein is by mass spectrometry or amino acid sequencing of proteins that are extracted from amyloid

deposits. These techniques are not available routinely. The most definitive method used in the clinical setting is immunofluorescence or immunohistochemical staining of tissue using antibodies that are directed against known amyloidogenic proteins. (Laura 2006) These methods are not available in our setting.

Lastly on the basis of history, clinical examinations and laboratory investigations- we have diagnosed this middle aged lady is a case of amyloidosis with nephrotic presentation due to primary amyloidosis.

Regarding management in case of AL amyloidosis - Several chemotherapeutic regimens have been evaluated, and high-dose intravenous melphalan followed by autologous stem cell transplantation

to support bone marrow recovery has emerged as the most likely to eliminate the clonal plasma cells. (Skinner 2004, Comenzo RL et al 1996, Dispenzicri A et al 2004) Experience from several treatment centers has suggested that 25 to 50% of patients who undergo such treatment have complete hematologic responses, meaning that there is no evidence of ongoing production of the monoclonal light chain. (Skinner 2004, Gertz MA et al 2002, Moreau P et al 1998)

The current treatment approach for AA amyloidosis is to treat the underlying inflammatory disease and thereby reduce production of SAA. In FMF, a disease that is associated with a high rate of AA amyloidosis, life-long treatment with colchicines to inhibit FMF-associated inflammation prevents the development of amyloidosis in many patients. (Ozen 2004)

Orthotopic liver transplantation has been performed in >660 individuals with TTR amyloidosis and is considered the definitive treatment for the disease. (Ericzon BG et al, 2003)

Ongoing amyloid deposition in the kidney is associated with progressive deterioration in renal function. In a group of patients who had AL amyloidosis and kidney involvement followed in the 1980s, progression to ESRD occurred at a median of only 14 months after diagnosis. (Gertz MA et al 1992)

So early diagnosis and appropriate treatment is essential to prevent further deterioration of renal function.

#### Conclusion:

Nephrotic syndrome due to amyloidosis is not common in our country but may possible. Details history, clinical examination, laboratory investigations including renal biopsy with light microscopic examination and immunofluorescence study will help physician for proper diagnosis of renal amyloidosis.

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# Prostatic Carcinoma with Metastasis to Colon Causing Obstructed Uropathy: A Case Report

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(*Bang. Renal J. 2013; 32(2): 28-30*)

## Introduction:

Prostate carcinoma is a slowly growing neoplasm therefore can easily be missed during its early stages and hence may present with metastasis. But it is very rare that prostatic carcinoma metastasize to nearby organ specially rectum. Here we present a case of prostatic carcinoma presented with acute kidney injury resulting obstructive uropathy from metastasis to colon.

## Case Report:

The 56-year-old patient was admitted with swelling of left lower limb and drowsiness. He was on haemodialysis (HD) for acute kidney injury (AKI) which developed after an episode of acute gastroenteritis for last one and a half month through left femoral access. The catheter was removed for development of swelling and tenderness of the left lower limb 6 days prior to admission in our unit. Since the removal of HD catheter, he had not received any form of renal replacement therapy and became drowsy for last 3 days. He had history of constipation and occasional passage of blood mixed with stool. He is a known patient of diabetes mellitus and hypertension and recently been diagnosed as a case of adenocarcinoma of prostate and stricture of urethra. He had history of transurethral resection of prostate (TURP) and optical internal urethrotomy (OIU) 2 months back and suprapubic cystostomy was done for retention of urine prior to hospitalization.

On examination, he was propped up in position, hemodynamically stable, moderately anemic and edematous. There was asymmetry of both lower limbs, circumference of left lower limb was 4 cm more (10 cm below tibial tuberosity) with erythema, tenderness and raised temperature. Suprapubic catheter was in situ. Temperature

was 98<sup>o</sup> F and bedside albumin was nil. Glasgow coma scale (GCS) was 12/15, planter response was bilaterally extensor. There was also bilateral basal crepitation on auscultation of lungs and abdomen was distended with exaggerated bowel sound. There was no associated history of fever, trauma, jaundice, vomiting, convulsion. There were neither any signs of meningeal irritation nor any focal neurological sign. Fundus was normal.

Immediately haemodialysis was given with preformed arteria-venous fistula and low molecular weight heparin was started for suspected left sided deep vein thrombosis of lower limb after sending urgent investigations. An annular growth was found on digital rectal examination after stabilizing the patient. Meanwhile all the investigations were available.

Hematological examination revealed high ESR 72 mm in 1<sup>st</sup> hour, Hemoglobin was 8.9 gm/dl, total leucocyte count was 3000/mm<sup>3</sup> with normal differentials, platelet was 2,65,000/mm<sup>3</sup>. Urine RME was normal. Urea was 305 mg/dl and S. creatinine was 18.5 mg/dl. Serum electrolyte showed S. Na+ 130 mmol/L, S. K+ 5.4 mmol/L, Cl- 100 mmol/L and TCo2 was 17 mmol/L. Doppler study of lower limb revealed deep vein thrombosis involving left iliac, common femoral and popliteal veins extending into left long and small saphenous vein. A soft tissue mass (62mm×55mm) in the pelvis and bilateral obstructive uropathy (mild) was found on USG of abdomen (Fig 1). His screening for infection, CXR (P/A View) and liver function test were normal. X-ray abdomen showed distended bowel loops (fig 2). Proctoscopy for anal growth and urethrocystoscopy for urinary retention was done which showed stenosis of anal canal and rectal growth and bladder neck contracture respectively. CT scan of abdomen revealed a large ill defined soft tissue mass measuring about 9cm×8.3cm×9.1

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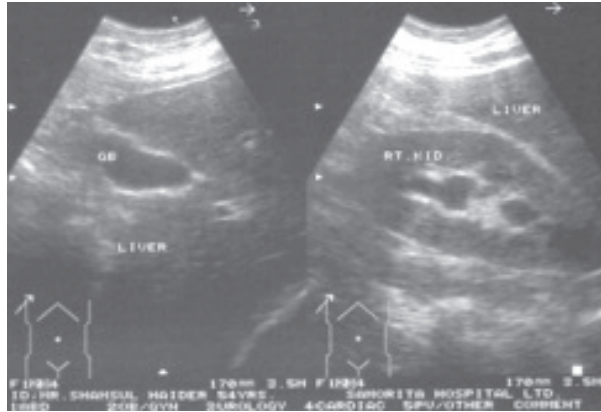
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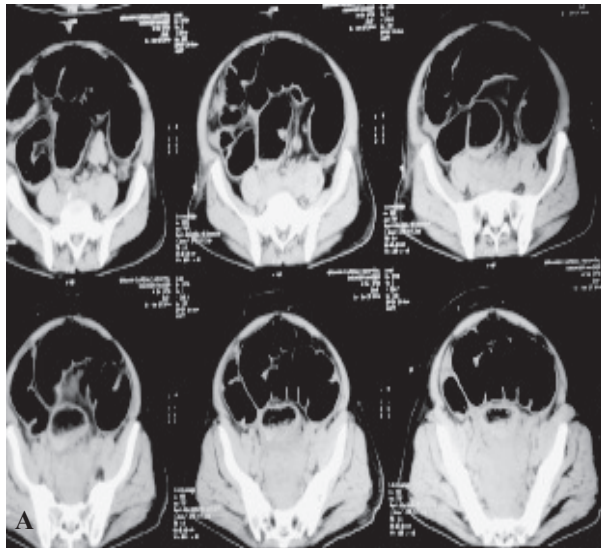
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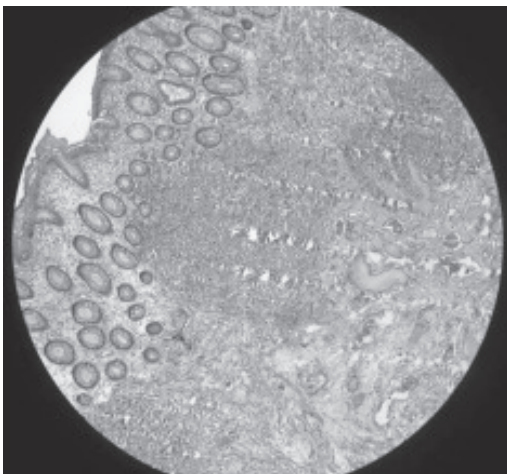
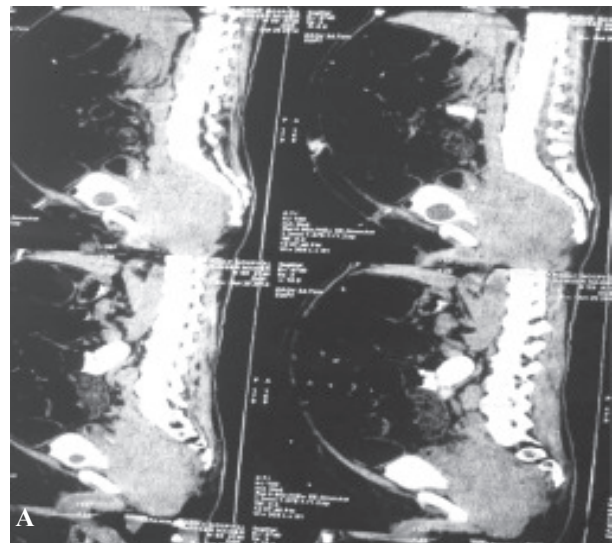
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**Fig.-1:** USG showing hydronephrosis of right kidney



**Fig 3:** CT scan of abdomen showing soft tissue mass in lower abdomen and posterior to urinary bladder (A,B)



**Fig 4:** Rectal tissue histopathology showing poorly differentiated adenocarcinoma

cm was seen in lower abdomen posterior to urinary bladder involving prostate, seminal vesicle, rectum and part of sigmoid colon. Multiple loco-regional enlarged lymph nodes were present. Ilium and jejunum were mild to moderately dilated and bilateral mild hydronephrosis with dilatation of upper 2/3<sup>rd</sup> of right ureter was also seen (Fig 3). Tumor markers were normal.

Meanwhile patient was getting haemodialysis each alternate day.

For his colonic growth, bladder neck contracture and prostatic carcinoma sigmoid loop colostomy with rectal biopsy, bladder neck incision and bilateral orchiectomy was done respectively and rectal biopsy revealed poorly differentiated adenocarcinoma (fig 4).

He had his last haemodialysis the day before the operation and post operatively his serum creatinine gradually decreased to 1.6 mg/dl.

We finally referred the patient to oncologist for further management.

#### Discussion:

Prostate cancer extension to colorectal tissue can occur through at least 3 potential routes. These are direct invasion through Denonvilliers fascia and infiltration into the rectum through lymphatics,<sup>1</sup> and spread through needle biopsy, by seeding into peri-rectal or rectal tissue along the needle, though it is extremely rare<sup>2,3</sup>. Prostate cancer metastasis to the recto-sigmoid region can occur by subserosal metastatic implant of the malignant tissues<sup>4</sup>. The incidence of rectal infiltration by prostatic

adenocarcinoma is extremely rare<sup>5</sup>. Our case is also an example of direct invasion of prostate cancer to rectum.

Acute renal failure due to bilateral ureteral obstruction is a common problem in palliative care. Malignant unilateral or bilateral ureteral obstruction may be secondary to direct tumorinvasion, extrinsic compression as in our case or encasement by metastatic retroperitoneal or pelvic lymph nodes<sup>6</sup>. Malignant ureteral obstructions usually require immediate ureteral decompression in order to restore renal function<sup>7,8</sup>. In our case there was also complete recovery of renal function.

### Conclusion:

Obstructive uropathy is a common cause of AKI in a patient with prostatic malignancy. Gastrointestinal and urologic complaints should be emphasized in such cases.

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