

## Evaluation of acute intradialytic complications, management & outcome in end-stage renal disease patients.

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### Abstract

Little is known about the challenges of routine renal replacement therapy in Bangladesh. We investigated the fatal and nonfatal acute hemodialysis complications in patients with end stage renal disease (ESRD) in dialysis centers in Mymensingh. 500 consecutive hemodialysis sessions incurred over a 4-month period by 50 patients with ESRD, receiving two weekly hemodialysis sessions of 4 hours each were considered. Personal and clinical profiles before, during, and within 24 hours after hemodialysis sessions were used to diagnose complications. The mean age of the patients was  $45.5 \pm 16.8$  years and the lowest and highest ages were 17 and 82 years respectively. Male was predominant of the patients and male to female ratio was 2:1. Hypotension, muscular cramps, pruritus, nausea and vomiting were the common complications in end-stage renal disease patients. Twenty eight percent of patients presented with hypertensive crisis, 34% fever, 18% bleeding, 44% headache, 32% vomiting, 16% lumber pain, 16% palpitations, 22% disequilibrium syndrome, 36% dyspnea, 28% chest pain, 20% syncope, 32% abdominal problem, 44% neurological problem, 46% electrolyte imbalance, 34% articular & musculoskeletal problems, 48% cramps, 38% convulsions and 20% loss of consciousness. The vascular access was the main bleeding site of the patients (44.5%), followed by 33.3% through nose and 22.2% digestive tract bleeding. Most of patients experienced muscular cramps, hypertensive crisis, pruritus, vomiting, palpitations, disequilibrium syndrome, dyspnea, chest pain, neurologic problem, electrolyte disorders, nausea, vomiting, convulsions and loss of consciousness in shorter duration of dialysis than those in longer duration of dialysis sessions. Bleeding, disequilibrium syndrome and cardiovascular disease were leading cause of death in end-stage renal disease patients. Those complications occurred mostly during understaffed periods. Urgent strategies are needed to quickly solve the human capital crisis in the health care sector.

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**Key words:** End-stage renal disease, hemodialysis, acute complications.

### Introduction

Chronic kidney disease (CKD) is a common and rapidly increasing public health problem, affecting 1 in 10 adults around the world. Reported incidence rates have more than doubled in many affluent countries over the past two decades, and forecasts for the years to come are alarming<sup>1,2</sup>. End-stage renal disease (ESRD) has reached epidemic proportion with more than 400,000 affected individuals in the United States and well over one million worldwide<sup>3</sup>. This staggering number represents only the tip of the iceberg, as the incidence of chronic kidney disease (CKD) is at least 30-fold higher than that of ESRD<sup>4</sup>. For instance, it is estimated that incidence rates for end-stage renal disease (ESRD) currently increase by 6% per year, which is much higher than the estimated growth rate for the global population (i.e., 1.2% per annum)<sup>5</sup>. Glomerulonephritis was the one of the leading causes of kidney disease several decades ago. Now-a-days, infections have become a less important cause for kidney disease, at least in the western world<sup>6</sup>. Moreover, current evidence suggests that hypertension and diabetes are the two major causes of kidney disease worldwide<sup>7,8</sup>. Given the pathogenic progression of kidney disease, patients with CKD are at high risk for progression to the end stage renal disease (ESRD) – a condition requiring dialysis or kidney transplantation to maintain patients'

long-term survival. In 2001, the average annual cost for maintenance of ESRD therapy was between US \$70 and \$75 billion worldwide excluding kidney transplantation, and the predicted number of ESRD patients will reach over 2 million in 2010. The enormous costs of treatment lead to a large burden for the health care systems, particularly in developing countries<sup>9</sup>.

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The complications of CKD are due to the disease itself as well as the mode of renal replacement therapy (RRT). Kidney function can only be partly replaced by maintenance dialysis, which provides only 5-10% of excretory renal function<sup>10</sup>. Hemodialysis, which is one of the renal replacement therapies, is a life-saving treatment. In the absence of this therapy, more than a million patients worldwide would have died within weeks. However, hemodialysis is accompanied by several complications. During the first years following the introduction of hemodialysis, complications were common due to the technical drawbacks associated with the dialysis machines and water systems. Currently, the advances in technology, particularly those in the last 20 years, have reduced the complications. However, complications caused by the reasons other than the dialysis machine and water system remain as a significant cause of morbidity and mortality in hemodialysis patients. Cardiovascular complications are currently the most common complication of hemodialysis. Among these complications, the rate of symptomatic intradialytic hypotension ranges between 20% and 50%, and it remains an important problem<sup>11</sup>. Another concern is the hemodialysis-associated arrhythmias, the rate of which was reported to be 5% to 75%. The common and lethal types of arrhythmias include ventricular arrhythmias and ectopies. The rate of hemodialysis-associated complex ventricular arrhythmia is around 35%<sup>12</sup>. The second most common type of arrhythmia is the atrial fibrillation, the rate of which is 27%<sup>13</sup>. Sudden cardiac death accounts for 62% of cardiac-related deaths and it is usually attributed to arrhythmias<sup>14</sup>. The first year of hemodialysis is of vital importance with respect to sudden cardiac deaths, which was determined in 93 of 1000 patients in the first year of hemodialysis<sup>15</sup>. While cramps were observed in 24%-86% of the cases during the first years following the introduction of dialysis therapy, recently it has been shown that only 2% of the patients having =2 hemodialysis sessions in a week suffer from cramps<sup>16</sup>. Other common complications include nausea, vomiting with a rate of 5%-15%, headache with a rate of 5%-10% and itching with a rate of 5%-10%<sup>17</sup>. Although cramps, nausea-vomiting, headache and itching do not result in mortality, they substantially deteriorate the quality of life of the patients. Although more common during the first years following the introduction of dialysis, Disequilibrium syndrome and complications associated with dialyser, water systems and dialysis machines are currently uncommon but may have fatal consequences.

## Methods

This was a cross sectional descriptive study of 4 months duration from September to December 2012 at a Private hospital hemodialysis unit, Mymensingh. During the study period analysis was carried out on data for 50 patients. They have a combined capacity

of four HD generators that use the Nipro Surdial 55 plus dialysis technology, that use the synthetic polysulfone dialysis membrane, and bicarbonate. The centers operate from Saturday to Thursday, from 9 a.m. to 10 p.m. (or beyond for emergency cases), and offer to registered patients two HD sessions of 4 hours duration each per week. All patients were dialyzed using standard (unfractionated) heparin with a starting dose of 2500 international units, followed by a maintenance dose of 500 international units per hour during the session. Where possible, patients are alternatively allocated to daytime and nighttime dialysis sessions. At the time of the study, each center was supervised by a nephrologist, one dialysis technician, four registered nurses and two nursing aid. Nurses were working in groups according to time schedules: The day time team (from 9:00 a.m. to 5:00 p.m.) and the night time team (from 5:00 p.m. to 10:00 p.m.)

## Data collection

During the study period, dialysis sessions for consenting patients who were on chronic dialysis were monitored. For practical reasons (single data collector), recruitments were limited to 10 days (five per center) per month. Therefore, only a sample of the dialysis sessions occurring during the study period was monitored for the purpose of the study. Dialysis sessions prematurely terminated for technical reasons and HD sessions of patients with acute kidney injury were excluded. Clinical profiles for each participant were recorded prior, during, and within 24 hours of dialysis session completion for the purpose of complications diagnosis, using a predesigned questionnaire. Individual information recorded included age, gender, etiological factors of CKD, and vascular access. The vascular access was either a native arteriovenous fistulae or a temporary catheter (femoral or jugular). Patients (or the accompanying family members) were advised to report all complications occurring during the 24 hours after dialysis according to a form they were provided with. During dialysis session, patients were examined at the beginning, 2 hours after the start, and at the end of the dialysis session. Blood pressure and heart rate were recorded hourly.

## Statistical analysis

Statistical analysis were performed using the SPSS® 9 software for Windows 7. We have reported results as mean, standard error of the mean, and count (percentages). Difference between variables was assessed using the t test and equivalents the level of significance was set at  $P < 0.05$ .

## Results

During the study period analysis was carried out on data for 50 patients. Of them, 24% was below 30 years of age, 36% between 30 – 50 years and rest 40% more than 50 years. The mean age of the patients was  $45.5 \pm 16.8$  years and the lowest and

highest ages were 17 and 82 years respectively. Male was predominant of the patients and male to female ratio was 2:1 (Table-I). Hypotension, muscular cramps, pruritus, nausea and vomiting were the common complications in end-stage renal disease patients. Twenty eight percent of patients presented with hypertensive crisis, 34% fever, 18% bleeding, 44% headache, 32% vomiting, 16% lumber pain, 16% palpitations, 22% disequilibrium syndrome, 36% dyspnea, 28% chest pain, 20% syncope, 32% abdominal problem, 44% neurological problem, 46% electrolyte imbalance, 34% articular & musculoskeletal problems, 48% cramps, 38% convulsions and 20% loss of consciousness (Table II). The vascular access was the main bleeding site of the patients (44.5%), followed by 33.3% through nose and 22.2% digestive tract bleeding (Figure 1).

Assessment of acute complications encountered by the patients illustrate that fever, bleeding, headache and lumber pain were significantly higher in shorter duration of dialysis (<5 months) compared to longer duration of dialysis (=5 months) sessions (57.1% vs. 25%,  $p=0.031$ ; 50% vs. 5.6%,  $p < 0.001$ ; 78.6% vs. 30.6%,  $p=0.002$  and 35.7% vs. 8.3%,  $p=0.018$  respectively). Most of patients experienced muscular cramps, hypertensive crisis, pruritus, vomiting, palpitations, disequilibrium syndrome, dyspnea, chest pain, neurologic problem, electrolyte disorders, nausea, vomiting, convulsions and loss of consciousness in shorter duration of dialysis than those in longer duration of dialysis sessions, although the difference did not turn to significance. In presenting complaints, fever was found significantly higher those who dialysis by catheter compare to arteriovenous fistulae (AVF) (83.3% vs. 18.4%,  $p < 0.001$ ). The higher rates of complications such as hypotension, muscular cramps, pruritus, headache, vomiting, palpitations, disequilibrium syndrome, abdominal problem, neurologic problem, electrolyte disorders, articular & musculoskeletal problems, cramps, vomiting, loss of consciousness were observed who received dialysis treatment during night time compared to day time (Table III).

A higher percentage of patients with age category less than 30 years was done dialysis during night time compared to daytime (28.6% vs. 18.2%). However, patients with age category 30–50 years and more than 50 years were somewhat higher daytime dialysis compared to nighttime (40.9% vs. 32.1% and 40.9% vs. 39.3% respectively) ( $p = 0.662$ ). The proportion of patients according to gender, diabetes, vascular access, duration of dialysis and ultrafiltration rate were almost similar between day and night time dialysis ( $p=0.981$ ;  $p=0.295$ ;  $p=0.919$  and  $p=0.477$  respectively) (Table IV). Over one-third (36%) of ESRD patients had a history of blood transfusion, 36% adjustment of medical dose, 23% analgesia and remaining 5% administered iodinated radio contrast agents (Figure 2). Three (13.6%) of 22 patients death occurred during day time and 4(14.3%) of 28 night time dialysis (Figure 3). Septicemia, hyperkalemia,

pulmonary edema were leading cause of death in end-stage renal disease (ESRD) patients (each of 28.6%) (Table V).

**Table I. Distribution of patients by demographic characteristics (n = 50)**

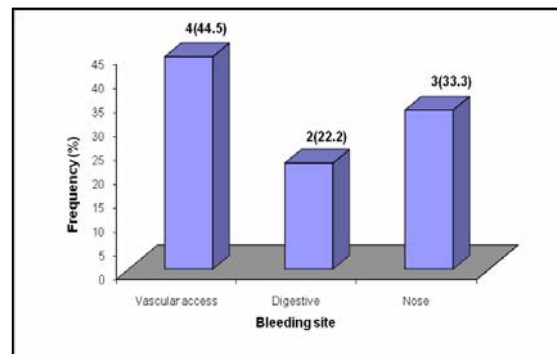
Demographic variables	Frequency	Percentage
<b>Age (years)</b>		
< 30	12	24.0
30 – 50	18	36.0
> 50	20	40.0
<b>Sex</b>		
Male	34	68.0
Female	16	32.0

\* Mean age = (45.5 ± 16.8) years; range = (17 – 82) years.

**Table II. Distribution of patients by acute complications (n = 50)**

Acute complications	Frequency	Percentage
Hypotension	33	66.0
Muscular cramps	31	62.0
Hypertensive crisis	14	28.0
Pruritus	34	68.0
Fever	17	34.0
Bleeding	09	18.0
Headache	22	44.0
Vomiting	16	32.0
Lumber pain	08	16.0
Palpitations	08	16.0
Disequilibrium syndrome	11	22.0
Dyspnea	18	36.0
Chest pain	14	28.0
Syncope	10	20.0
Abdominal problem	16	32.0
Neurologic problem	22	44.0
Electrolyte disorders	23	46.0
Articular & musculoskeletal problems	17	34.0
Cramps	24	48.0
Nausea	28	56.0
Vomiting	26	52.0
Convulsions	19	38.0
Loss of consciousness	10	20.0

# Total will not correspondents to 100% because of multiple responses



**Fig. 1: Distribution of patients by bleeding site (n = 9)**

**Table III. Comparison of acute complications in duration of dialysis, vascular access and time of dialysis**

Acute complications	Duration in dialysis (sessions)			Vascular access			Time of dialysis		
	=5 (n=14)	>5 (n=36)	P	AVF (n=38)	Catheter (n=12)	P	Day (n=22)	Night (n=28)	P
Hypotension	9(64.3)	24(66.7)	0.873	26(68.4)	7(58.3)	0.520	13(59.1)	20(71.4)	0.361
Muscular cramps	11(78.6)	20(55.6)	0.132	23(60.5)	8(66.7)	0.702	11(50.0)	20(71.4)	0.121
Hypertensive crisis	6(42.9)	8(22.2)	0.145	10(26.3)	4(33.3)	0.637	7(31.8)	7(25.0)	0.594
Pruritus	12(85.7)	22(61.1)	0.094	23(60.5)	11(91.7)	0.044	15(68.2)	19(68.9)	0.981
Fever	8(57.1)	9(25.0)	0.031	7(18.4)	10(83.3)	<0.001	8(36.4)	9(32.1)	0.754
Bleeding	7(50.0)	2(5.6)	<0.001	5(13.2)	4(33.3)	0.113	7(31.8)	2(7.1)	0.024
Headache	11(78.6)	11(30.6)	0.002	15(39.5)	7(58.3)	0.251	9(40.9)	13(46.4)	0.696
Vomiting	7(50.0)	9(25.0)	0.089	11(28.9)	5(41.7)	0.410	7(31.8)	9(32.1)	0.981
Lumber pain	5(35.7)	3(8.3)	0.018	4(10.5)	4(33.3)	0.060	3(13.6)	5(17.9)	0.686
Palpitations	4(28.6)	4(11.1)	0.131	5(13.2)	3(25.0)	0.329	1(4.5)	7(25.0)	0.050
Disequilibrium syndrome	6(42.9)	5(13.9)	0.026	7(18.4)	4(33.3)	0.277	4(18.2)	7(25.0)	0.563
Dyspnea	7(50.0)	11(30.6)	0.198	12(31.6)	6(50.0)	0.246	10(45.5)	8(28.6)	0.217
Chest pain	5(35.7)	9(25.0)	0.449	10(26.3)	4(33.3)	0.637	7(31.8)	7(25.0)	0.594
Syncope	2(14.3)	8(22.2)	0.529	8(21.1)	2(16.7)	0.741	5(22.7)	5(17.9)	0.669
Abdominal problem	4(28.6)	12(33.3)	0.746	12(31.6)	4(33.3)	0.910	7(31.8)	9(32.1)	0.981
Neurologic problem	8(57.1)	14(38.9)	0.243	16(42.1)	6(50.0)	0.631	9(40.9)	13(46.4)	0.696
Electrolyte disorders	8(57.1)	15(41.7)	0.324	18(47.4)	5(41.7)	0.730	7(31.8)	16(57.1)	0.075
Articular & musculoskeletal problems	5(35.7)	12(33.3)	0.873	14(36.8)	3(25.0)	0.450	6(27.3)	11(39.3)	0.373
Cramps	6(42.9)	18(50.0)	0.650	19(50.0)	5(41.7)	0.614	9(40.9)	15(53.6)	0.374
Nausea	9(64.3)	19(52.8)	0.462	19(50.0)	9(75.0)	0.128	13(59.1)	15(53.6)	0.696
Vomiting	10(71.4)	16(44.4)	0.086	17(44.7)	9(75.0)	0.067	11(50.0)	15(53.6)	0.802
Convulsions	7(50.0)	12(33.3)	0.276	13(34.2)	6(50.0)	0.326	9(40.9)	10(35.7)	0.707
Loss of consciousness	4(28.6)	6(16.7)	0.345	6(15.8)	4(33.3)	0.185	4(18.2)	6(21.4)	0.776

# Data were analysed using Chi-square ( $\chi^2$ ) test. Figures in the parentheses denoted corresponding percentage.

**Table IV. Profile of patients according to dialysis time when complication occurred**

Parameters	Dialysis		p-value
	Day time (n = 22)	Night time (n = 28)	
<b>Age (years)</b>			0.662
<30	4(18.2)	8(28.6)	
30 – 50	9(40.9)	9(32.1)	
>50	9(40.9)	11(39.3)	
<b>Gender</b>			0.981
Male	15(68.2)	19(67.9)	
Female	7(31.8)	9(32.1)	
<b>Diabetes</b>	7(31.8)	13(46.4)	0.295
<b>Vascular access</b>			0.852
AVF	17(77.3)	21(75.0)	
Catheter	5(22.7)	7(25.0)	
<b>Duration of dialysis</b>			0.919
=5	6(27.3)	8(28.6)	
>5	16(72.7)	20(71.4)	
<b>Ultrafiltration rate (mL/h)</b>			0.477
=1000	3(13.6)	6(21.4)	
>1000	19(86.4)	22(78.6)	

# Data were analysed using Chi-square ( $\chi^2$ ) Test.

Figures in the parentheses denoted corresponding percentage.

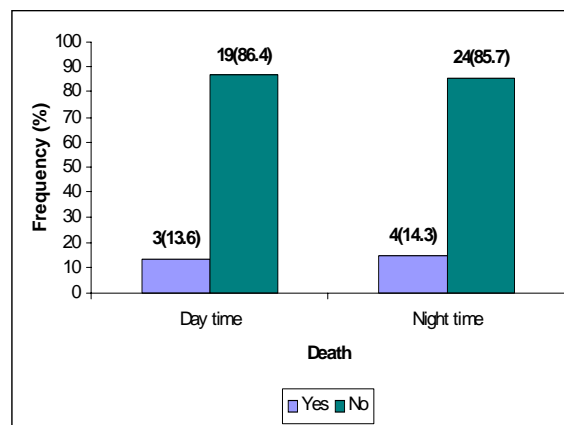
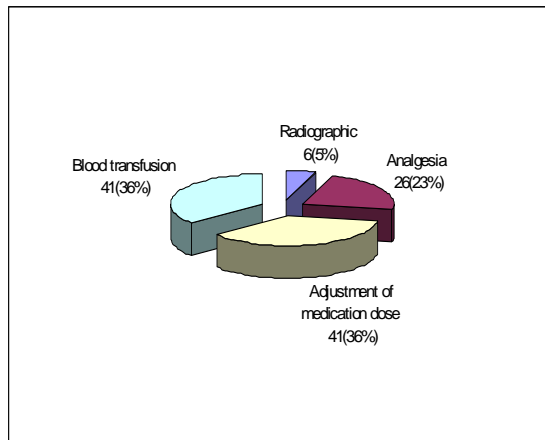


Fig. 3: Comparison of death between day time and night time

Table V. Distribution of patients by causes of death (n = 7)

Causes of death	Frequency	Percentage
Septicemia	02	28.6
Hyperkalemia	02	28.6
Acute MI	01	14.2
Pulmonary edema	02	28.6

## Discussion

There is a dearth of published literature on acute HD complications in ESRD patients in Bangladesh, particularly in those receiving fewer than recommended HD sessions per week. Acute complications were defined as any clinical manifestation linked to HD occurring during the dialysis session or within the first 24 hours after dialysis. Our study has revealed the high frequency of acute HD complications in ESRD patients on two weekly 4-hour HD sessions, some which were fatal. These complications, with profiles similar to those reported elsewhere<sup>18,19</sup>, were more likely to occur during nighttime dialysis when centers were particularly understaffed, and were determined by a combination of both patient-related and health service-related factors. Hypotension was the leading complications with reported frequency similar to those from the literature<sup>20</sup>.

It is favored by the feeding less than 2 hours before dialysis, the higher ultrafiltration rate more than 1000 mL/hour and diabetes. Feeding less than 2 hours or during dialysis leads to blood sequestration in splanchnic vein with reduce effective blood volume and can be linked to the reduction of systemic vascular resistance<sup>21</sup>. Meanwhile, higher ultrafiltration more than 1000 mL/hour generates hypovolemia, which should be normally compensated by refilling rate; the occurrence of hypotension is favored by the inadequately refilling in these patients. The plasma refilling rate often increases in correlation with the ultrafiltration rate, depending on the hydration status to counteract intravascular volume depletion<sup>22</sup>.

A large number of diabetic patients suffer from autonomic neuropathy, which is the main factor for the occurrence of hypotension in HD through impaired blood pressure regulation<sup>23</sup>. The prevalence of hypotension remained high in our study despite the systematic use of cold dialysate, which has been shown to be effective and safer<sup>24</sup>. Muscles cramps were the most frequent complication recorded in the study. They were significantly associated with the longer duration in dialysis, the presence of diabetes, the higher ultrafiltration rate, and the dialysis with arteriovenous fistulae(AVF). The association with longer duration in dialysis could be explained by the improved appetite as uremia state is relieved by dialysis and the inadequate dry weight while with diabetes, it can be related to the higher prevalence of peripheral neuropathy in such patients. The higher ultrafiltration rate to compensate interdialytic weight gain caused by less frequent and shorter dialysis is another factor for the occurrence of muscle cramps<sup>25</sup>.

Catheter access in the study settings is used primarily for emergency dialysis in patients referred late as

previously described<sup>26</sup>. These catheters are foreign body in immunodepressed uremic patients and constitute a source of infections. Those emergency dialyses are also likely to be conducted during nighttime when the centers are understaffed and received only minimal and distance supervision. Disequilibrium syndrome is one of the major and potentially fatal complications at the initiation of dialysis<sup>29</sup>. It is favored by the severe uremic state, which can be illustrated in our setting by emergency dialysis with catheter and can lead to death as also observed. The present study has some limitations. We were unable to monitor the biological parameters of the patients and accordingly were unable to account for derangements in those parameters that could explain some of the observed complications. The current report is also based on repeated observations from the same participants, which means some of the high frequency of complications may actually be due to the same group of participants who repeatedly developed the same complications during subsequent dialysis sessions. For this reason, we did not derived coefficients for potential determinants, which would have required accounting for this clustering. This however is unlikely to affect the major conclusions from this study as well as any ensuing recommendations.

## Conclusion

In conclusion, this study has revealed the rather high frequency and diversity of acute complications of HD in patients undergoing chronic RRT in our settings. These complications are a consequence of essentially controllable patient-level and health service-related factors; the essential being that they tend to occur during nighttime under-resourced dialysis sessions. The present study however outlines the fact that complications do occur during hemodialysis but they are not very common in our patients and many of them are not of a severe nature. So we can conclude that hemodialysis with all its advancements is a safe and tolerable procedure in the management of ESRD patients.

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