Late initiation of dialysis in diabetic Egyptian patients
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Introduction
The number of chronic kidney disease (CKD) patients has been increasing over the past two decades, both globally and in Egypt. In our current study we tried to identify the pattern of end-stage renal patients [chronic kidney disease stage 5 (CKD5)], who presented at a tertiary referral center (Cairo University Hospital, Kasr-Alainy School of Medicine), to identify the epidemiological characteristics, clinical presentation, hospital course, and outcome.

Patients and methods
This is a prospective analysis of all medical admissions through the emergency department (Department 6) of Kasr-Alainy School of Medicine, Cairo University, in 1 year from July 2010 to July 2011. We included patients with proven CKD 5 who needed to be started on renal replacement therapy.

Results
A total of 571 patients were identified, of whom 82 patients (36 males and 46 females) proved to have CKD5 and needed to be started on renal replacement therapy. The mean age of the included patients was 51.63 ± 14.7 years. Oliguria and vomiting were the most frequent symptoms, as seen in 52 cases (63.4%), followed by symptoms of volume overload in 24 patients (29.3%) and disturbed level of consciousness and fever in six patients (7.3%). Diabetic nephropathy was the most common cause of renal failure in our studied cohort (51.2%), followed by hypertension (22%); the cause was unknown in 25% of patients. Four patients (4.9%) died during their hospital stay.

Conclusion
In conclusion, our study showed that there is delayed referral for nephrology care and delayed initiation of dialysis when patients presented through the emergency department. Of particular interest was the fact that diabetic patients were most often subjected to this practice.

Keywords:
diabetic nephropathy, late referral, outcome

Introduction

Chronic renal failure is a devastating medical, social, and economic problem for patients and their families. The number of chronic kidney disease (CKD) patients has been increasing over the past two decades, both globally and in Egypt [1–4]. Delayed diagnosis and failure of institutions to initiate measures to slow down the progression of renal failure has resulted in a predominantly younger CKD population. Late referral of patients with CKD to nephrologists is a major public health problem [5].

Diabetes mellitus is the most frequent cause of chronic kidney failure in both developed and developing countries [6]. Careful monitoring of diabetic patients with CKD and timely planned initiation of renal replacement therapy (RRT) are of utmost importance, as delayed initiation of dialysis is associated with excess mortality, morbidity, and cost [7–9].

In our current study we tried to identify the pattern of end-stage renal patients (CKD5), who presented to a tertiary referral center (Cairo University Hospital, Kasr-Alainy School of Medicine), to identify the epidemiological characteristics, clinical presentation, hospital course, and outcome.

Patients and methods

This is a prospective analysis of all medical admissions to one medical unit (Department 6) at Kasr-Alainy School of Medicine; Cairo University, through the emergency department in 1 year from July 2010 to July 2011. We evaluated all patients admitted to Department 6 through the emergency department every Thursday from 8 p.m. to 8 a.m.

The total number of patients admitted to this unit through the emergency room during the study period was 571. We included patients with proven end-stage renal disease (CKD5) for whom RRT had to be initiated.

The evaluation of patients included:

(1) Demographic data (name, age, sex, special habits of medical importance).

(2) History, physical examination, and previous relevant investigations.
(3) Etiology of renal disease, previous nephrology care and targets achieved, and any intervention needed during hospital stay.
(4) Comorbid conditions like diabetes mellitus, hypertension, cardiovascular diseases, liver diseases, lung diseases, neoplasm, and vascular diseases.
(5) Type of dialysis needed, access-related problems, complications during dialysis, duration of hospitalization, and cause of death if any.
(6) Laboratory investigations on admission, including blood urea and serum creatinine, estimated glomerular filtration rates, serum electrolyte estimation, Ca^{++}, PO_4^+, uric acid, albumin, blood gases, and complete blood picture.
(7) Fundus examination, ECG, plain chest radiography, abdominal ultrasound.

Results

A total of 82 patients were identified and recruited into our study, of whom 36 were male and 46 were female.

The mean age of the included patients was 51.63 ± 14.7 years (16–87 years) and age distribution Table 1 comorbid conditions, etiology of renal disease, laboratory and ultrasonography findings are shown in Tables 2–5.

Clinical presentation

Oliguria and vomiting were the most frequent symptoms, seen in 52 patients (63.4%), followed by symptoms of volume overload in 24 patients (29.3%) and disturbed level of consciousness and fever in six patients (7.3%) (Table 2).

Hospital stay

The average duration of hospital stay was 6.3 ± 1.5 days (2–12 days) (Tables 3–5).

Dialysis modalities

Hospital intermittent hemodialysis (HDX) modality was the most frequent dialysis modality used (81 patients, 98.8%). Only one patient underwent acute peritoneal dialysis. Sustained low-efficiency dialysis (SLED) and continous renal replacement therapy (CRRT) were not employed in our studied cohort.

The total number of HDX sessions performed during the study period was 322, with an average of 3.98 ± 0.91 (range, 1–6) sessions per patient.

Table 1 Age distribution of patients

Age group (years)	Male [number of cases (%)]	Female [number of cases (%)]
16–29	2 (5.6)	5 (10.9)
30–49	16 (44.4)	9 (19.6)
50–65	14 (38.9)	24 (52.2)
66–87	4 (11.1)	8 (17.4)
Total	36 (44)	46 (56)

Table 2 Comorbid condition

Comorbid condition	Number of cases (%)
HTN	18 (22)
DM	11 (13.4)
DM and HTN	31 (37.8)
Analgesic abuse	8 (9.8)
Ischemic heart disease	6 (7.3)
Vascular diseases[a]	8 (9.8)
Hepatitis C virus infection	8 (9.8)
Neoplasm	3 (3.7)

DM, diabetes mellitus; HTN, hypertension; [a]Previous cerebrovascular accident and peripheral vascular disease.

Table 3 Etiology of CKD patients

Causes	Number of cases (%)
Diabetic nephropathy[a]	42 (51.2)
Unknown etiology	21 (25.6)
Hypertension	18 (22)
Polycystic kidney disease	1 (1.2)

CKD, chronic kidney disease; [a]Fundus examination was performed and confirmed diabetic retinopathy changes.

Table 4 Laboratory parameters of patients

Laboratory parameters	Mean values	Range values
Serum creatinine (mg/dl)	13.8 ± 4.8	5.4–28.3
Blood urea level (mg/dl)	253.5 ± 73.9	84–466
Serum Na^+ (mEq/l)	133.8 ± 6.9	110–147
Serum K^+ (mEq/l)	5.1 ± 0.98	3–7.3
Hemoglobin level (g/dl)	8 ± 1.7	4.5–11.4
TLC level/mm^3	9.7 ± 5.2	2.8–26.4
Platelet level/mm^3	261.8 ± 86.1	110–480
pH	7.19 ± 0.12	6.9–7.47
HCO_3 level (mmol/l)	9.6 ± 4.04	2.6–24
Serum calcium (mg/dl)	6.51 ± 1.01	5–9
Serum phosphorus (mg/dl)	6 ± 2	2–10
Serum uric acid (mg/dl)	6.84 ± 2.67	2.5–14
Serum albumin (g/dl)	3.28 ± 0.46	2–4

Table 5 Abdominal ultrasound findings

Abdominal ultrasound findings	Number of cases (%)
Liver cirrhosis without focal lesions, splenomegaly	6 (7.3)
Bilateral small-sized kidney with no evidence of obstruction	81 (98.8)
Bilateral polycystic kidney disease	1 (1.2)

As regards dialysis access, the right internal jugular vein was the most frequent path of access, as it was used

in 50 patients (61.7%), followed by the left internal jugular vein (16 patients, 19.8%) and the arteriovenous fistula (15 patients, 18.5%).

The incidence of hemodialysis complications: 18.7% (Table 6).

Transfusion of blood products
The total number of units of packed red blood cells transfused to the patients was 147; the average number of units per patient was 2.53 ± 1.08 (1–5 U).

Previous nephrology care
Only 15 patients (18.7%) had undergone previous nephrology care (Table 7).

Mortality
Four patients (4.9%) suffered a sudden cardiac arrest during their hospital stay, of whom three (75%) were female and one (25%) was male. Their average age was 52.5 ± 7.5 years (43–59 years). Two patients (50%) arrested during sessions of HDX. One patient (25%) had septicemia (leading to septic shock with hemodynamic instability) and one patient (25%) suffered a massive cerebral hemorrhage.

Discussion
CKD is a growing problem [10]. The timing of nephrology referral in the predialysis stage of CKD is increasingly being considered as an important variable related to prognosis [11]. The definition of 'late' is somewhat arbitrary and varies in the literature, ranging from less than 1 month to 1 year before kidney

Table 6 Complications during hemodialysis therapy

The complications during HDX sessions	Number of cases (%)
Infected central line	4 (4.9)
Cramps	6 (7.4)
Hypotension	4 (4.9)
Palpitation	2 (2.5)
Infected arteriovenous fistula (abscess formation)	1 (1.2)
Convulsions	1 (1.2)

HDX, hemodialysis.

Table 7 Prior nephrology care

Duration	Number of cases (%)
Less than 6 months	3 (3.6)
6–12 months	2 (2.4)
13–36 months	5 (6)
37–60 months	2 (2.4)
More than 60 months	3 (3.6)

replacement [12]. One argument in favor of early evaluation is that the management of chronic renal insufficiency and its complications could be improved. Early evaluation might lead to improved patient education about dialysis, provide more time for an informed decision about the type of dialysis, and permit timely placement of permanent vascular access [13].

Results showed that 90% of included patients were under the age of 65 years; 45% of male patients were under 50 years; of the elderly patients above 65, 11% were male and 17% were female; the mean age of the patients was 51.63 ± 14.7 years. This pattern of age distribution drew our attention to the fact that CKD is mostly prevalent in the younger population, affecting their productive life. In a Jordanian study the mean age of dialysis patients was 49.1 years, which is comparable to our results [14]. This finding contrasts with the western industrialized countries where there is a growing elderly population. The average age of the patients undergoing dialysis in the USA has been steadily increasing over the last several decades. In 2000, the average age was ~62 years [15]. Another study from Switzerland, spanning 40 years, observed an increase in age of initiation of dialysis from 48 years in the 1970s to 64 years between 1999 and 2008 [16].

Our results showed that patients presented with frank classical uremic symptoms: vomiting (63.4%), volume overload (29.3%), and even uremic encephalopathy (7.3%). This constellation of clinical presentations reflects deficient nephrological care before reaching the point of needing RRT. The laboratory data also reflected delayed referral and poor prior follow-up and control of metabolic conditions (mean serum creatinine 13.8 mg, mean valves of hemoglobin 8 g, Ca 6.5 mg, P 6 mg). Only 15 patients (18.7%) had received prior nephrology care more than 6 months before presentation, but despite that their renal disease was poorly controlled.

One reason behind this may be the reluctance of physicians to inform patients of the severity of their disease, as CKD is progressive and physicians are aware that patients will eventually reach the point where they require RRT. Moreover, patients themselves resort to herbal and nontraditional treatment regimens in an effort to control the symptoms, which leads to late presentation. Early referral to an experienced nephrologist who can handle the situation and gradually convince the patient is the only solution. Also, it is of utmost importance to construct special multidisciplinary clinics to follow-up CKD patients, including social, dietary, and psychiatric support. Public education about the causes, courses, and options of treatment will help to fix this problem.

The positive finding was a prior vascular access that had matured and was suitable for use in 15 patients (18.5%). In Germany 72% of incident dialysis patients who had arteriovenous access at time of start of dialysis, was 69% whereas in Japan, 26% and in Canada, 16% [17]. We still need more awareness among practicing nephrologists to plan for access creation when dialysis is expected within 6 months, as it reduces the cost, facilitates better blood flow, and leads to fewer complications.

HDX is still the preferred and prevalent method of RRT, especially in the acute setting. The rate of complications is 18%. The poor condition on presentation and delayed start mandate that patients remain hospitalized for 6 days and frequently require blood transfusion of 2 U or more.

Mortality rates among HDX patients exceed 20% per year [18], and a higher mortality rate within the first year after initiation of HD has been reported [19]. Identifying the period of highest risk for death after initiation of HD and factors that are associated with this higher risk are important for the care of patients who are new to HD (incident). In our study, the mortality rate during the short hospital stay was 4.9%. The rate is relatively low as compared with the published data, but might be explained by the short follow-up time and hospital stay of around 1 week. Unfortunately we do not have data on longer follow-up periods. Studies also have supported the importance of early nephrology referral in the predialysis period for reducing mortality after HD initiation [20,21]. Because these studies have typically included prevalent rather than incident patients, only limited information is available concerning mortality rates and factors that influence mortality immediately after HD initiation. Few studies have assessed mortality rates and mortality predictors in incident HD patients [22,23].

The percentage of diabetic nephropathy patients in our studied cohort represents the majority (51.2%). However, the published data from the Egyptian registry estimates the percentage to be around 12%. According to an extensive review made by Barsoum and Francis, [24] chronic glomerulonephritis and interstitial nephritis are currently the principal causes of CKD in developing countries, reflecting the high prevalence of bacterial, viral, and parasitic infections that affect the kidneys [25].

The explanation of this unexpected finding may be that patients with previous kidney disease – for example chronic glomerulonephritis and obstructive uropathy – are under direct nephrology care from the start and therefore get a better quality of care; further, should they require RRT, it is performed in an elective and carefully planned manner. In contrast, diabetic patients are usually under the care of a non-nephrologist (mostly general practioners, especially outside big cities) and they are more prone to delayed presentation.

The incidence of CKD with unknown cause was seen in 25% of patients. There are several studies worldwide on CKD prevalence and its prevention but very few studies have been conducted on CKD of unknown etiology (CKDu), which may be due to poor documentation [26]. According to Jha *et al.* [27], several countries including Malaysia, Italy, Austria, Argentina, and the UK report that about less than 30% of CKD cases are due to unknown reasons.

The WHO has declared hepatitis C a global health problem, with ~3% of the world's population (roughly 170–200 million people) infected with hepatitis C virus (HCV). Egypt has the largest burden of HCV infection in the world, with a 14.7% prevalence of chronic HCV infection among individuals aged 15–59 years [28]. Our results showed a slightly lower prevalence of HCV infection in our cohort of incident dialysis patients (10%).

The limitations of our study are its single-center design, limited number of patients, and short follow-up duration. Another limitation is that we mostly employed one modality of RRT (acute HDX) and did not study other modalities such as SLEED and CRRT. The Egyptian nephrology community, however, is in need of a large nationwide registry and epidemiological data on CKD patients.

Conclusion

Our study showed that there was delayed referral for nephrology care and delayed initiation of dialysis in patients presenting through the emergency department. It is noteworthy that diabetic patients were most subjected to this practice. This observation mandate that the key leaders of nephrology in collaboration with the Egyptian society of nephrology develop clear guidelines for CKD care at different stages and on when to refer for nephrology care. We, as nephrologists, should be considering more active, early nephrological management of diabetic patients with greater cooperation with diabetologists as part of the holistic management of this group of patients.

Acknowledgements

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