DISCUSSION

The term chronic kidney disease (CKD) refers to a condition of irreversible kidney damage that usually progresses to end-stage renal disease (ESRD), a life-threatening condition without proper renal replacement therapy.[9,13] Accordingly, children with CKD are at risk of increased morbidity, mortality, and decreased quality of life.[69]

Recent years have shown a tremendous increase in the amount of available data on CKD in children. However, most of the available information stem from ESRD registries, and information on the earlier stages of pediatric CKD is still limited. In fact, the early stages are often asymptomatic, or have non-specific symptoms; and therefore are under-diagnosed and under-reported worldwide. [9]

The magnitude of CKD varies from one geographical area to another due to genetic and environmental factors.[13] The incidence and prevalence of all stages of CKD in children are increasing worldwide. [9,21] The prevalence has been reported to be rising with a steady annual increase rate of 8%.[70]

In Egypt, as well as in most developing countries, the epidemiology of CKD in children is not known as there are no national data systems in place to collect, analyze and report disease information. In Alexandria, children with CKD are admitted to the Alexandria University Children's hospital (AUCH) as well as several other hospitals. The milder cases are treated in hospitals' outpatient clinics and private clinics; and frequently the diagnosis of CKD is not recognized. Severe cases from Alexandria and neighboring governorates are usually referred to the AUCH. Accordingly, admissions to the AUCH do not reflect the prevalence of CKD among children in Alexandria.

However, studying cases of CKD admitted to the AUCH is essential to help plan strategies for early diagnosis, retarding progression and improving management of children with CKD. Therefore, it was decided to study the earlier stages of CKD (stages II-IV) admitted to the AUCH. Stage V cases (on dialysis) are currently under study separately, and at present, there is no available information on stage I cases. In fact, until recently, all studies performed on childhood CKD excluded stage I (kidney damage for ≥3 months with normal or increased GFR), which may be incorrect.[71]

To our knowledge, the present study is the first in Egypt on pediatric CKD stages II-IV. There are no published studies in the international literature on CKD in Egyptian children. Moreover, a search of the data base of the Egyptian Universities Libraries (EUL) revealed no studies on CKD stages II-IV in children.

In the present study, data of children with CKD stages II-IV, who were admitted to the AUCH over a period of 10 years (2002-2011) were collected and analyzed. Stages of CKD were defined according to the K/DOQI guidelines, and based on the estimated GFR using Schwartz formula.[6] They were 65 children, a relatively small cohort with an average of 6.5 cases per year. In fact, many cases were not included in the study when the follow-up period was less than 3 months, or the information in the file was insufficient.

The number of children with CKD stages II – IV in the second 5 years of the present study (2007-2011) was more than double that in the first 5 years of the study (2002-2006)

(44 and 21 cases, respectively). This may be attributed to increasing awareness of CKD as well as the increasing incidence of CKD world-wide. [9,21]

A comparative analysis of the demographic features and etiology of our patients and of patients from some other countries is summarized in Tables 32 and 33. The disparity between the results of the studies from different countries could be attributed to differences in: (1) genetic factors (2) environmental factors (3) definition of CKD and its stages (4) determination of GFR (5) stages of CKD included in the study (usually stage V included) (6) age range of the patients (7) period of the study (8) whether the study was referral center-based (majority) or true population-based (9) etiologic classification of CKD, and (10) definition of cut off levels for some parameters such as short stature, malnutrition, hypertension and anemia.

Prior to the introduction of the NKF-K/DOQI classification system for CKD, [6] various definitions for CKD were used. For example the ItalKid project, a prospective population-based Italian study on CKD epidemiology, and the North American Pediatric Renal Transplant Cooperative Study (NAPRTCS), defined CKD as having a GFR of below 75mL/min/1.73m^2.[7,78] Others based their definition on serum creatinine levels or on other thresholds of GFR.[15,74,75]

In the present cohort, males (69%) were significantly more than females, with male: female ratio of 2.25:1. This is in conformity with the results of almost all studies on childhood CKD, which reported male gender predominance with frequencies ranging between 56% and 71%. Male predominance may be attributed, at least in part to the fact that congenital anomalies of the kidney and urinary tract (CAKUT), a main cause of CKD, occur with higher frequency in boys than in girls.[7,9,73] In addition, male predominance may be explained by the high frequency in some countries of nephrotic syndrome and hereditary nephropathies, which occur more in males.[16,18,79-81]

The mean age of the children at diagnosis of CKD in the present series was 5.7±3.9 years. More than half of the cases (57%) were 5 years old or less, and this was statistically significant. In Europe, the great majority of the cases are below 5 years, with a mean age at diagnosis of 3.9-6.9 years; as the majority of the cases are due to CAKUT and hereditary diseases.[7,9,73,76] On the contrary, in most developing countries, the majority (56%-87%) of the patients are 5 years and above.[18,19,76,80-82] In Nigeria, 54% of the patients were over 10 years of age reflecting the frequency of infection-related nephropathy and possibly late diagnosis as well.[83]

The great majority of the cases at presentation were in stages III and IV (46.2% & 41.5% respectively), and a minority (12.3%) were in stage II. This reflects late diagnosis in our cases. It has been stated that in the absence of screening programs, children with CKD stages I & II and often stage III may not receive medical attention.[84]

The distribution of patients in the different stages of CKD at diagnosis varies in the different published studies. In a study from Iraq,[85] 50% of the cases were in stages II & III and 50% in stages IV & V. In a study from Turkey,[76] 38% of the cases were in stages II & III and 62% in stages IV & V. In a report from South Africa,[80] 62% of the cases were in stages II & III and 38% in stages IV & V. In a cross-sectional study in a single center in Canada, [86] 86% of the cases were in stages I & II and 4% in stages IV and V. Two recent

studies from Nigeria, [19,83] reported that 68% and 46% of the cases respectively, were in stages I & II and 21 and 45% of the cases, respectively, were in stages IV & V.

The children in stage II were significantly older than those in stages III & IV (9.3±3.65 years, 5.8±3.93 years and 4.4±3.22 years, respectively). This may be attributed to the relatively late diagnosis of the milder cases of CKD, and the fact that the severer cases e.g., CAKUT present early.

Identifying the important causes of CKD in our country is essential as it may guide planning strategies for prevention and early detection of CKD. Congenital anomalies of the kidney and urinary tract were the most frequent cause of CKD in the present study (responsible for 47.7% of the cases). Glomerulopathies, hereditary nephropathies and other renal/urologic diseases were the causes of CKD in similar percentages of patients (12.3-13.8%). The etiology in a minority of the cases was either multisystemic diseases or unknown (7.7% and 6.2% respectively).

The great majority of the cases were from Beheira (50.7%) and Alexandria (46.2%) governorates, and a minority (3.1%) from Kafr-El-Sheikh. This pattern parallels the general pattern of admissions in the AUCH. The great majority of the cases (91%) had no family history of renal disease. This is not against the presence of hereditary causes of CKD in the present series.

It has been reported that CAKUT and hereditary nephropathies, are responsible for about two thirds of all cases of CKD in developed countries, while acquired causes predominate in most developing countries.[9] In a report of the NAPRTCS, [77] congenital causes including CAKUT (48%) and hereditary nephropathies (10%) were the most common, and glomerulonephritis accounted for 14% of the cases. A fairly similar distribution of causes has been reported in Europe by the Italian [7] and Belgian [72] registries. However the proportions of CAKUT (58-59%) and hereditary nephropathies (15-19%) were slightly higher, while the proportions of glomerulonephritis were lower (5-7%) than in the NAPRTCS data base, possibly because of the difference in racial distribution. [7,72]

Table (32): The demographic features in the present study compared to the epidemiology of CKD stages II-V in Europe [9]

Country [reference]	Alexandria*	Italy [7]	Belgium [72]	Spain [73]	Sweden [74]	France [75]	Turkey [76]
Period	2002-2011	1990-2000	2001-2005	2007-2008	1986-1994	1975-1990	2005
Number of cases	65	1,197	143	605	118	127	282
Inclusion criteria	0-14 years GFR≤ 60	0-19years GFR< 75	0-19years CKD 3-5	0-17years CKD 2-5	0.5-15years GFR<30 or SCr>120 (<3years),>150 (3-9 years) >180(>10years)	0-15years SCr>133(<2 years) or 175 (> 2 years)	0-18years GFR <75
Pediatric population covered (millions)		16.8	2.4	11.3	1.7	0.5 (Lorraine)	24.0
Incidence (pmarp)		12.1	11.9	8.7	7.7	10.5	11.9
Prevalence (pmarp)		74.7	56	71.1	59	66	
Male/ female ratio	2.25	2.0	1.3	1.9	1.6	1.4	1.3
Age at diagnosis (years)	5.7 (mean)	6.9 (mean)	3.0 (median)	3.9 (mean)	3.3 and 11.3 in congenital and acquired disorders (median)	6.3 and 10.6 in congenital and acquired disorders (median)	8.0 (mean)
GFR or CKD stages at diagnosis	CKD II :12% CKD III :46% CKD IV :42%	GFR42 (mean)	CKD 3:67% CKD 4: 19% CKD 5: 14%	GFR52(mean) CKD2-3:82% CKD4-5: 18%	Pre-RRT:57%	Pre-RRT: 76%	CKD2-3: 38% CKD 4 :30% CKD 5: 32%

* Present study; CKD: Chronic kidney disease; RTT: Renal replacement therapy; GFR: Glomerular filtration rate (mL/min/1.73 m^2); SCr: Serum creatinine (µmol/L)

Table (33): Comparison between the causes of CKD in the present study and those in some other studies [9]

	Causes of CKD			
Study (reference)	**Alexandria***	**NAPRTCS [77]**	**Italian Registry[7]**	**Belgian Registry[72]**
Population		CKD (GFR<75)	CKD (GFR<60)	CKD (GFR<60)
Age range (years)	0-14	0-20	0-19	0-19
Patients	Incident	Registered 1994-2007	Incident 1990-2000	Incident 2001-2005
Number of cases	65	7,037	1,197	143
Etiology				
CAKUT	31 (48%)	3,361 (48%)	689 (58%)	84 (59%)
Hypodysplasia ± reflux nephropathy		1.907	516	66
Obstructive uropathy		1,454	173	18
Glomeulonephritis	12 (18%)	993 (14%)	55 (5%)	10 (7%)
HUS	2 (3%)	141 (2%)	43 (4%)	9 (6%)
Herediatary nephropathy	8 (12%)	717 (10%)	186 (15%)	27(19%)
Congenital NS		75	13	5
Metabolic disease	2 (3%)			5
Cystinosis		104	22	2
Cystic kidney disease		368 (5%)	101 (8%)	13(9%)
Ischemic renal failure		158 (2%)	49 (4%)	3 (2%)
Miscellaneous	6 (9%)	1,485 (21%)	122 (10%)	10 (7%)
Missing/unknown	4 (6%)	182 (3%)	40 (3%)	

* Present study; CKD: Chronic kidney disease; GFR: Glomerular filtration rate (mL/min/1.73m^2); CAKUT:Congenital anomalies of the kidney and urinary tract; HUS: Hemolytic-uremic syndrome; NS: Nephrotic syndrome; NAPRTCS: North American Pediatric Renal Trials and Collaborative Studies.

In countries in the Middle East, CAKUT is the leading cause of CKD (47-62%) with a clear predominance of uropathies over hypodysplasia, followed by hereditary nephropathies. [15,16,71,76,90,91] The higher proportion of genetic diseases found in the Middle East than in Europe, was explained by a higher prevalence of consanguineous marriages.[9]

Chronic glomerulonephritis is the main reported cause of CKD in various studies from India,[87] South East Asia, [17,18,82] Latin America, [88] Caribbean area, [89] and Sub-Saharan Africa, [80,81,83,90] with a percentage ranging from 30% to almost 64%. Such high proportions of glomerulonephritis may be related to high prevalence of bacterial, viral and parasitic infections that commonly affect the kidneys in these developing countries.[9]

In the present study, although CAKUT, hereditary nephropathies, and multisystemic diseases, were more frequent in children 5 years old or less, there were no significant differences in age distribution (up to 5 years and above 5 years of age) within the different etiologic groups of CKD. This may be due to the small numbers of patients. In the NAPRTCS report, the distribution of causes varied with age, whereas CAKUT predominated in younger patients, glomerulonephritis was the leading cause in children older than 12 years of age.[77]

In accord with the fact that CAKUT occur with higher frequency in males,[7,93] the present study showed that within the group of CAKUT males were 4 times more than females, however statistically the difference was insignificant and this is difficult to

explain. Within the group of glomerulopathies, females were more than the males (double), but the difference was statistically insignificant; and this is again difficult to explain except by the small number of patients.

Among our stage II patients, glomerulopathy was the most frequent etiology. This is probably because the diagnosis of glomerulopathy is usually evident and hence not delayed. The frequencies of various etiologies among patients in stages III and IV were not statistically different.

The mean weight and height (or length) standard deviation scores of our cases of CKD were within the normal range. Nevertheless, more than 1/3 (36.9%) of the studied patients were short and nearly 1/5 (18.5%) of them were underweight. The proportions of underweight and short stature were least among stage II patients. However, there were no statistically significant differences in the proportions of underweight and short stature between the 3 stages of CKD studied, apparently because of the small numbers of patients compared.

The frequency of growth retardation varies in studies from different countries. In a study from Canada, [86] growth failure (height Z-score < -2 SD) occurred in 11.5% of children with CKD stages I-V and the frequency increased with worsening stage of CKD (5.3% in stage I to 13.3% in stages IV & V). In a study from Spain on children with CKD stages II-V predialysis, 25% of the patients had a height Z-score of ≤ -1.88 and growth deficit was directly related to the disease stage. [73] In contrast, in USA, 36% of children with CKD had short stature, [77] and in Turkey 49.6% of children with CKD stages II-V had growth retardation. [76]

The prevalence of protein-energy malnutrition among children with CKD varies between 6% and 65% in the different studies. [73,94] In Spain, 7% of children with CKD stages II-V were malnourished (Body Mass Index Z-score ≤ -1.88). Children under 2 years of age were those of poorer growth and most malnourished. [73] In a study from Nigeria, [19] on children with CKD, the frequency of protein-energy malnutrition increased from 32.4% in stage I to 50% and 40.4% in stages IV and V, respectively.

Apart from short stature and underweight, the most frequent clinical manifestations in the present cohort, were pallor (67.7%), fever (33.8%) (due to urinary or other infections), edema (27.7%) and hypertension (21.5%). Oliguria and polyuria were infrequently complained of (9.2% & 7.7%, respectively).

The differences in the frequency of the various clinical findings among the 3 stages of CKD studied were statistically insignificantl. However, the frequency of pallor increased almost significantly from stage II to stage IV.

In a Nigerian study, edema (85%), hypertension (51%), and oliguria (37%) were the most frequent clinical features, as the most common etiology of CKD there was glomerular diseases. [83] In childhood CKD, the prevalence of hypertension may range between 20% and 80% depending on the degree of renal dysfunction and underlying renal disease. [24] In a Canadian study, it was noted that hypertension was common even in stage I CKD (63%).[86] In contrast in a study on CKD stages III-V in Belgian children, hypertension was found in only 14% of the cases, and this was attributed to the fact that 2/3 of their cases

were in stage III.[72] Also, in a population-based survey in Turkey on children aged 5-18 years with CKD stages III-V, the prevalence of hypertension was 6.1%.[20]

Proteinuria (40%), pyuria (26.2%) and hematuria (15.4%) were the most frequent urinary findings in the present study. Among the 17 cases with pyuria, the results of urine culture were found in only 8 files and were positive in 6 cases. Colony count was done in only 2 cases and was $>10^5$/mL in both. Pyuria was found mostly in association with CAKUT. The differences in the frequency of the various urinary findings among the 3 stages of CKD were not statistically significant.

In a study from Canada, the overall prevalence of proteinuria (defined as >1g/day) was 11.5% and ranged between 5.8% in stage I and 40% in stages IV & V. [86] The investigators pointed out that the finding that proteinuria does increase with worsening stage of CKD despite a decline in the prevalence of glomerular disease is consistent with other studies which suggest that proteinuria is related to the severity of kidney disease. [95]

The mean hemoglobin level in the present series (8.9 ± 1.33 g/dL) was low, and was significantly lower in stage IV than in stages II & III. Anemia was found in > 2/3 (70.8%) of the cases. Although the frequency of anemia increased from stage II to stage IV, yet the differences were not statistically significant. This may be attributed to the small numbers of the patients.

In a Canadian study, [86] the overall prevalence of anemia (hemoglobin < 12 g /dL) was 36.6% (increased from 31% in CKD stage I to 93.3% in stages IV & V). In the CKD in children (CKiD) prospective cohort study in USA, anemia was found in 21% of cases in stage II, 39% of cases in stage III and 73% of cases in stage IV.[96] An overall prevalence of anemia among children with CKD of 58.4% was reported in a study from Nigeria,[19] (increased from 41.4% in stage I to 100% in stage IV and 97% in stage V).

The mean blood pH (7.33 ± 0.08) and bicarbonate (19.6 ± 5.28 mEq/L) in our study were low. One third (33.8%) of the cases had metabolic acidosis. Metabolic acidosis was significantly more frequent in stage IV than in stage III (51.9% and 26.7%, respectively), and was absent in stage II. In a Canadian study,[86] metabolic acidosis was found in 4.4% of the cases (increasing from 1% in stage I to 54.6% in stages IV & V). Acidosis develops early in children with CKD due to obstructive or tubulointerstitial renal disease.[84]

The mean serum calcium in the present study (8.7 ± 1.01 mg/dL) was low, but the mean levels of serum phosphorus and alkaline phosphatase were within the normal range. One third (33.8%) of the cases had hypocalcemia, the frequency of hypocalcaemia increased significantly from stage II to stage IV. Hyperphosphatemia and elevated serum alkaline phosphatase were found in nearly 1/5 (18.5%) of the cases. The parathyroid hormone was not measured in any of the cases. Noteworthy, alkaline phosphatase shows good correlation with bone histology and is more readily available and cheaper than the parathyroid hormone measurement.[84]

In a study from Canada, metabolic bone disease requiring treatment was found in 16.9% of children with CKD, even in the early stages (6.3% in stage I, 15% in stage II, 29% in stage III and 100% in stages IV & V). The authors attributed the prevalence of bone disease in the early stages of CKD to somatic growth and phosphate wasting with

tubular disease. [86] In Belgium, oral alfacalcidol to suppress the parathyroid hormone was needed in 32% of the children with CKD, mostly in stages IV&V.[72]

The mean level of serum triglycerides was high (168.9 ± 120.58 mg/dL), but the mean level of serum cholesterol was within the normal range. Hypertriglyceridemia and hypercholesterolemia were found in 12.3% of our cases with no significant differences in frequency between the 3 stages of CKD. In the CKiD cohort study, 45% of the children had dyslipidemia (defined as triglycerides >130 mg/dL, HDL cholesterol < 40 mg/dL or non-HDL cholesterol > 160 mg /dL). [97]

All the children in the present study had normal serum sodium levels. Hyperkalemia was found in 10.8% of the cases, mostly in stage IV. Hypokalemia was encountered in only one case in stage II. In a Canadian cohort of childhood CKD, hyperkalemia was found in 1.6% of the cases (ranging from 0.5% in stage I to 18% in stages IV&V predialytic) and hyponatremia in 5.7% of the cases (raging from 3.4% in stage I to 13.3% in stages IV&V).[86] Of note, 57% of the patients in this Canadian cohort were in stage I.

Renal biopsy was done in 15 of our patients (23%). Nine of them (60%) had idiopathic glomerulopathies/glomerulonephritis, 3 (20%) had lupus glomerulonephritis, 2 (13.3%) had hemolytic-uremic syndrome, and one (6.7%) had chronic pyelonephritis.

In a study from South Africa,[80] on 126 children with CKD stages II-IV, the most frequent indications for renal biopsy were steroid-resistant nephrotic syndrome, HBV-or HIV-associated nephropathy, SLE, and unexplained CKD or hypertension. Focal segmental glomarlosclerosis was the most dominant histological form of nephrotic syndrome resulting in CKD. In one-third of biopsies for nephrotic syndrome, categorization was not possible because of global glomarlosclerosis or inadequate biopsy specimen.

With regard to imaging studies in the present series, ultrasonography for the urinary tract was done in all cases. More than half (58.5%) of the cases had bilateral increased renal parenchymal echogenicity, and one third (33.8%) had bilateral hydronephrosis. Voiding cystourethrogram was performed in nearly 2/3 (61.5%) of the cases and showed abnormalities in the majority (70%) of these cases. The abnormalities included urethral valves, neurogenic bladder and bilateral primary vesicouretral reflux.

Renal scintigraphy was done in 21.5% of the cases and CT scan of the abdomen and pelvis in 6.2% of the cases. Echocardiography was performed for murmurs in 5 cases (7.7%), 4 of them had associated acyanotic congenital heart disease. None of the cases had bone X-rays.

In the CKiD study, eccentric left ventricular hypertrophy (LVH), characteristically associated with volume overload and anemia was seen in 11% of the cases, while concentric LVH typically considered to result from hypertension was present in 6% of the children. The authors recommended the use of 24-hour ambulatory blood pressure monitoring and echocardiography to help determine cardiovascular risk and to guide blood pressure therapy in children with mild to moderate CKD. [98]

The treatment given to the patients in the present cohort was frequently incomplete. This could be mainly due to the cost of the drugs and/or incomplete assessment of the

patients. Alfacalcidol and calcium carbonate were given to about 2/3 of the patients (63% &67.7% respectively), the majority of them were in stages III & IV. However, 22.2% &18.5% of the patients in stage IV did not receive these two drugs respectively. Sodium bicarbonate was given to 1/3 of the patients (33.8%), more frequently in stage IV, yet 48.1% of the patients in the latter stage did not receive sodium bicarbonate.

Erythropoietin, an expensive hormone was given to 30% of the patients in stage III and 37% of those in stage IV, although anemia was found in 73.3% and 77.8% of the patients in these 2 stages, respectively. Other vitamins and iron were given to less than half of the cases (47.7% and 43%, respectively). Astonishingly, in a study from Spain on 605 children with CKD revealed that 33% of anemic patients received no treatment for anemia, while the rest received insufficient treatment.[73]

Antihypertensive drugs were needed in 20% of our cases. Steroids and cyclophosphamide were given to a minority (with glomerulopathies). Antibiotics were given to 1/3 of the cases (for urinary tract or other infections). Surgical intervention was carried out in 21.5% of the cases. Acute peritoneal dialysis was done to 36.9% of the cases on presentation. This was apparently to tide the patients over aggravated renal dysfunction caused by a reversible factor.

None of the cases received growth hormone, a very expensive hormone. In Canada, growth hormone was given to 20 % of patients with CKD stages IV & V.[86] There was no mention in the files of our patients of any dietary instructions or psychological support.

The mean duration of follow- up in the present study was 3.2 ± 2.5 years. Follow- up was irregular in nearly half (47.7%) of the cases. More than half (55.4%) of the cases showed deterioration of kidney function during follow- up, and 13.8% of them (9cases) required maintenance dialysis. The kidney function in the rest of the cases (44.6%) was stationary up to the last follow-up visit, but the actual fate of these cases was uncertain. Although the frequency of progression increased from stage II to stage IV, yet the differences were not statistically significant. This may be due to the small number of patients in each stage. Within the limitations of follow-up in the present series, there was no significant relation between the etiology and frequency of progression of CKD.

It has been noted that progression of CKD is variable and depends on the underlying disease, the severity of the initail injury, and the presence of additional risk factors. [9] In the ItalKid project the incidence of renal replacement therapy (in ESRD) was 7.3 per year per 100 patients with CKD, and the risk of ESRD was 68% by the age of 20 years.[7]

Data from the NAPRTCS on more than 4000 children with CKD stages II-IV showed a progression rate to ESRD of 17% at 1 year and 39% at 3 years following registration, with a median time to ESRD of 4.5 years. The rate of progression was inversely proportional to base-line GFR.[25] In a very recent study from Japan, 12.5% of 447 children with predialysis CKD (stages III – V) progressed to ESRD with a median follow-up of 1.49 years. Children with advanced CKD (stages IV&V) were particularly likely to progress. [99]

CONCLUSIONS

From the results of the present study on chronic kidney disease (CKD) in children, it could be concluded that:

1. There are deficiencies in the clinical and work-up data in some of the files.
2. Some important investigations were not done e.g., urine culture and colony count (in some of the patients), echocardiography (in most of the patients) and skeletal X-rays (in all of the patients).
3. The onset of CKD was in the first 5 years of life in the majority of the cases.
4. Congenital anomalies of the kidney and urinary tract were the commonest cause of CKD.
5. There was delay in the diagnosis of CKD.
6. Anemia, proteinuria, growth retardation, metabolic acidosis and hypocalcemia were the most common findings at presentation.
7. Treatment given to the patients was frequently incomplete, compared to the international (K/DOQI) guidelines.
8. Follow-up was irregular in nearly half of the patients.
9. CKD progressed in the majority of the patients followed-up.