

Effect of Demographic Data on the Outcome of Chronic Hemodialysis in Children, A Multicentric Study

- **Dr.AsmaaSalihKhudhur**, *Pediatric Nephrologist, Al-Karamaa teaching hospital*
Pediatric Nephrology Department, Baghdad, Iraq. Email: Asmaash77@yahoo.com

Corresponding Author:

Dr.AsmaaSalihKhudhur, *Pediatric Nephrologist, Al-Karamaa teaching hospital*
Pediatric Nephrology Department, Baghdad, Iraq. Email: Asmaash77@yahoo.com

Abstract

Background :The use of chronic dialysis to sustain the lives of children with end-stage renal disease(ESRD) has been available in developed countries for more than 30 years. During the past few decades , advances in technology have made long-term dialysis a viable treatment option for pediatric ESRD patients of all ages, from newborns to adolescents.While a successful kidney transplant remains the treatment of choice for all pediatric ESRD patients, almost three-fourths of these children require chronic dialysis while awaiting transplantation for periods ranging from a few months to several years . Pediatric dialysis carries a significantly higher mortality than that for the age – adjusted population.

Objectives:-To know the effect of demographic data on 4 years outcome of pediatric patients on chronic hemodialysis program.

Patients and Methods:-

A cross – sectional study of all chronic hemodialysis patients who started dialysis in pediatric age, in hemodialysis centers in Al Kharkh side of Baghdad city extended between the 1st of January of 2011 to 31th of December 2014. During which 94 patients were collected. Clinical and laboratory data were obtained from medical records and by direct interview with each patient by questionnaire.

The questionnaire include variables in the patients demographics data and factors that may influence outcome.

Causes of death was taken from the pediatric nephrologist of each center data was observed and analysis was carried out using spss-21.

Result:-During the period of the study, a total of 94 patients on chronic HD program were studied according to patients demographics data, where the age group ≤ 7 years were (26.6%) while these ≥ 14 years were (7.44%).

Male form (63.82%) while female (36.17%). (75.5%) of patients were from Baghdad city.

The cause of end stage renal disease was small size kidneys (15.95%), unknown causes (13.82%), urological problems (29.59%), SRNS were (11.70%), Cystinosis were (6.38%), recurrent renal stones (6.38%) and (19.14%) were due to other causes.

The sample studied according to the effects of these factors on the outcome of the patients on the chronic HD program. Were the primary cause of ESRD have a significant correlation with the patients outcome dead or alive. Overall survival rate was (51.1%).

Conclusions:- primary cause of ESRD were associated with a significant correlation with the patients outcome. No effect of age at start of hemodialysis, sex, on the outcome of the pediatric patients on chronic HD program enrolled in this study.

Key words:(Demographic data ,Outcome ,Hemodialysis in Children)

Aim of the study:To know the effect of demographic data on the outcome of chronic Hemodialysis in children.

Introduction

Long - term outcome of chronic dialysis in children

The use of chronic dialysis to sustain the lives of children with end-stage renal disease (ESRD) has been available in developed countries for more than 30 years. During the past few decades, advances in technology have made long-term dialysis a viable treatment option for pediatric ESRD patients of all ages, from newborns to adolescents. While a successful kidney transplant remains the treatment of choice for all pediatric ESRD patients, almost three-fourths of these children require chronic dialysis while awaiting transplantation for periods ranging from a few months to several years.

Pediatric dialysis carries a significantly higher mortality than that for the age – adjusted population.

Mortality in children on Dialysis

Survival data for paediatric patients on chronic dialysis from both national registries and single centre studies provide us with essential information. Data system (USRDS), a compulsory registration system which includes children ≤ 19 years; the North American pediatric renal trials and collaborative studies (NAPRTCS), which allows voluntary data reporting and includes children ≤ 21 years; the United Network for organ sharing (UNOS), which collects data on all patients registered for renal transplant in USA; the European renal Association – European Dialysis and transplant association (ERA-EDTA), a voluntary organization which coordinates a national European registry for all patients; the Australia and New Zealand dialysis and transplant association (ANZDATA), that is a comprehensive, compulsory database including children up to 20 years of age, and other national registries the United Kingdom renal registry, the National Dutch registry and the Italian registry.

Cardiopulmonary events and infection were cited as the most common causes of death by all registries, accounting for at 21% of deaths seen significantly more infections causing death in the youngest children(1).

Cardiovascular disease accounted for 57% of deaths in children on hemodialysis and 43% of those on peritoneal dialysis, compared to 30% in those with a functioning transplant, in whom malignancy was responsible for 14% of deaths(2).

Factors influencing outcome:-

Overall mortality in dialysis patients compared to normal and transplanted children:-

Pediatric dialysis carries a significantly higher mortality than that for the age-adjusted population.

Dialysis treatment was also associated with a mortality risk more than four times higher than for children who have been transplanted (3).

Era of Dialysis:-

The continued improvement in survival with time may be underestimated, as younger children and those with significant non-renal comorbidity are taken onto dialysis program.

Age at start of Dialysis:-

All registries report a significantly higher mortality in infants starting dialysis.

It must be kept in mind that treatment thresholds vary amongst different centers, making uniform comparisons of survival data difficult and reflection the varying opinions amongst nephrologists towards offering RRT to the very young or those with comorbidity (4).

Comorbidity:-

In recent years, patients with non-renal comorbidity such as multi system involvement from inherited disorders, prematurity or CKD following over whelming infection with multi-organ damage are increasingly offered RRT.

Both renal (i.e. oligoanuria) and non-renal comorbidities (e.g pulmonary hypoplasia, severe developmental delay) have been identified as significant risk factors for increased mortality in infants and young children (5,6).

The anuric infant is particularly difficult to manage, and anuria has been discussed as an important risk factor for survival . long – term dialysis outcome data from Great Ormand street hospital for children showed that 30 children of a cohort of 98 on chronic dialysis has significant non-renal comorbidity including neurodevelopmental delay, syndromes with multisystem involvement, congenital cardiac disease, malignancy and inherited metabolic disorders. Of the 17 deaths reported, 76% were in those with associated comorbidities, a 7.5 fold greater risk of death in this group (7). In a long – term follow-up study from Miami of 52 infants on dialysis, oligoanuria gave an odds ratio for death 41 times greater than that of infants with residual renal function.

Major comorbidities (e.g. pulmonary hypoplasia or central nervous system disease) were also associated with an increased odds ratio for mortality of 4.4 (8). Low birth weight (LBW) was not a significant risk factor in this group, although LBW has been identified by others as an independent risk factor for death in infants age < 9

months with severe CKD ($\text{GFR} < 20\text{ml/min/1.73m}^2$) or requiring dialysis in first 2 years of life (9). The effect of comorbidity on survival extends into adulthood as childhood survivors of dialysis with comorbidity have a significantly higher risk of death compared to those with only primary renal disease(3).

Primary Renal Disease

The 2006 USRDS report sites primary diagnosis as an independent determinant of mortality for paediatric patients on dialysis with glomerulonephritis and hereditary or congenital disease having a better 5-year survival than those with secondary glomerulonephritis or vasculitis.

Autosomal recessive polycystic kidney disease has an odds ratio of 20 for mortality compared with other diagnosis in infants, but this may be due to the oliguria and pulmonary hypoplasia associated with this diagnosis (8). Proteinuria secondary to focal segmental glomerulosclerosis requiring bilateral nephrectomies for effective management will increase mortality risk as children are rendered anuric.

Demographics

Two studies have suggested but are not conclusive that African – American infants have higher mortality rate. In a 2003 NAPRTCS study, African – American infants age 2-12 months at initiation of dialysis were three times more likely to die compared to Caucasian and Hispanic infants, although this significant difference was not observed if age at dialysis initiation was > 2 years (10). In a single centre long – term follow – up infant dialysis study, decreased survival of infants of African – American ethnicity compared to the predominantly Hispanic patients was also reported but was not felt to be due to the home or socioeconomic environment as the deaths occurred mainly in hospital with all patients receiving identical care (8).

Patients and Methods

A multicenteric descriptive, observational cross – sectional study of all chronic hemodialysis patients who started dialysis in pediatric age, in hemodialysis centers in AL kharkh side of Baghdad city extended between the 1st of January of 2011 to the 31th of December 2014. We collected 94 patients undergoing hemodialysis in 3 centers:-

- Al – karama teaching hospital center.
- Al – zohoor center in pediatric teaching hospital
- Al – Emamaen Al- khadhemean teaching hospital center

Clinical and laboratory data were obtained from medical records and from data collected from patients by direct interview with each patient during hemodialysis session and by questionnaire.

The causes of death was taken from the nephrologist of each center.

The patient population include all children younger than 20 years old who survived at least 90 days after starting hemodialysis.

Patient were excluded from the study if they underwent transplantation but returned to dialysis.

Cases whose medical records were not available were excluded.

Children with aprior kidney transplantation were excluded (preemptive transplanted patients were excluded). There is deficient in the three centers ranging from missing some information like basic or clinical data to miss whole medical record which was excluded from the study.

Patients demographics data included age, sex, residency, primary cause of ESRD and comorbidities obtained.

Data Statistical analysis

Statistical analysis was performed using spss – 21 (statistical packages for social sciences – version 21) and Microsoft office excel (Microsoft office Excel for windows; 2010). One way analysis of variance (ANOVA) and student t-test was used to assess significant difference among means in regards with duration. Proportions were compared by chi-square, $P < 0.05$ was considered statistically significant.

Results

During the period of study, a total number of 94 patients undergoing chronic hemodialysis were studied.

We study: the distribution of patients according to demographics data as shown in table (3.1).

According to age at start of hemodialysis, age group ≤ 7 years were (26.6 %), from 8-10 years were (30.85 %), from 11-13 years were (35.10), and those from 14 years till 20 years were (7.44 %). The mean age of our patient was (10.99) year ,and the mean age at start of hemodialysis was (9.60) year.%. With an age extreme between 3 years and 20 years.

According to gender, males forms (63.82%) of the sample, whereas females form (36.17%).

According to the residency, 71(75,55%) of our patients were from Baghdad, whereas the rest from different province in Iraq like Anbar, Dialla, Kutt, Salah El -deen and Diwania (24.46%).

According to the primary cause of ESKD, (15.95%) were due to small size kidneys, (13.82%) were due to unknown causes, (26.59%) were due to urologic problems, (11.70%) were due to SRNS (6.38%) were due to cystinosis (6.37%) were due to recurrent renal stones, (19.14%) were due to other causes like RTA, cystic disease &ARPKD, nephrocalcinosis, nephronophthies, HUS, primary Hyperoxaluria, Mitochondrial cytopathy, diabetic nephropathy andrenovascular dis.

According to co-morbidities (3.19%) have hypothyroidism, (2.12%) have epilepsy, (4.25%) have cerebral palsy, (8.51%) have other morbidities like (Down syndrome & enzymatic defects). (81.91%) were without co.morbidities.

Table (3.1): Distribution of patients according to demographics data:-

Variable	No.	%
Age at start of hemodialysis (yrs)		
≤ 7 years	25	26.59
8 – 10 years	29	36.85
11- 13 years	33	35.10
≥ 14 years	7	7.44
Overall	94	99.99
Gender		
Male	60	63.82
Female	34	36.17
Overall	94	
Residency (Province)		
Baghdad	71	75.53
Others	23	24.46

Overall	94	
Primary cause of ESRD		
1. Small size kidneys	15	15.95
2. Unknown cause	13	13.82
3. Urologic problems	25	26.59
4. SRNS	11	11.70
5. Cystinosis	6	6.38
6. Recurrent renal stones	6	6.38
7. Others	18	19.14
8. Overall	94	
Co – morbidities		
Hypothyroidis	3	3.19
Epilepsy	2	2.12
C.P	4	4.25
Others (syndromes + enzymetic defects)	8	8.51
Without	77	81.19
Overall	94	

Table (3.2) show the distribution of patients according to outcome.

48(51.1%) of our patients were alive, 34(70.8%) of them still on hemodialysis till the time of the end of the study, 2(4.1%) were stop hemodialysis(improved), and 12 (25%) were transplanted.

46 (48.9%) of our patient were died. The median survival time of patients who died during follow up was 2 years.

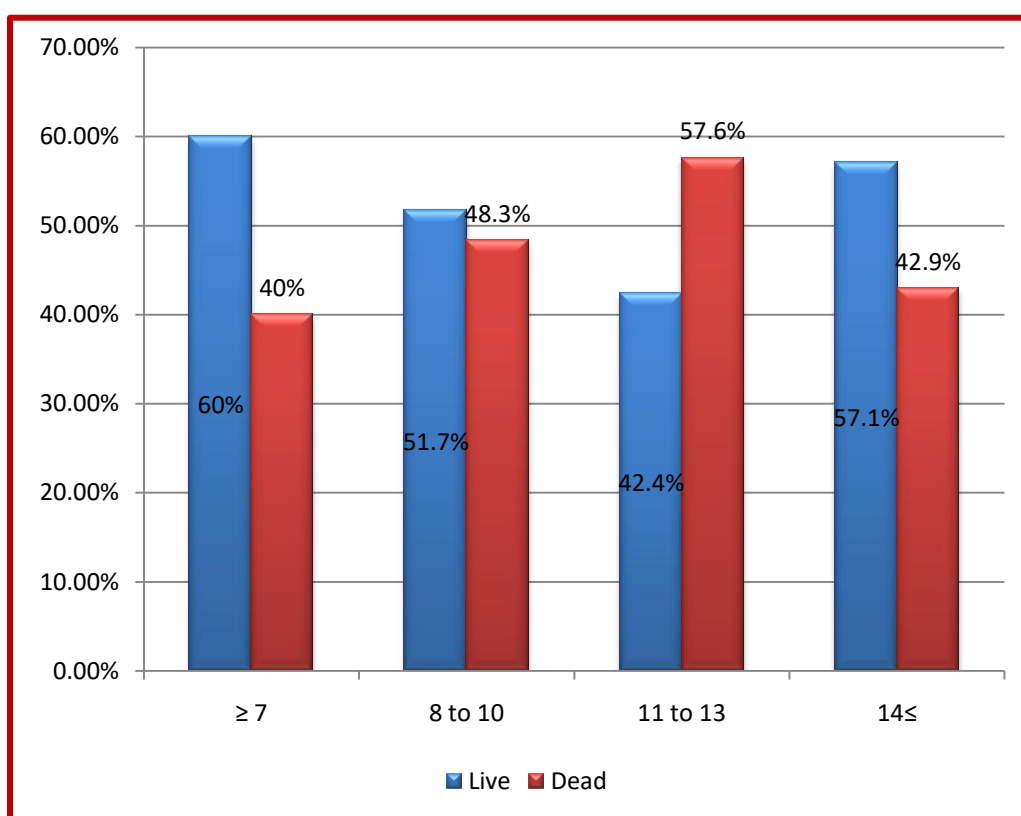
Table (3.2) distribution of patients according outcome

Variable	No	%
Alive	48	51.1
▪ Still on H.D	34	70.8
▪ Stop H.D	2	4.1
▪ Transplanted	12	25
Dead	46	48.9
Overall	94	

Correlation or (association) between patients demographic data and patients outcome.

As shown in figure(3-1) regarding the correlation between age at start of hemodialysis and outcome (died, alive), age group ≤ 7 years (26.59%). (60%) were alive, and (40%) were dead. Age group 8-10 years (30.85%), (51.7%) were alive, while (48.3%) were dead. Age group 11-13 years (35.10%), (42.4%) were alive, while (57.6%) were dead. Age group ≥ 14 years (7.44%), (57.1%) were alive, while (42.9%) were dead.

(P. value = 0.92 which is NS) so there was no association between the age at start of HD and Patient outcome.



Fig(3.1) Correlation between age at start of hemodialysis and patients outcome.

Fig (3.2) shows the correlation between gender and outcome, where in male (59.57%), (53.6%) were alive and (47.4%) were dead.

While in female (40.42%), (46.4%) were alive and (52.6%) were dead. (P.value = 0.55 which is NS) so there was no association between the gender of the patients and outcome.

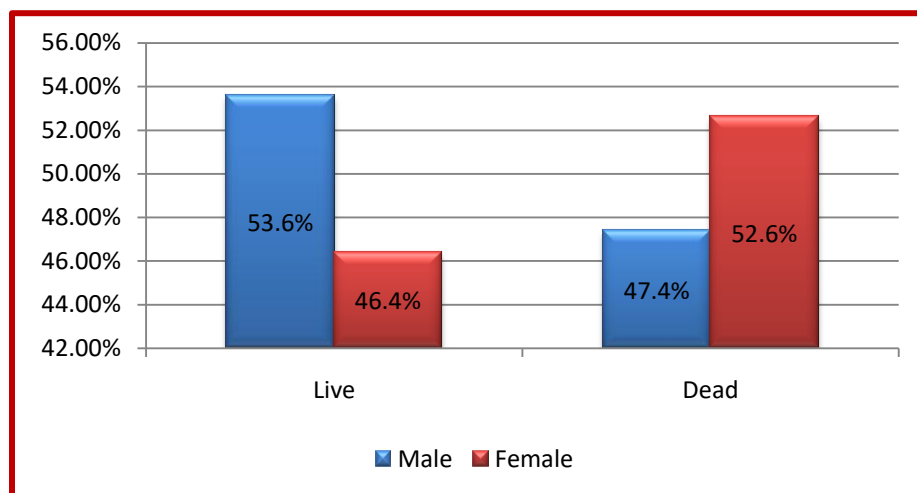


Fig (3.2) Association between gender and patients outcome.

Fig (3.3) shown the association between residency and outcome, where in patients from Baghdad (75.5%); (50.7%) were alive and (49.3%) were dead. While in patients from other province (36.17%); (52.2%) were alive and (47.8%) were dead.

(P. value = 0.9.25 which is NS)

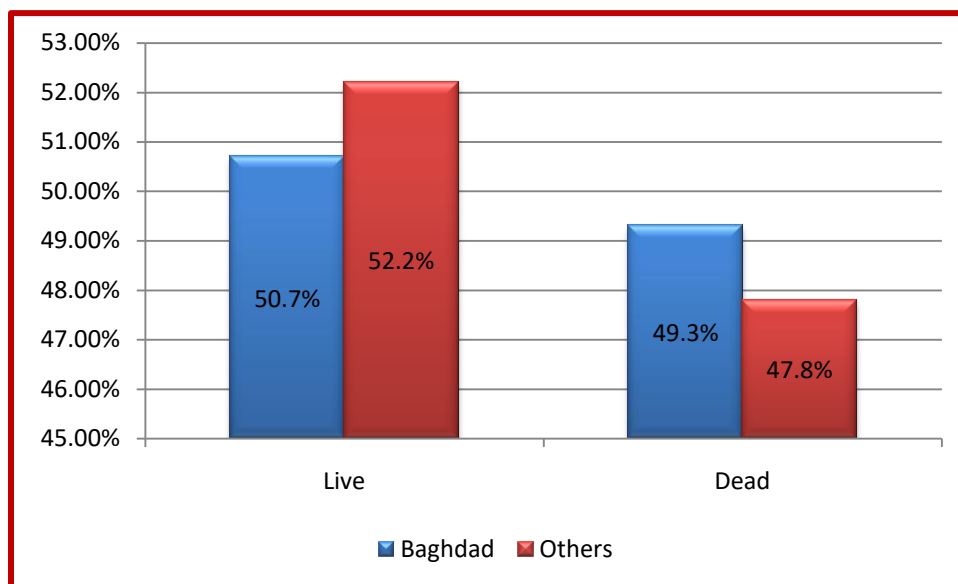


Fig (3.3) shows the residency and outcome.

Fig (3.4) shows the association between the primary cause of ESKD and patients outcome where in small size kidneys (15.95%); (60.0%) were alive and (40.0%) were dead.

In unknown cause (13.82%); (30.8%) were alive and (69.2%) were dead.

In urologic problems (26.59%); (44.0%) were alive and (56.0%); were dead.

In SRNS (11.70%); (63.6%) were alive and (36.4%) were dead.

In cystinosis (6.38%); *50.0%) were alive and (50.0%) were dead.

In recurrent renal stones (6.38%) ; (66.7%) were alive and (33.3%) were dead. In other causes (19.14%) ; (55.6%) were alive and (44.4%) were dead.

(P. value = 0.04 which is S) so there is correlation between the primary cause of ESKD and patients outcome.

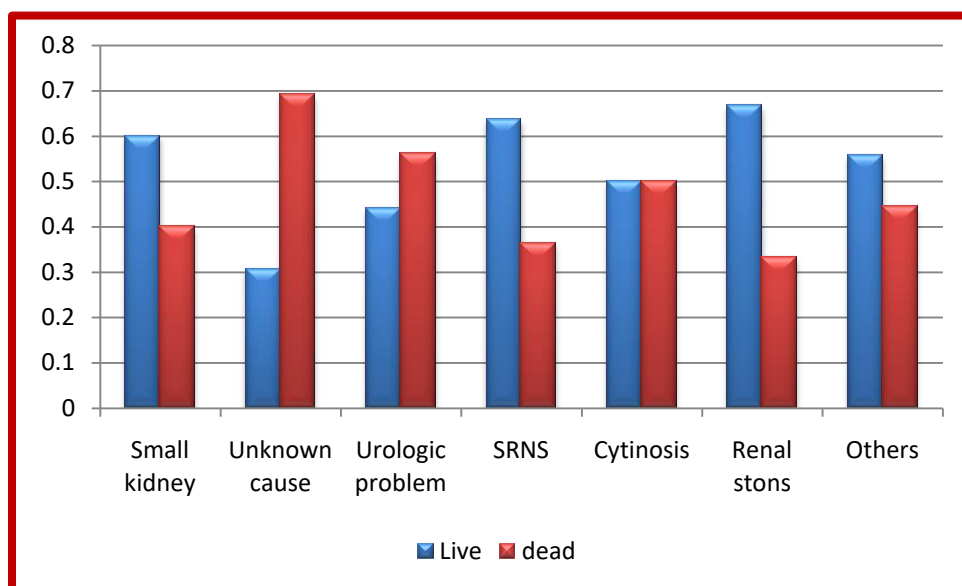


Fig.(3.4) Correlation between the primary cause of ESRD and the patients outcome.

Discussion

This study performed in three Hemodialysis centers in Al- Kharkh side of Baghdad to outline the effect of demographic data on the outcome of Long – term chronic Hemodialysis program in pediatric patients.

In this study, patients were divided according to the age at start of hemodialysis into four groups, age group ≤ 7 years, 8-10 years, 11-13 years and ≥ 14 years.

Regarding the percentage of each group the present study shows (26.6%), (30.8%), (35.10%) and (7.44%) respectively. With an age extreme ranging from 3 yrs to 20 yrs.

The present data shows that the age group ≤ 7 years have an acceptable percentage. Which is slightly more than that reported by the NAPRTCS (22.9%) (11) , and slightly lower than that reported by Rukshanashroff study (55.10%) (12).

This finding disagreed by Moroccan survey study which shows that only 3% of the patients were younger than 5 yrs (13). And ANZDAT registry which shows (9.3%)(14).

The reason behind they have few children aged less than 5 years old in these studies, is that they are generally not considered as eligible for dialysis. And that in our dialysis centers which included in the study, we have the opportunity to offer hemodialysis program to younger age patients with ESKD. Due to the availability of small size dialyzer, lines, and the trained personnel in addition to the availability of vascular surgeons trained well in inserting CVC for small childs.

It must be kept in mind that treatment thresholds vary amongst centers, reflecting the varing opinions amongst nephrologist toward offering RRT to the very younger and those with co-morbidity.

On the others hand, the age group ≥ 14 years have the smallest percentage in this study.

This finding disagree with the finding of the Morrocan survey study (13), and the finding of the NAPRTCS register (11), which shows that the largest number of cases was between 15 and 18 years old.

The reason behind our finding is that the patients in this age group mostly werereferred to the adult dialysis unit.

The present study found no correlation between the age at start of hemodialysis and patients outcome.

This result disagreed by Dr. Mark M.Mitsnefes study (15) and Stephen P. McDonald study (14). Which shows that the crude mortality rate during dialysis treatment were higher among children younger than 5 years at start of hemodialysis compared with those who were 5 years and older.

This association observed between mortality and age in children with ESKD mirrors the association observed in the general pediatric population: mortality risk

increase with decreasing age less than 5 years and increase with increasing age beyond about 10 years(16).

In this study, we noticed a male predominance with (63.82%), while female form (36.17%). This finding goes with the result of the Moroccan survey (13) .

These result can be explained by the high incidence of congenital anomalies of the kidney and urinary tract among boys (17).

There is no significant correlation between the gender and the patients outcome.

This finding goes with the finding of daugirdas J. et al in HEMO study (18) which shows that the overall mortality was not associated with gender. This result is disagreed with the finding of Dr. Mark M. Mitsnefes et al study which shows that the female sex were associated with a high mortality risk. (15).

The present study shows that (57.5%) of our sample study were from Baghdad while (24.46%) of them were from other Iraqi province.

This might be due to the long distance that prevent most patients form enrolling in our Dialysis centers in Baghdad.

Regarding the primary cause of end stage renal disease, (15.95%) were due to small size kidneys, (13.82%) were due to unknown causes, (29.59%) were due to urological problems. (11.79%) were due to SRNS, (6.38%) were due to cystinosis, (6.38%) were due to recurrent renal stones while (19.14%) were due to other causes.

This study shows that urological problems are the most common primary cause of ESRD. The urological abnormalities represents also the most found etiology in morocco survey (34%) Of cases (13), as well as in different countries (USA 57% of cases) ,(Italy 68% of cases).

(India (47%) of cases), and(Iran 52% of cases). (19)(20) (21) (22) .

Probably the reason behind our results similarity with other studies due to delay in the diagnosis and treatment of urological problems.

In other countries such as vietnam, Nigeria and South Africa, Glomerulonephritis represents the main cause of ESRD with (66.4%) ,(58%), (56.4%) respectively.

This difference is due to a higher prevalence of infections disease. (23) (24) (25) .

Other studies shows that among the causes of CKD, congenital malformations of the urinary tract were the most prevalent, consistent with data obtained in developed and developing countries .however, neurogenic bladder was the second most prevalent cause observed in Johathan S. de Freitas et al. study, and by researchers in Turkey. While GN and hereditary nephropathies were observed in developed countries. (26).

These etiologies we have found may be underestimated because of (13.82%) of unknown etiologies In this study.

This study found significant correlation between the primary cause of ESRD and outcome of the patients.

This result goes with A Dutch cohort study (27), which shows that there is association between the primary cause of ESRD and increased mortality.

According to the patients outcome (alive or died),48(51.1%) were alive .Of them (70.8%) still on hemodialysis,(4.1%) stop hemodialysis and (25%) of them were transplanted.

While 46(48.9%) of the patients were dead. The median survival time of patients who died during follow up was 2 year, which is slightly similar to 2.78 year found in the Taiwan's study(28).

The USRDS of 2006(29)reported a mortality rate of 56.5 per 1000 patient-years for pediatric dialysis patients.

The overall mortality rate was 22.8% per 1000 patient-years for pediatric dialysis patients in the Italian study (30).

Taiwan's mortality rate for pediatric dialysis patients was 24.66 per 1000 patients –years.And the rate was 15.7 per 1000 patient-years in another cohort study from Netherlands (27).

Beside,the mortality rate in the NAPRTCS study (deaths/1000 patient-years) varied with age,from 13.6 in infants to 2.2 in adolescents (31)

Conclusions

- 1- Primary cause of ESRD were associated with a significant correlation with the patients outcome.

- 2- No effect of age at start of hemodialysis, sex, on the outcome of the pediatric patients on chronic HD program enrolled in this study.

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