

Management and outcome of children with end-stage renal disease in northwest Iran

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ABSTRACT

Outcome of end-stage renal disease (ESRD) in children has considerably improved since the development of dialysis and kidney transplantation. This study was conducted to evaluate the management and outcome of ESRD children in a referral pediatric center in northwest Iran. A cross-sectional study of medical records of ESRD children (glomerular filtration rate less than 15 ml/min/1.73 m²) younger than 16 years who were admitted in Children's Hospital of Tabriz between October 1999 and October 2009 was performed. Ninety-four children with ESRD including 51 boys (54.3%) and 43 girls (45.7%) with a mean age of 7.9 ± 3.49 years were studied. Parents of nine patients (7.8%) refused treatment. Eighty patients underwent renal replacement therapy (RRT) and were followed for a mean period of 4.86 ± 2.77 years. Initial modality of RRT was hemodialysis in 81.25%, continuous ambulatory peritoneal dialysis in 16.25%, and preemptive kidney transplantation in 2.5%. Thirty-two patients (34%) underwent renal transplantation. The mean duration of staying on dialysis before transplantation was 12.4 ± 11 months. Twenty-nine of kidney donors (90.6%) were living unrelated donors. The 1- and 3-year graft survival rates were 81.2% and 68.8% and the 1- and 3-year patient survival rates were 96.9% and 93.8%, respectively. Thirty-one patients died (33%). The mortality of girls was significantly higher than boys ($P=0.04$). There was a significant negative correlation between age and mortality ($P=0.01$). Heart failure and infections were the most common cause of death. This study showed that ESRD children in our area have a poor outcome in comparison with developed countries.

Key words: Children, end-stage renal disease, outcome, renal replacement therapy

Introduction

End-stage renal disease (ESRD) is the stage 5 of chronic kidney disease (CKD) in which renal replacement therapy (RRT) becomes necessary for sustaining of life.^[1] ESRD is a major health problem with multiple medical, social, and financial problems.^[2,3] Children constitute about 1–2% of total ESRD population,^[4,5] but devastating effects of ESRD in children are more significant than in adults. The lifespan and outcome of ESRD children have dramatically improved since the development of dialysis techniques and

kidney transplantation. However, the mortality of children on dialysis is estimated to be 30–150 times higher than for general pediatric population.^[5–8] Outcome of children with ESRD varies depending on socioeconomic factors and the degree of financial support by governmental resources. In a report from North America, 75% of ESRD children were transplanted within 3 years of RRT initiation.^[5] While in a 5-year study in Sudan, only 3.9% of ESRD children underwent transplantation^[9] and in Vietnam more than 70% of pediatric ESRD patients did not benefit from RRT due to limited facilities for RRT in children.^[10,11]

Hemodialysis (HD) and transplantation in Iranian adults began about 30 and 22 years ago, respectively.^[12] However, use of these procedures has developed in children only recently. Pediatric nephrology and dialysis ward in Children's Hospital of Tabriz started its work in September 2000. This hospital is a referral center for pediatric CKD in East Azarbaijan province and nearby provinces in northwest of Iran. There are little data about the outcome of ESRD children in our area. This study was conducted to evaluate the management and outcome of ESRD children referred to our institution during the past 10 years.

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Materials and Methods

We reviewed the medical records of all ESRD children younger than 16 years who were either admitted or were on outpatient follow-up in children's Hospital of Tabriz/Iran from October 1999 to October 2009. ESRD was defined as glomerular filtration rate (GFR) less than 15 ml/min/1.73 m² for more than 3 months.^[1] GFR was estimated by Schwartz formula using height (cm) and serum creatinine.^[1] The variables including sex, age of ESRD diagnosis, family history, renal replacement modality, duration of dialysis, duration of follow-up, and patient's outcome were collected in designed forms. Besides the RRT, all patients underwent supportive treatments including management of underlying disease, treatment of hypertension, administration of 1,25(OH) D3 and phosphate binders, and treatment of anemia by iron compounds and erythropoietin. Patients who lived in other cities of the province were introduced to their regional dialysis center after establishment of an access for HD or continuous ambulatory peritoneal dialysis (CAPD). All patients were followed every 1–2 months in outpatient service by the same pediatric nephrologist. This study was approved by ethical committee of Tabriz University of Medical Sciences. The data were analyzed by statistical package for the social sciences (SPSS). Chi-square and Pearson's tests were used for data analysis. Quantitative variables were presented as mean ± SD and *P* value <0.05 was considered as significant.

Results

Ninety-four children with ESRD including 51 boys (54.3%) and 43 girls (45.7%) were studied. Fifty-five patients (58.5%) had already reached ESRD at first presentation. The mean age of patients at the time of ESRD diagnosis was 7.9 ± 3.49 years (range 9 months to 16 years). Fifteen patients (15.9%) had a family history as having a sibling with CKD. Etiologies of ESRD in total patients were congenital urologic anomalies in 33 (35.1%), glomerular diseases in 23 (24.5%), hereditary nephropathies in 20 (21.3%), and systemic diseases in 7 (7.4%) patients. Etiology of ESRD remained unknown in 11 (11.7%) patients. Fourteen patients (14.9%) were less than 4 years old at diagnosis in whom hereditary nephropathies and congenital urologic anomalies accounted for 57% (8 patients) and 43% (6 patients) of etiologies, respectively.

Nine patients (eight girls and one boy) were not followed because their parents refused the treatment. Five patients died before initiation of RRT. The remaining 80 patients underwent RRT and were followed for a mean period of

4.86 ± 2.77 years (range 5 months to 9.5 years). Initial modality of RRT used was HD in 65 patients (81.25%), CAPD in 13 patients (16.25%), and preemptive kidney transplantation in 2 patients (2.5%). Type of HD access was permanent HD catheter in 16 (24.6%) and arteriovenous fistula in 49 (75.4%) patients. The average duration of HD and peritoneal dialysis (PD) was 19.8 ± 11.6 months and 30.76 ± 19.88 months, respectively.

Thirty-two patients (34%) underwent renal transplantation and were followed for 3.4 ± 1.84 years (1–8 years). Twenty-nine of kidney donors (90.6%) were living unrelated and three (9.4%) were living related. The mean age of patients at the time of transplantation was 11 ± 3.3 years (range: 4–16 years). The mean duration of staying on dialysis before transplantation was 12.4 ± 11 months (range: 1.5–54 months). Acute rejection episode occurred in 10 patients (31%). The 1- and 3-year graft survival rates were 81.2% and 68.8% and the 1- and 3 year patient survival rate were 96.9% and 93.8%, respectively.

Thirty-one patients (20 girls and 11 boys) died (33%). Mortality of girls (20/43, 46.5%) was significantly higher than boys (11/51, 21.5%) (*P*=0.04). Mortality of transplanted patients was significantly less than untransplanted patients (*P*=0.01). There was a significant negative correlation between age and mortality (*P*=0.01). Causes of death were heart failure in 14 (14/31, 45.2%), systemic infections in 9 (9/31, 29%), infections due to HD or PD access in 5 (5/31, 16.1%), and pulmonary hemorrhage in 3 patients. The condition of patients at the end of the study period is demonstrated in Table 1.

Discussion

In our country, the ESRD patients are supported by health ministry and “foundation of special disease” and most parents tend to follow their children's treatment. In our study only 7.8% of parents refused treatment. In study of Gulati in 1999, in India^[13] 40% and in Vietnam^[10] 50% of parents refused from further therapy because of financial problems.

Table 1: Condition of ESRD children at the end of study period

Condition	Number (%)
Treatment refusal	9 (9.6)
On hemodialysis	20 (21.3)
On CAPD	6 (6.3)
Functioning allograft	28 (29.8)
Died	31 (32.97)
Total	94 (100)

ESRD = End-stage renal disease, CAPD = Continuous ambulatory peritoneal dialysis

Initial modality of dialysis varies among nephrology centers depending on technical and nursing facilities. Peritoneal dialysis (PD) is the most common modality in most European countries and North America for dialysis of children.^[5,6] Also in some developing countries such as Tunisia and Jordan, PD was used in most of children needed RRT.^[14,15] While in our study HD was initial RRT modality in 82% of patients. In an Iranian multicenter national study, 93.5% of all dialysis patients (including children and adults) received HD and only 6.5% received PD.^[12] Also in a single-center study in Tehran/Iran, HD was the predominant form of RRT in children.^[16] The higher use of HD in our patients may be explained by nephrologist bias, lack of adequate nursing and technical support and noncompliant families. Automated PD (APD) which is the most frequently used form of PD in children in developed countries^[5] has led to considerable reduction of peritonitis rate. In our study, CAPD (instead of APD) was the sole modality of PD due to lack of cyclor machines. Similar to our results, CAPD was the initial PD modality of choice in 92.6% of Turkish children as reflected in the report of the Turkish Pediatric Peritoneal Dialysis registry.^[17]

In this study, 34% of patients and in an 8-year study in Tehran/Iran, 32.5% of ESRD children underwent transplantation.^[16] According to the report of Turkish Pediatric Peritoneal Dialysis registry,^[17] only 15.4% of Turkish ESRD children were transplanted that is less than our study. While in an 11-year study in Kuwait,^[18] a country with high level of treatment facilities, 76% of pediatric ESRD patients underwent renal transplantation. In a study in the United Kingdom, 56% of ESRD children younger than 2 years received transplant at mean age of 2.6 years and 87% were transplanted between 1 and 4 years.^[19] While in our study, from 14 patients younger than 4 years, no one was transplanted before 4 years of age. Lower rate of transplantation in this study in comparison with some countries may be attributed to lack of cadaver donors and high cost of living unrelated donors.

Preemptive transplantation is optimal treatment of pediatric ESRD for maintaining growth and development of children. In a report from North America^[5] 16% and in Kuwait^[18] 26% of ESRD children underwent preemptive transplantation. Contrary to these reports, relative frequency of preemptive transplantation was only 1.4% in Turkey^[20] and 2.5% in our study. The less number of preemptive transplantation in this study may be explained by late referral. Most of our patients (58.5%) presented at terminal stage, so needed dialysis before preparing for transplantation. Similar findings have been reported

from other developing countries.^[9] In Vietnam^[11] 85%, in India^[13] 54% and in Paraguay^[21] over 60% of ESRD children were already in ESRD before first admission. Late referral indicates the failure of primary healthcare systems to diagnose CKD and conditions leading to ESRD in early stages.

Survival rate of children younger than 20 years on chronic RRT has increased over the past years and varies from 79% to 82% at 10 years in developed countries.^[5,22] In this study that included children younger than 16 years, only 67% of patients were alive at the end of study period. It should be noted that a younger age at onset of RRT is a considerable mortality risk factor in all studies.^[22] Moreover, higher mortality in our study may be attributed to prolonged stay on dialysis and some socioeconomic factors. In some countries such as Jamaica^[22] and Nigeria,^[23] mortality rate of ESRD children is even higher than our results and is about 44.4% and 47%, respectively.

Cardiovascular disease is the most common cause of death in ESRD children and is responsible for 21.5–50% of mortalities in different studies followed by infections that account for 20% of mortalities.^[24,25] In accordance to other studies, heart failure and infections were the most frequent causes of death in our study.

Conclusion

This study shows that a great effort is necessary to improve the outcome of ESRD patients in our area. Delayed referral is one of our major problems. Continuing education and increasing awareness of referring physicians and families about early sign and symptoms of renal diseases are necessary to decrease the number of patients who are referred at end stage. High cost of transplantation results in a long staying time on dialysis that impairs the quality of life in our patients. Limited well-educated nursing and social workers and lack of technical support restrict employment of CAPD and APD in our area. Other studies are necessary to evaluate the long-term outcome of transplanted children.

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