Chronic Kidney Diseases in Iraqi Children

Jinan Soaod Orabi Hassan*, Najla Ibrahim Ayoub **, Asaad Abdullah *, Ammar Abdulateef Hussien****, Ala'a Abdul-Hussein Al-Enbari*****

ABSTRACT:

BACKGROUND:

Chronic renal insufficiency (CRI) causes substantial morbidity in virtually every major organ system of the body. Moreover; CRI is inevitably progresses to end stage renal disease.

OBJECTIVE:

To find out the frequency of chronic renal failure in pediatric age group and their risk factors.

METHODS:

One hundred ten infants, children and adolescents with chronic renal failure age between 1 mo.-17 yr. visiting Al-Karama Teaching Hospital in nephrology, urology, dialysis and transplant units for the period from1st May 2004 until 30th April 2006 were included in this study. Patient's notes were reviewed for: Age, sex, age at first presentation, age at referral to pediatric nephrologists , medical and social history including mode of their RRT, then the cause of their renal failure. Every patient was clinically examined and blood pressure. Measurement was taken, followed by taking anthropometric measurements which includes body weight (Kg) and height (cm) in addition to assessment of sexual maturity rate stages lastly we record laboratory investigation which include blood urea, S. creatinine, Hb. level , S. Ca^{+2}, S.Ph., and GFR in addition to any investigations regarding original renal disease.

RESULTS:

In this study we found that males are more affected than females in a ratio of 3.2/1. The mean age at their 1^{st} presentation were 3.5 ± 3.7 yrs. while their mean age when they referred to pediatric nephrologists were 5.2 ± 4.4 yrs. Below 5 yrs. constituting 44.5% and age group between 6-10 yrs constituting 29.1% while in age group above 10 yrs were 26.4%. Mean value of GFR in this study was 14.2 ± 7.5 ml/min/ 1.73m^2, 36.4% patients were in ESRD. Obstructive uropathy as a cause of CRF were in 34.5% of total patients, followed by glomerular diseases that involves 21.8% and congenital anomalies of urinary system in 20.9% of our patients in this study. About 80% of our patients were found to be anemic with Hb concentration ≤ 10 g/dl and 48.1% of patient having hypocalcemia with S. Ca^{+2} level <9.5 mg/dl and hyperphosphatemia with S.Ph. >5.5 mg/dl found in 32.7% of patients.This study shows a significant relationship between hypocalemia and hyperphosphatemia and anemia with progression of renal insufficiency to ESRD. About 45.5% and 53.6% were below 3^{rd} centile for Wt. and Ht. respectively and more than 50% had delayed puberty on SMR staging of Tanner and those patient's with growth retardation are significantly increased in number as the disease progressed to ESRD.Hypertension considered in patient with BP > 95^{th} percentile according to task force table for age and sex and wt. and Ht. percentile and accordingly our study show that about 45.5% of patients were HTN. Mode of RRT is mainly conservative and intermittent peritoneal dialysis in 41.8% and 40% of our patients respectively. While only one patient was on APD and 11 patients were on HD and 8 patients received lived related & unrelated renal transplant.

CONCLUSION:

The obstructive uropathy is the commonest cause for CRF especially in children <5 yrs. Most of our patients were of delayed referral to pediatric nephrology and they are poorly managed, severely affected and growth retarded. We have limited diagnostic resources & options regarding pediatric dialysis programs & renal transplant.

KEY WORDS: (Kidney Diseases, Iraqi Children)

*Department Of Pediatrics Nephrology , Central Teaching Hospital Of Pediatrics ,Baghdad.
**Head Of Pediatrics Department In Al- Mustansyria University, Baghdad.
*** Department Of Medicine, Baghdad Teaching Hospital.
**** Department Of Pediatrics Nephrology , Al-Karama Teaching Hospital, Baghdad.
***** Department Of Pediatrics Cardiology In Ibn-Al- Bittar Hospital, Baghdad.

INTRODUCTION:

Chronic renal failure (CRF) is a devastating medical, social, and economic problem for patients and their families [1].Chronic renal insufficiency (CRI) once established, tends to progress to end stage renal failure. The rate of decline in glomerular filtration varies in groups of patients with different nephropathies and also in patients with the same disease [3].Chronic renal failure and CRI are clinical terms used to describe renal dysfunction of varying degrees from mild to severe in nature. In some cases, it is progressive and common to all forms of kidney injury, including that due to developmental, genetic, immunologic, metabolic, traumatic, & infectious processes[4]. Incidence**:**The real incidence of chronic renal failure in children is uncertain. Most estimates are based on the number of patients accepted into dialysis and transplantation programs. Available reports reveal striking geographic differences in the incidence and recognition of renal diseases. In developed countries the incidence of CRF decreases slowly owing to early diagnosis, improved conservative treatment, and prevention of genetically transmitted disease. The median annual incidences of CRF from 4.5-12.5 / million population, male predominance among children with congenital structural diseases, whereas no such gender related difference for other disease. The proportion of children below 5 years of age has increased to 40-50% as renal replacement therapy (RRT) has become more common in very young children .(5) This study done to: To identify the etiology of chronic in the studied group, to assess their growth in relation to degree of renal impairment, to study some factors that influences the progression of renal disease and to high light the difficulties faced in their management.

PATIENTS AND METHODS:

This is a prospective study ,one hundred ten (110) patients with chronic renal failure age 1 mo.-17 yr attend mostly as a referred cases from different hospitals in Iraq to Al-Karama Teaching Hospital in nephrology, urology, dialysis& transplant units in Baghdad city during the study period (from May 2004 – April 2006) were enrolled in this study.CRF was defined as GFR below 50 ml/min./1.73 m^2 [6] and presence of any of the following (i) bilateral small contracted kidneys or single contracted kidney (ii) radiographic evidence of bony deformities[7] (iii) persistence of GFR below 50ml/min/1.73m^2 over ensuring 3 months[8].The information about each patient was selected using a well-structured questionnaire (appendix) which includes: (1) name, (2) age, (3) sex, (4) age at presentation for first time, (5) age at referral to pediatric nephrologists, (6) Primary renal diagnosis determined from the previous medical history& clinical features which includes pallor, edema, oligurea, hematuria, abnormal urinary stream and laboratory data including blood chemistry, urinalysis , blood pictures, radiographic and scientigraphic studies and renal histopathology, and any laboratory investigations. done by patients according to their original disease were recorded, (7) Renal replacement therapy type for each patient was recorded, (8) level of blood urea, serum creatinine, S. Ca^{+2} , S. Pi., Hb level at presentation, (9) GFR at presentation (GFR is measured in ml/min/1.73m^2) by using Schwartz *et al.* formula which based on the length of patient – an estimate of muscle mass and plasma creatinine concentration. GFR = K x L/PCr L=length, PCr=plasma creatinine K is an empirical constant depending on sex and age of the child, because of different ratios between length and muscle mass over different ages, several values for the constant have been proposed. 0.45 for full term normal size infants, 0.33 for low birth wt. infants, 0.55 for girls aged 1-20 yrs and boys aged 1-13 yrs, 0.7 for boys aged 13-20 yrs[9], (10) stage of chronic renal insufficiency for each patients were determined according to this classification (Update 2006) **Stage I**(CRI (GFR < 90)m1/min /1.73$m^{2)}$,**Stage II(**CRI (GFR 60-89) m1/min /1.73m^2), **Stage III(**CRI (GFR 30-59) m1/min /1.73m^2),**Stage IV(**CRI (GFR 15-29) m1/min /1.73m^2**),Stage V**(CRI (GFR less than 15 ml/min./1.73m^2) End stage renal disease (ESRD) (GFR below 10ml/min/1.73m^2), (11) Length for infants, the measurement of linear growth is length taken by two examiners with the child supine on measuring board, for older children the measure is stature, taken with a child standing on a stadiometer, (12) weight: for those children was measured by Seca Germany scale. The data are presented on standard charts: (i) weight for age and sex , (ii) height for age and sex, (13) adolescence between 10-20 yr proceeds across three distinct periods – early (10-13 yrs) , middle (14-16 yrs), and late (17-20 yrs), and SMR stage (sexual maturity rate) for each patient's in these groups determined by using classification of SMR stages for girls and boys tables adapted by Tanner JM; growth at adolescence, 2nd, Oxford, England, Black Well scientific publications[20], (14) blood pressure: by sphygmomanometers before BP measurements are taken the child should rest for 3-5 minutes and a child in seated position (supine for infants) from a fully exposed right arm resting on a supportive surface at heart level with back supported & feet

firmly on the floor, one must ensure that the inflatable bladder that encircles the circumference of the arm is wide enough to cover more than 40% of the distance from the acromion to the olecranon and neither obstructs the placement of the stethoscope bell at the antecubital fossa nor interferes with the axilla, K1 (Korotkoff) (SBP) is recorded when the first tapping sound is heard. K5 (is the disappearance of all sounds) identified as a reliable definition of DBP for children and adolescents, and K4 is a low-pitched, muffled sound as DBP in infants [2]. Then we use task force tables which is probably the most widely used source of information on BP in children and provides us with statistical definitions of HTN (hypertension) these tables gives systolic and diastolic 90^{th} &95^{th} percentiles for age ,sex &Ht percentile. To use these tables, a child BP is measured and the height percentile is calculated using standard growth charts for age and sex:1 - If BP is below 90^{th} percentile, the child is normotensive. 2 - If the measured BP is between the 90^{th} and 95^{th} percentile, the patient is considered to have high normal BP. 3 - Measurements higher than 95^{th} percentile diagnosed as hypertension [17] (15) The etiological classification of CRF was as follows: 1 - Obstructive uropathy was diagnosed if urinary tract dilatation was demonstrated by radiography or scintigraphy, in the absence of vesicoureteric reflux and bladder dysfunction. 2 -Chronic G.N. → defined by presence of nephrotic range proteinuria and gradually deteriorating renal function with or without red blood cells and casts and/or HT. If possible a definitive diagnosis of chronic GN was established on a renal biopsy [8, 9]. 3 - Reflux nephropathy was considered in the presence of scarred kidney (irregular renal out line) demonstrated by U/S, intravenous pyelography or radionucleotide imaging [10] and either of the following: (a) Primary vesicoureteric reflux demonstrated on micturating cysto- urethrography (MCU) and (b) History and laboratory evidence of past urinary tract infection. 4 -Neurogenic bladder was considered in patients with MCU showing a large capacity bladder without any obstruction, and contracted bladder wall with trabeculations, urodynamic studies including cystometry and electromyography of the pelvic and abdominal musculature were done to confirm the diagnosis of neurogenic bladder dysfunction, the type of neurogenic bladder was determined by urine flow rate, residual urine volume and intravesical pressures, external urethral sphincter, pelvic and abdominal electromyography and urethral pressure profile were recorded simultaneously[11]. 5 -CRF was considered secondary to hemolytic uremic syndrome in patients with previous history of acute renal failure, microangiopathic anemia and typical renal biopsy [15]. 6 -Other inherited or multisystem disease is considered according to every disease, clinical feature, biochemical analysis, blood gas analysis renal histology if available, urine analysis and immunological study, radiological and U/S results. 7 -Patients in whom the cause of CRF could not be identified were classified as unknown etiology. Statistical analysis: All data were coded and entered to the computer. Data arranged and tabulated by using statistical package for social science (SPSS). Associations between different variables were measured by using chi-square test. Differences between continuous variables were measured by using analysis of variance (ANOVA test). P value < 0.05 considered to be significant.

RESULTS:

In this study a total of 110 patients with CRF are distributed according to their gender .We found that male more affected than female with a sex ratio of about 3:1 The mean age at presentation of CRF in this study was 6.65 ±5 years (range 1 month- 17 years) .The mean (SD) age at onset of the underlying disease(1st presentation age) was 3.5 ± 3.7 years(range 1 month-14.5 years)while the mean age at referral to pediatric nephrologists was 5.2±4.4years(range 1month -16.5years) So there were considerable delay (about 2 years) between initial presentation & referral age. According to their age our patients were distributed to 4 groups (<1y) with frequency of 14(12.7%),(1-5y)with frequency of 35(31.8%),age group from(6-10y)about 32(29.1%)&group of patients above 10 y account for 29(26.4%)so patients less than 5y with highest No.49(44.5%). Obstructive uropathy was the most prominent cause of CRF in this study which account for 34.5% and about 50% of them with ESRD. Posterior urethral valve seen in 22.7% which mean that it's a major cause for obstructive uropathy. While glomerular disease was found in 21.8% of patients in this study &nephrotic syndrome with focal segmental glomerulosclerosis was the most frequent cause of glomerular disease which account to 9%.Congenital abnormalities of urinary system was the 3rd common etiology for CRF &VUR with a highest frequency. All these causes & other causes of CRF with No. of patients distribution according to stages of CRF are listed in table No. (1) Obstructive causes to urinary tract is the prominent cause of CRF in pediatric children with age group < 5yr. with 50% while glom. Cause is the least in this age group, but we can see that glom. Disease as a cause of CRF mainly in 6-10 yrs age group. Congenital abnormalities like

obstructive disease also predominantly in age group < 5yrs. and VUR is the most frequent cause of this group as in table No. (2). In table No. (3) The mean GFR of our patients was 14.22 ± 7.5 (range 6.2-46.7) ml/min./1.73m^2 while mean blood urea 154.7 ± 76.5 mg/dl with a range of (47-370) mg/dl and mean S.cr. 4.77 – 2.15 (range 1.5-10.5) mg/dl According to GFR level CRI patients classified to stages, from stage I-ESRD as mentioned previously. We see that no. of patient with end stage disease group in higher frequency than other group. We can see that no patient in stage I or II and the no. of patient in stage III was with the least frequency. Classification of our patient no. with their different age groups according to the stages of renal failure depending on their GFR values. Study show that the younger age group those <1y and 1-5 yrs have higher incidence and development of end stage renal disease. It was found that male more severely affected than female in stage III male 2.4% and female 7.7% of the total no. while in end stage renal disease male was 38.1% while female 30.8%. The median blood levels of calcium and phosphate were 8.8 ± 1.2 and 5.1 ± 1.2 respectively Table (3). The no. of patient with S.Ca^{+2} <9.5 mg/dl was 53 (48.1%) and we found that no. of our patient with S. Ph. > 5.5 were 36 (32.7%). We can see in this study the means& (SD) of hemoglobin concentration was 8.34 g/dl and 2.1 with a range between (4.2-14) g/dl as shown in Table (3). In Table (4) the frequency of patient with Hb conc. 5-10 gm is the predominant, their no. and percentage 77 (70%), and so the patient with Hb concentration ≤ 10 g/dl was 88 (80%). In this study we found a significant relationship between laboratory value of Hb concentration and S. Ca^{+2} and S. Ph. With progression of renal failure to end stage renal disease, anemia and hypo Ca^{+2} more significant association with progression of renal disease than hyperphosphatemia. Table (5) Nearly half of CRF patient in this study was hypertensive as this table shown that 45.5% of our patient considered as HTN as they have blood pressure above 95th percentile while patients with blood pressure <90th percentile considered as normotensive constituting 41.8%, and the group who account 12.7% of total patient called high normal blood pressure with blood pressure ≥ 90th percentile as shown in table no.12. Also we found that >50% of our patients with ESRD were HTN. In this study we can see that the higher frequency of our patient below 3rd centile for weight and height 50 (45.5%) and 59 (53.6%) respectively, so this mean that >50% of our patients were of stunted growth. The mean for height percentile in this study is 10.2 (SD. 13.3) with a range of ≤ 3rd percentile, ≤73 percentile and the mean for wt. 13.6 with (SD. 17.2) and the range for wt. between ≤ 3 percentile and ≤ 90 percentile. Patients with short stature more frequently seen in end stage renal disease, that's mean as the disease progress toward ESRD the patient no. with short stature increase in frequency. Also in this study the body wt. and final Ht. are significantly affected by progression of renal failure to ESRD, as shown in Table (7, 8, 9, and 10) SMR evaluated for each patients aged 10-20 yrs and according to early , middle and late adolescence periods from 10-13 yrs (normal SMR stage 1-2) in this age group we have 23 patient 69.5 % of them with SMR stage I . In 14-16 yrs (normal SMR 3-5) we have in this group 50% of them SMRI and 50% SMRII. In 17-20 yrs (normal SMR 5) in our study we have 2 patients in this age group both with SMRII. Table (11) In this study we have 44 patients 40% received intermittent peritoneal dialysis and 46 patients 41.8% still on conservative medical line of management and only 1 patient undergo APD while 11 patients had vascular access and put on hemodialysis program. Finally we have 8 patients with CRF undergo lived related & unrelated renal transplants as shown in Table (12).

Table 1: Distribution of patients No. according to causes & stages of CRF

Causes	Stage 3	Stage 4	Stage 5	End stage	Total No.	%
1.obstructive uropathy -PUV	_	2	10	13	25	22.7
-PUJ(Pelvi-ureteric junction obstruction)	_	2	4	5	11	10
-Bladder neck obstruction	_	_	1	1	2	1.8
- Congenital Multiple obstructive anomalies	–	-	1	1	2	1.8
2.Glomerular diseases-(Chronic GN)	-	-	1	-	1	0.9
-Congenital NS		-	1	3	4	3.6
-FSGN	1	4	3	2	10	9

-MCD		1	_		1	0.9
-MPGN	2	1	-	-	3	2.7
-MSPGN	-	-	1	-	1	0.9
-RPGN	_	1	_	1	2	1.8
3.CONGENITAL ABNORMALITIES OF URINARY SYSTEM -VUR		7	4	2	13	11.8
-Neurogenic bladder	1	2	2	2	7	6.3
-Congenital dysplastic kidney	_	1	_	_	1	0.9
4.INHERITED DISEASES -Alport syndrome		_	1	_	1	0.9
-Bartter syndrome	–	1	1	_	2	1.8
-Cystinosis	_	3	_	_	3	2.7
-Nephrocalcinosis	_	1	1	2	4	3.6
5.MULTISYSTEM DISEASES -Amyloidosis	-	-	2	1	3	2.7
Causes	Stage 3	Stage 4	Stage 5	End stage	Total No.	%
-HUS	–	-	-	2	2	1.8
-Lupus nephritis	_	1	1	_	2	1.8
6.PARENCHYMAL DISEASES -Chronic pyelonephritis	–	1	_	_	1	0.9
-Chronic interstitial nephritis	_	1	1	-	2	1.8
7.UNKNOWN	-	1	-	4	5	4.5

Table 2 : Causes of CRF at different age groups

Diagnosis	1mo.-5Y	6-10Y	>10Y	Total No.(%)
Obstructive uropathy	24	11	3	38(34.5%)
Glomerular diseases	6	11	7	24(21.8%)
Congenital abnormities of urinary system	13	6	4	23(20.9%)
Inherited disease	2	4	4	10(9.1%)
Multisystem diseases	2	0	5	7(6.4%)
parenchymal disease	0	2	1	3(2.7%)
Unknown	1	1	3	5(4.6%)

Table 3: Mean biochemical parameters for patients with CRF.

	N	Minimum	Maximum	Mean	*Std. Deviation*
B.UREA	110	47mg/dl	370mg/dl	154.7mg/dl	67.5
S.CREATININE	110	1.5mg/dl	10.5mg/dl	4.7mg/dl	2.15
GFR	110	6.2ml/min/1.73m2	64.7ml/min/1.73m2	14.2ml/min/1.73m2	7.53
HB	110	4.2gm/dl	14gm/dl	8.34gm/dl	2.14
SCA	110	5.3mg/dl	10.6mg/dl	8.81mg/dl	1.25
S.PH	110	3.3mg/dl	8.1mg/dl	5.18mg/dl	1.28

Table 4: Frequency of CRF patients according to their Hb concentration.

	Patients number	Percent
<5 gm/dl	11	10.0
5-10 gm/dl	77	70.0
>10 gm/dl	22	20.0
Total	110	100.0

Table 5: Correlation between different labs. values &CRF stages.

			NO.	MEAN	SD	P
HB	STAGE	stage 3	4	9.9500	4.0220	
		stage4	31	8.9839	1.9012	
		stage5	35	8.3429	1.9556	
		end stage	40	7.6725	2.1036	0.028
SCA	STAGE	stage 3	4	10.1000	.4163	
		stage4	31	9.2355	.9701	
		stage5	35	8.9114	1.0698	
		end stage	40	8.2650	1.4100	0.01
S.PH	STAGE	stage 3	4	4.0250	.1708	
		stage4	31	4.9097	1.0753	
		stage5	35	5.3000	1.1458	
		end stage	40	5.3875	1.5112	0.110

Table 6: Distribution of patients according to BP centile

		Patients No.	Percent	Valid Percent	Cumulative Percent
Blood pressure	<90th%	46	41.8	41.8	41.8
	≥90th%	14	12.7	12.7	54.5
	>95th%	50	45.5	45.5	100.0
Total		110	100.0	100.0	

Table 7: Distribution of patients according to their height centile.

		Patients No.	Percent
Height percentile	≤3rd%	59	53.6
	≤5th%	5	4.5
	≤10th%	28	25.5
	≤25th%	11	10.0
	≤50th%	6	5.5
	≤75th%	1	.9
Total		110	100.0

Table 8: Distribution of Patients No. according to weight centile

		Patients No.	Percent
Weight percentile	≤3rd%	50	45.5
	≤5th%	1	0.9
	≤10th%	31	28.2
	≤25th%	19	17.3
	≤50th%	5	4.5
	≤75th%	3	2.7
	≤90th%	1	0.9
Total		110	100.0

Table 9: Relation between No. of patients with short stature & stage of renal failure.

			HT.SCORE		Total
			Normal	Short stature	
STAGE	stage 3	No.	2	2	4
		%	50.0%	50.0%	100.0%
	stage4	No.	20	11	31
		%	64.5%	35.5%	100.0%
	stage5	No.	20	15	35
		%	57.1%	42.9%	100.0%
	end stage	No.	9	31	40
		%	22.5%	77.5%	100.0%
Total		No.	51	59	110
		%	46.4%	53.6%	100.0%

p=0.002(S)

Table 10: Relationship between underweight&CRF stage.

			WT.SCOR		Total
			normal	low wt	
STAGE	stage 3	no.	4		4
		%	100.0%		100.0%
	stage4	no.	24	7	31
		%	77.4%	22.6%	100.0%
	stage5	no.	21	14	35
		%	60.0%	40.0%	100.0%
	end stage	no.	11	29	40
		%	27.5%	72.5%	100.0%
Total		no.	60	50	110
		%	54.5%	45.5%	100.0%

p=.00006(S)

Table 11: Distribution of patients No. with their SMR according to their adolescent age group

Age group	Patients No.					
	Total	SMR1	SMR2	SMR3	SMR4	SMR5
(10-13Y) M	14	12	2	-	-	-
F	9	6	3	-	-	-
(14-16Y) M	7	-	3	4	-	-
F	4	-	3	1	-	-
(17-20Y) M	2	-	2	-	-	-
F	-	-	-	-	-	-

Table 12: Distribution of No. of patients according to RRT.

Mode of RRT	No. of patients	%
Ambulatory peritoneal dialysis	1	0.9
Conservative medical treatment	46	41.8
Hemodialysis	11	10
Peritoneal dialysis(intermittent)	44	40
Renal transplant	8	7.2

DISCUSSION:

Progressive renal disease occurs in all age groups. The incidence of chronic renal insufficiency among children younger than 16 years varies from 1.5-3 per million [(2)]. The precise incidence of CRF in our country is not known. The epidemiologic information concerning CRF in children is scanty, particularly with regard to the less advanced stages of renal impairment that are potentially more susceptible to therapeutic interventions aimed at changing the course of the disease and avoiding ESRD. So the incidence is lacking because no national registries exist. In the present study CRF is more predominant in male (76.4%) than female (23.6%) in a ratio of 3.2/1 this result is in agreement with other studies of (Gianluigi, 2003 & Kamoun, 1996). [(21, 16)] The mean age of the studied patients was 6.6 ± 5 yrs. (range 1 mo.-17 yrs). In this study age of onset of the underlying disease (presentation age) range (1 mo.-14 yrs) with a mean of 3.5 ± 3.7 yrs. While their referral mean age to pediatric nephrologists was 5.2 ± 4.4 yrs. with a range between (1 mo. – 16.5 yrs) this suggesting delayed detection and referral of our

patients by about 2 yrs. And this is true for other studies done by Jameela, (2006[18], while this result is higher in comparison to reports from developed country. Forty four and half percent of registered children with CRF in this study were below 5 yrs of age and this is consistent with other study done by Pankaj Hari in 2003.[11] Mean GFR in this study was 14.2 ± 7.5 ml/min/1.73m^2 and after the classification of our patients according their stages of CRF depending on their GFR we noticed that 36.4% of CRF were in ESRD and children <5 yrs appear to be with higher incidence and development of ESRD in comparable with other age group. This mean delayed diagnosis and failure to institute measures to slow the progression of renal failure which have resulted in a predominantly young ESRD population, these result is in agreement with study done by Sakhujav, (2006) but higher in compared to NAPRTCS report. [1,15] Also we noticed that children with age group <1 yrs 1-5 yrs show higher incidence of development and progression to ESRD. Also male more severely affected than female because (38.1%) of male developed. ESRD in comparison to female constituting (30.8%), these result may be as a consequence of causes lead to CRF, as this study show that obstructive uropathy and congenital abnormalities of urinary system is a major cause of CRF in children less than 5 yrs. and these causes most predominantly in male than female, and this true for other study done by Pankaj, (2003).[11] Obstructive uropathy and congenital abnormalities is a cause of CRF in younger age group < 5y, while glomerular disease play as a prominent cause in older age > 5 yrs and this consistent with report from Agnes A and Fogo, (2003).[2] Similar to other international studies done by Mouin, G. (NAPRTCS) 2003[12] and Gianluigi, (2003)[14] and Kai Ronnholm(2004)[5], Obstructive uropathy is the prominent etiology for CRF in Iraqi children which may seen in 34.5% of patient in this study cases of CRF other congenital abnormalities like reflux nephropathy were 11.8% of our patients while in Turkish children(1995)[19], VUR account for 32.4% which was a major cause of CRF in their study. Glomerulopathy is a cause of CRF in 21.8% of children in our study, and hereditary nephropathy were in 9% of our patient this in contrast to study done for Tunisian child that show that the chief etiology for CRF as the hereditary nephropathy (29%) and (19%) for the glomerulopathy.[16] Also hereditary disorder is a common cause of CRF in Swedish children (17%) and reported three times more frequently than in Europe, while preventable causes like obstructive nephropathy and VUR contribute to less percentile of CRF cases in developed countries (Italy) in comparison to reports from developing countries (Nigeria Jamaica).([13,15] This is chiefly due to prompt detection and management of urinary tract infections, followed by careful screening for underlying anomalies. Screening for urinary tract anomalies by antenatal ultrasonography is likely to detect significant structural disorders which can be treated postnataly; early and appropriate management of these disorders would prevent their progression to CRF and ESRD. Focal segmental glomerulosclerosis (FSGS) is a major cause lead to CRF among glomerulopathy with N.S about 9% of cases CRF and this in agreement to study of NAPRTCS in which FSGS account 7.7% of total patient in their studying they consider it as a risk factor that increase the rate of progression to ESRD because FSGS cause neprhons degradation and degeneration with evidence of glomerulo-to-tubulo interstitial transfer of the disease accounting for disease progression[22]. Neurogenic bladder were seen in 6.3% of cases ECRF in this study while in study of Saudi Arabia by Jameela she noticed neurogenic bladder in 19.6% of her patients.[18] In this study mean Hb concentration was 8.3 g/dl ± 2.1 g/dl with a range between (4.2-14) g/dl and 88% of our patients were anemic with Hb concentration of <10 g/dl, this in agreement with study done by Pankaj, (2003).[11] The mean blood level of calcium was 8.8 ± 1.2 mg/d where is plasma phosphate level show a mean of 5.1 ± 1.2 mg/d. and our study show that hypocalcemia occur in 48.1% of our patient with S.Ca^{+2} < 9.5 mg/dl and hyperphosphatemia seen in 32.7% with S. ph. >5.5 mg/dl which mean in adequate management and this consistent with other study from NAPRTCS by Mouin and Amirtejani.[12] The correlation anemia, hypo Ca^{+2} and hyperphosphatemia with rate of progression to ESRD, in our study we found a significant relationship between these parameters and progression of renal insufficiency which was similar to Agnes, A. & Fogo (2003).[2] We see that mean Hb concentration significantly decreased when the ESRD was the end point, that has an advance effect on school attendance, cognition, exercise tolerance and leads to regression of ventricular hypertrophy. Similar correlation were found with presence of hypocalcemia and hyperphosphatemia that mean S.Ca^{+2} decrease gradually when the renal function goes toward ESRD, so as S.Ph. increased as the condition progress for ESRD& this is in agreement with what's done by Mouin G.(2003)([12] .

So anemia, hypo Ca^{+2} &hyperphosphatemia, can be considered as risk factors for both deterioration of

renal function and as predictor for growth in impairment. The presence of all these risk factors indicate that our patient are in adequately managed and delayed care for their CRF due to delayed diagnosis and delayed referral. Hypertension was defined as either SBP or DBP ≥ 95th percentile for gender, age, and height. As in adults, hypertension is a frequent complication in children with CRF. In this study 45.5% of CRF children considered as hypertensive this result is similar to other comparable study done by Mark Mitsnefes (NAPRTCS study)[15] who demonstrated a high prevalence (48%) of H.T. and show close correlation of hypertension with progression of renal failure and this result in agreement with adult studies demonstrating that high BP is associated with accelerated deterioration of kidney function. In children with CRF, the elevated BP is considered to be simply a marker of severity of the disease. The study of NAPRTCS and our study show that H.T.N is not only a marker, but also a significant risk factor for progressive renal dysfunction, so the present study (show that > 50% of patient with ESRD are hypertensive). The study demonstrates the potential value of BP on long-term outcome in pediatric patients with CKD, especially in those with mild renal impairment. So to delay progression we need a target BP below 50th percentile or between 50th and 95th to be controlled by 24h ambulatory BP.Stunted growth in CRF contributed to protein and calorie malnutrition, metabolic acidosis, growth hormone resistance, renal osteodystrophy , anemia , age at onset of CRI and primary renal disease[2].So in this study (53.6%) of CRF are short stature and their height below 3rd percentile and 45.5% of patients enrolled in this study where below 3rd percentile for weight as demonstrated on growth charts of Ht. and wt. and for age and sex.

So more than 50% of them are of stunted growth and when we study mean wt. and Ht. percentile for patient's in different stages of renal failure we found that significant increase in no. of patient with growth retardation (for Ht. & wt.) correlated with the decline of GFR of those patient. So severity of CRI or long standing CRI correlate positively with increase percentage of growth retardation. In our patients and this is also noticed in other study of Mouin, G. NAPRTCS.[12] The study shows that >50% of children ≥ 10 yrs of age were with delayed puberty according to SMR stages for age and sex at least by 2 yrs than normal and this is consistent with a report who demonstrated that the onset of puberty was delayed by 2 to 2.5 yrs on average, the start of genital maturation (Tanner stage G2) was delayed by 1.8 yrs in uremic boys and 2.5 yrs in boys after renal transplantation, unlike the development of secondary sexual characteristics which is delayed but not permanently halted in CRF,the reproductive function may be permanently impaired[2].In this study 40% of CRF children underwent intermittent peritoneal dialysis (as APD and CAPD program are not available in our country.) 41.8% of patient in this study were on conservative medical line of management and one patient only went to other center and put on APD program in north of Iraq.Ten percent of CRF children put on program of hemodialysis, this low percent because vascular access are limited in children due to the small size of their blood vessels, and lastly 7.2% of children enrolled in this study prepared and underwent lived related& unrelated renal transplantation.While the choice of replacement therapy in children is variable the registry of NAPRTCS reports that:

- 1/4 of children underwent pre emptive renal transplantation.
- 1/2 was started on peritoneal dialysis.
- 1/4 was started on hemodialysis [4].

So when pre-emptive transplantation is not an option, the choice between two forms of dialysis is generally dictated by technical, social, and compliance issues, as well as family preference [4].

CONCLUSION:

1. Obstructive uropathy is the most important cause of CRF in Iraqi children especially those less than 5 yrs.
2. Majority of our patients are considerably delayed referral to pediatric nephrology and they were presented malnourished and stunted growth which reflect severity of the disease and delayed management of treatable complication of renal failure as hypertension, anemia, hypocalcemia and hyperphosphatemia.
3. Renal replacement therapy facilities are deficit especially for dialysis program for pediatric age group as CAPD, APD and hemodialysis in addition to inadequate pediatric transplant centers to enhance pre-emptive transplant program.

Recommendations

1. Development of a comprehensive treatment plan between primary care physicians and pediatric nephrologists for children with CRF in order to provide optimal care.
2. To emphasize the necessity of an early referral of patients with CRI to the nephrologists, so that the health team can intervene to delay the decline of renal function and arrest disease progression by dietary modification and blood pressure control.

3. Enhance diagnostic & therapeutic tools for both nephrology & urology pediatric units.

a. As established good antenatal care and postnatal care facilities.

b. Advanced laboratory tool for all investigation as hormonal assay, E/M, immunofluorscent, cytology, virology, biochemistry, hematology, histopathology, blood gas analysis.Cystoscopy, contrast media , urodynamic study, urinary catheters with all size, radiographic

c. facilities pediatric size line and filter for hemodialysis and all dual lumen catheter size.

d. Drugs for RRT as G.H and EPO and immunosuppressive drugs for renal disease and transplant.

e. Availability of wide range metabolic screen for metabolic and inherited disease.

f. Dietitian for chronic renal failure cases.

4. Enhance CAPD and APD and hemodialysis program to increase the dialysis option for pediatric age group.

5. Creation of pediatric transplant units and provide it will all facilities.

REFERENCES:

1. Sakhuja V, Kohli HS. End-stage renal disease in India and Pakistan, Incidence, causes, and management, Ethn. Dis. 2006 ; 16(2 Suppl. 2) : 2-20-3.
2. Agnes, B., Fogo & Valentinakon. Pathophysiology of pregressive renal disease. 1269-1290 – Fraz Schaefer. Endocrine and Growth Disorders in chronic renal failure 1313-1346. Pediatric Nephrolgy Philadelphia: Ellis D. Avnger, M.D., William E. Harmon, M.D., Patrick Niavdet, M.D., 5th ed. 2003.
3. David B. Cundall, J. Trevor and John M.H. Buckler. Which bone age in chronic renal insufficiency and end-stage renal disease? IPNA Pediatric Nephrology (198812: 200-204).
4. Tarak Srivastava, MD , Bradley A Warady, MD overview of the management of chronic kidney disease in children, UptoDate February 2006, Online 13.3.
5. Kai Rönnholm and Christer Holmberg. Chronic renal failure and dialysis options. KIDNEY DISORDERS IN CHILDREN AND ADOLESCENTS. 2004; 10, 193-201.
6. Schwartz GJ, Haycock GB, Edelmann CM, Sptizer A. A simple measure of glomerular filtration rate in children derived from body length and plasma crentinine. Pediatric (1976); 58: 259-263.
7. Mehls O. Renal osteodystrophy in children: etiology and clinical aspects. In: Fine RN, Gruskin AB, editors. End stage Renal Disease in children, Philadelphia: W.B. Saunders, 1984, P. 227-250.
8. Baucer SB. Neurogenic bladder dysfunction. Pediatr. Clin. North. Am 1987; 34: 1121-1132.
9. Srivastava RN, Moudgil A, Bagga A, Vasudev, AS. Hemolytic uremic syndrome in children in Northern India Pediatric Nrphrol. 1991; 5: 284-288.
10. Hamed RM. The spectrum of chronic renal failure among Jordanian children. J. Nephrol. 2002; 17: 316-321.
11. Pankaj Hari, Ish Kumar Singla, Mukta Mantan, Madhuri Kanitkar, Bobby Betra and Arvind Begga., Chronic renal failure in children. Indian Pediatrics. 2003; 40: 1035-1042.
12. Mouin G., Seikaly, P.L. Ho. Lea Emmett, Richard N. Fine. Amir Tejani. Chronic renal insufficiency in children: The 2001 Annual Report of the NAPRTCS. Pediatric Neprhol. IPNA 2003, 18: 796-804.
13. Cristina M.B., Eduardo A. Oliveira, Jose S. Diniz, Monica M.V., Gilce R.O. Predictive factors of progression of chronic renal insufficiency: a multivariate analysis, Pediatric Nephrol. IPNA (2003); 18: 371-377.
14. Gianluigi Ardissino, MD, PhD, FAAP, Valeria Daccy MD, Alberto. E, MD and Emanuela Taioli, MD. Epidemiology of chronic renal failure in children: Data from Italkid project, Pediatrics. 2003; 111 ,382-387.
15. Mark Mitsnefes, Ping-Leung Ho and Paul T. McEnery. Hypertension and progression of chronic renal insufficiency in children, A report of the North American Pediatric Renal Transplant Cooperative Study NAPRTCS. J. American Society of Nephrology (JASN) 2003; 14: 2618-2622.
16. Kamoun A, Lakhoua R. End stage renal disease of the Tunisian child. Epidemiology, etiologies and outcome. Pediatr. Nephrol. 1996;10: 479-482.
17. Howard Trachtman, Bernard Gauthier. Monographs in clinical pediatrics. Pediatric nephrology volume 10 Editors by Philip Lanzkowsky, M.D. in Schneider children's hospital of long Island, 1998 OPA (over seas publishers association)pages:189-214.
18. Jameela A. Kari. Chronic renal failure in children in the western Area of Saudi Arabia. Saudi J. Kidney Dis. Transplant. 2006; 17: 19-24.
19. Aydan Sirin, Sevine Emre, Ahmet Nayir. Etiology of chronic renal failure in Turkish children. Pediatr. Nephrol. 1995; 9: 549-552.

20. Robert D. Needlman. Growth and development Nelson textbook of pediatrics. 16th edition Philadelphia , Pennsylvania Co. 2002; 7 ,23-61.

21. Giuliana Lama. Michele Adolfo T. Reflux nephropathy and hypertension : correlation with the progression of renal damage. Pediatr. Nephrol. 2003; 18 : 241-245.

22. Wilhelmkriz. Progression of chronic renal failure in focal segmental glomerulosclerosis : Consequence of podocyte damage or of tubulo interstitial fibrosis ? Pediatr. Nephrol. 2003; 18: 617-622.