INTRODUCTION

Chronic renal failure (CRF) is defined as the progressive destruction of renal mass with irreversible sclerosis and loss of nephrons over a period of months to years depending on the underlying etiology. Glomerular filtration rate (GFR) progressively decreases with nephrons loss and the term CRF is more specifically used for patients whose GFR is less then 30ml / min. End stage renal disease (ESRD) is the point in this progression when the kidneys no longer function well enough to support life. ESRD usually associated with sign and symptoms of uremia, is defined as when the GFR has declined to levels less then 10ml /min.

During the last few years an international consensus has emerged staging chronic kidney disease (CKD) into five stages. Stage 1 being glomerular filtration rate (GFR) 90ml/min and signs of kidney damage. Stage 2 GFR 60-89 ml/min and signs of kidney damage. Stage 3 being GFR 15-29 ml/min and stage 25 GFR <15ml/min.

The prevalence of CRF in pediatric population is 18 per million. The etiology of chronic renal failure in childhood correlates closely with the age of the patient at that time when renal failure is first detected. CRF in children younger than five years is commonly due to anatomic abnormalities...
(Hypoplasia, Dysplasia, Obstructions, Malformation) and in children after five years is commonly the result of acquired glomerular diseases (Glomerulonephritis, Hemolytic Uremic Syndrome) or hereditary disorders (Alport Syndrome, Cystic disease). Congenital urological malformations are most common causes of chronic renal failure in children with congenital obstructive uropathy accounting for more than 50% of these cases.

Exact incidence of CRF in Pakistani children is not known however one study reported that most common causes of CRF was congenital structural anomalies (26%) out of which posterior Urethral Valves was leading cause followed by dysplastic, hypoplastic kidneys. Another study showed common cause of CRF bilateral renal stones. In one study common presenting symptoms were anemia and growth retardation but in another study acidotic breathing was common presentation at all ages followed by fever in infants, failure to thrive in pre-school and edema in older children.

The goals of management of CRF in children is not only to prevent progression to ESRD but to fulfill the physiological and emotional needs of children to the best possible quality of life. These goals can be achieved by:

- Early and appropriate treatment of reversible causes of CRF like vesicourethral reflux, posterior urethral valves and urolithiasis.
- Early and appropriate conservative management of CRF may help to achieve normal growth and development and periodic monitoring for rate of progression to end stage renal stage disease to help plan for renal replacement therapy.

MATERIAL AND METHODS
Setting
The study was conducted in pediatrics medicine department of Allied Hospital Faisalabad which is a 100 bedded tertiary care unit.

Duration of study
Duration of study was 1 year from March 20th 2007 to March 2008.

Sample Size
The study included 40 patients.

Sampling Technique
It was convenience (non-probability) sampling.

Inclusion Criteria
Patients over 6 months and under 15 years of age with GFR <25% of the normal for that age and sex were included.

Exclusion Criteria
1. Patients with acute renal failure.
2. Children with transplanted kidneys.

Study design
It was a cross sectional study.

Method of data collection
All patients with chronic renal failure admitted either through emergency or from out patient department who fulfilled the inclusion criteria were included.

After the diagnosis of CRF informed consent was taken from parents. The parents were informed about the study and the procedure of the study. They were assured about confidentiality and were informed about outcome of the disease. All these patients were stabilized initially taking care of their acute problems. A detailed history was taken with the view to reach the probable underlying cause and to assess the common clinical features with which the patients of CRF presents. A detailed examination was undertaken to identify any causative factor of CRF. Height, weight. Blood pressure was taken in each case. CBC, Peripheral film, serum calcium, phosphate, alkaline phosphatase, blood urea, serum creatinine, serum electrolytes, X-Ray wrist joints, Abdominal USG and urine C/E was done in each case. Other investigations like renal scan, CT scan, ABGs were done where relevant. Renal biopsy was done after taking the consent of the parents.
Chronic renal failure was defined as GFR < 25% of the normal per that age and sex. GFR was calculated by the following formula = GFR = body length (cm) / serum creatinine (mg/dl) x k (constant). Hypertension was defined as systolic or diastolic blood pressure above 95th percentile for that age and sex. Short stature was defined as height less than 5th percentile for that age and sex.

**Data Analysis**
All the data was recorded in predesigned performa. Data analysis was computer based. SPSS-Version 10 was used for analysis. Continuous variables like age, height, weight and blood pressure were expressed as mean ± standard deviation. Discrete variables like sex, risk factors and findings of examination were presented as frequency and percentages. For comparison with other study Chi-Square was used. PC 0.05 was taken as significant.

**RESULTS**
A total of 4000 patients were admitted in pediatrics medicine department during the period March 2007 to March 2008. Out of these 40 patients fulfilled the inclusion criteria. Male (n-28) to female (n-12) ratio was 2.33: 1 and were included in the study. 9 patients (22.5%) were below 5 years of age, 22 (55%) were between 5-10 years of age and 9 (22.5%) were above 10 years of age. Mean age in male was 7.36±3.98 and in female was 8.96±2.65 years.

Depending upon the clinical evidence and available laboratory support the etiology was determined in 34 (85%) patients but no cause was found in 6 (15%) patients the most common cause of CRF was congenital malformation and out of which PUV (Posterior Urethral Valves). were 7 (17.5%) and pelvicureteral junction obstruction (PUJ) in 2 (5%).

The second most common cause was urolithiasis in 8 (20%). The reflux nephropathy was found in 6 (15%). Glomerulopathies were found in 3 (7.5%). Among glomerulopathies chronic glomerulonephritis 1 (2.5%). Crescentic glomerulonephritis 1 (2.5%) and rapidly progressive glomerulonephritis (RPGN) (1-2.5%).

Neurogenic bladder was found in 2 (5%) cases. Among inherited causes 1 (2.5%) with Fanconi syndrome and 1 (2.5%) with polycystic kidney disease. 1 (2.5%) with renal artery stenosis also found among other causes 1 (2.5%) with acquired stricture due to trauma and 1 patient of Down syndrome also had CRF.

Among all these cases 6 (15%) no etiology was found.

Most common symptoms of CRF were failure to thrive 31 (77%), respiratory distress 30 (75%), pallor 30 (75%), fever 30 (75%), vomiting 25 (62%), body swelling 20 (50%), anorexia 17 (42%), fits 10 (25%), and carpopedal spasm 2 (5%).

In 33 (82%) patients weight was below 5th percentile. In males mean weight was 15.79±7.76 kg and in females was 18.29±6.41 kg. In 30(75%) patients height was below 5th percentile. Mean height in males was 103.89±23.36 and in females was 113.42±17.93 cm.

Hypertension was a frequent finding in CRF patients. Systolic blood pressure in male 123.93± 20.78 and in female 125.83±17.81 and diastolic blood pressure was in males 81.96±15.41 and in female 85.83±16.76 mmHg. Systolic blood pressure above 95th percentile noted in 21 (52%) and diastolic blood pressure above 95th percentile in 28 (65%). In about 20 (50%) both systolic and diastolic were raised above 95th percentile.

On clinical examination pallor was found in 35 (87%) and out of which 28 (70%) had hemoglobin between 5-10gm/dl and 7 had below 5gm/dl.

Serum calcium level was noted < 7mg/dl in 20 (50%) patients.

Serum bicarbonate level below 15meq/L was in 26 (65%) out of which 10 (25%) had between 6-10meq.
The average duration of patients stay in hospital was 8 days. 3 patients (8%) expired during stay in hospital 1 due to hypertensive heart failure and encephalopathy and sepsis. 37 (92%) patients were on regular follow up.

**DISCUSSION**

Chronic renal failure is an irreversible progressive renal disorder which ultimately leads to end stage renal disease. Renal replacement therapy in the form of dialysis or renal transplant are the ultimate options for the management of these children. The treatment options are very costly and available in only few centers in Pakistan. The age of the patients presentation closely correlates with the underlying cause.

Primary renal diseases that lead to chronic renal failure are quite different in children compared with adults because of the higher proportion of congenital and hereditary nephropathies. Congenital trace anomalies are associated with high mortality rates. Geographical location may also influence the distribution of the diseases which lead to CRF. The incidence and etiology are age-dependent and vary according to geography, socioeconomic and ethnic background. Males are affected more, 8-25/million, while in females the incidence is 4-21/million children. Our study is in confirmation with this data whereby male to female ratio is 2.33:1 (P-.614).

Most studies show that obstructive uropathy is the major cause of CRF in children out of which the major causes are congenital malformations stricture and renal calculi. Congenital structural anomalies are most common cause of chronic renal failure in children. The common congenital causes reported in literature include PUV,
### Table-I. Etiology of patients of chronic renal failure (n=40)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Total no. of patients</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Malformations</td>
<td>9</td>
<td>22.5</td>
</tr>
<tr>
<td>Posterior urethral valves</td>
<td>7</td>
<td>17.5</td>
</tr>
<tr>
<td>Pelviureteral junction (PUJ) obstruction</td>
<td>2</td>
<td>5.0</td>
</tr>
<tr>
<td>Urolithias</td>
<td>8</td>
<td>20</td>
</tr>
<tr>
<td>Reflux Nephropathy</td>
<td>6</td>
<td>15</td>
</tr>
<tr>
<td>Glomerulopathies</td>
<td>3</td>
<td>7.5</td>
</tr>
<tr>
<td>i. Chronic Glomerulonephritis</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>ii. Crescentic Glomerulonephritis</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>iii. RPGN</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Neurogenic Bladder</td>
<td>2</td>
<td>5.0</td>
</tr>
<tr>
<td>Stricture</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Miscellaneous Causes</td>
<td>5</td>
<td>12.5</td>
</tr>
<tr>
<td>i. Renal Artery stenosis</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>ii. Down syndrome with CRF</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>iii. CRF with Hypo plastic kidney</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>iv. Fanconi syndrome</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>v. Polycystic kidney</td>
<td>1</td>
<td>2.5</td>
</tr>
<tr>
<td>Unknown Etiology</td>
<td>6</td>
<td>15</td>
</tr>
</tbody>
</table>

### Table-II. Etiology of CRF patients according to age (n=40)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Age under 5 years (n=9)</th>
<th>Age above 5 years (n=31)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Anomalies</td>
<td>3(7.5%)</td>
<td>6(15%)</td>
</tr>
<tr>
<td>Urolithias</td>
<td>------</td>
<td>8(20%)</td>
</tr>
<tr>
<td>Reflux Nephropathy</td>
<td>1(2.5%)</td>
<td>5(12.5%)</td>
</tr>
<tr>
<td>Glomerulopathies</td>
<td>0(0%)</td>
<td>3(7.5%)</td>
</tr>
<tr>
<td>Neurogenic bladder</td>
<td>1(2.5%)</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Urethral stricture</td>
<td>0(0%)</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Polycystic kidney</td>
<td>1(2.5%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>Renal Artery stenosis</td>
<td>0(0%)</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Hypoplastic kidney</td>
<td>0(0%)</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Fanconi Syndrome</td>
<td>1(2.5%)</td>
<td>0(0%)</td>
</tr>
<tr>
<td>CRF with Down Syndrome</td>
<td>0(0%)</td>
<td>1(2.5%)</td>
</tr>
<tr>
<td>Unknown Etiology</td>
<td>2(5%)</td>
<td>4(10%)</td>
</tr>
</tbody>
</table>

### Table-III. Etiology of chronic renal failure (Comparison with other studies)

<table>
<thead>
<tr>
<th>Etiology</th>
<th>Faisalabad (our study) (n = 40)</th>
<th>Lahore (n = 42)</th>
<th>Karachi (n = 78)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congenital Anomalies</td>
<td>9 (23%)</td>
<td>11(26%) (P &gt; 0.697)</td>
<td>18(23%) (P &gt; 0.944)</td>
</tr>
<tr>
<td>Urolithias</td>
<td>8 (20%)</td>
<td>5(12%) (P &gt; 0.316)</td>
<td>11(14%) (P &gt; 0.409)</td>
</tr>
<tr>
<td>Reflux Nephropathy</td>
<td>6 (15%)</td>
<td>4(10%)</td>
<td>19 (24.5%)</td>
</tr>
<tr>
<td>Glomerulopathies</td>
<td>3 (8%)</td>
<td>4 (10%) (P &gt; 0.743)</td>
<td>12 (15%)</td>
</tr>
<tr>
<td>Neurogenic Bladder</td>
<td>2 (5%)</td>
<td>2 (5%) (P &gt; 0.960)</td>
<td>-</td>
</tr>
<tr>
<td>Unknown Etiology</td>
<td>6 (15%)</td>
<td>9 (21%)</td>
<td>-</td>
</tr>
<tr>
<td>Miscellaneous</td>
<td>5 (12%)</td>
<td>5 (12%)</td>
<td>-</td>
</tr>
</tbody>
</table>

*Chi-Square is used to compare with other studies.*
pelviureteral junction obstruction, urethral atresia, prune belly syndrome and megacystis. Hafeez F reported congenital structural anomalies as the most common cause of CRF. Our results are similar as 23% (P > .697) of our patients has the same etiology. A study in Kuwait shows that congenital malformations are the leading cause of CRF. Other studies in Poland & Saudi Arabia also shows that posterior urethral valves and other malformations of urinary tract are the leading causes of CRF. Similarly other studies also showed that obstructive uropathy was the most common cause of CRF in pediatric age. One study in Karachi in Jamro S also shows the same results (P > .944). Our figures are consistent with internationally and locally reported data in that the PUV were the leading cause and that the majority of cases of obstructive uropathy were males. As obstructive uropathies are both preventable and reversible to some extent, early detection can prevent the onset of renal failure in most cases of obstructive uropathy. Early detection is possible if the clinician has high index of suspicion and by using antenatal screening followed by postnatal ultrasonography and renograms. Some degree of reversal of renal failure is possible if the obstruction in the urinary passages is removed. If recognized at a timely stage, complications of obstructive uropathy like hydronephrosis with progressive renal damage and urinary ascites can be prevented. In USA, 16.5% of all pediatric renal transplants were due to obstructive uropathy. Unfortunately, we still see many children with advanced renal damage due to obstructive uropathy, which could have been prevented if early diagnosis and intervention has been made possible.

Urolithiasis or renal calculi are the second most common cause of CRF due to obstructive uropathy after congenital formation in our study out of 43% are obstructive uropathy cases 20%
were reported with Urolithiasis. This is confirmed by the international & local studies. A study in Lahore shows that renal calculi are the second most common cause of Chronic Renal Failure.6 (P > .316). In other study in Mayo Hospital Lahore & Karachi also confirm these results10,18 (P > .409).

Reflux nephropathy is responsible for a significant percentage of end-stage renal disease in late childhood as well as being the most common cause of severe hypertension in childhood and adolescence. To prevent reflux nephropathy, it is imperative to discover reflux at the youngest age possible and preferably before any urinary tract infections have occurred. Vesico-ureteric reflux (VUR) is diagnosed with increasing frequency in infants, typically during postnatal investigation of antenatal hydronephrosis. Jemro S et al conducted a study in Larkana Pakistan which shows that the reflex neuropathy is common cause of Chronic Renal Failure. There is a significant relationship between grade II VUR & higher primary renal damage in boys and girls. Association between renal damage and VUR is more important in boys but UTI and renal inflammation is seems to be more important in girls19. A study in Rome Italy shows the reflux and febrile UTI in First year of life are at great risk of developing CRF in long term4. Reflux nephropathy is an important cause of CRF in our study and 15% of the cases presented with this cause.

Glomerulopathies are also one of the most common cause of CRF in some series. In Bangladesh and Saudi Arabia Glomerulopathies are also important causes of CRF20. Focal segmental glomerulosclerosis, chronic glomerulonephritis and nephrotic syndrome with minimal glomerular changes were reported as primary renal pathologies in the patients with end-stage renal disease. In our center, glomerular diseases were the forth most common cause of CRF(7.5%). (P > .745) Chronic Glomerulonephritis, RPGN and crescentic Glomerulonephritis which were established on renal biopsy where the causes of CRF in our study. Another study also confirm these results21. Neurogenic bladder is also an important cause of CRF in children and in our study 2 cases (5%) reported with this problem and these results are consistent with other studies (P >960).6

The other causes like tubular causes (Fanconi Syndrome), Renal Artery Stenosis and Polycystic kidney also found. One patient of Down Syndrome also diagnosed as case of CRF.

A large number about 15% cases in our study found no cause of CRF which shows further research and investigation should be done in this regard to save the lives.

The clinical presentation of CRF is quite varied and dependent on the underlying renal disease. The patients are relatively asymptomatic in the earlier stages. In our children, the most common presenting complaints of the patients were respiratory distress, fever, swelling of body, vomiting and pallor. Almost 50% of the patients had these symptoms at the time of presentation. Metabolic acidosis and growth retardation are common complications of CRF6. Despite recent advances in management of Children which chronic kidney diseases growth remains suboptimal22. In our study, 75% of the patients had acidotic breathing at the time of presentation and on doing blood gases, about 77% of the patients were having metabolic acidosis. Growth is affected in CRF even the patient does not have any other clinical manifestations. Growth retardation is the result of a variety of abnormalities in growth hormone regulation including changes in its plasma concentration, in regulation of its release and end organ unresponsiveness. The other factors associated with growth impairment are age, race, primary diagnosis & reduced renal functions at the time of diagnosis22. A study in Bangladesh Shows that children with congenital anomalies are more stunted as compared to acquired causes23. In our study, 82% of the patients had weight that was below 5th percentile and 75% of the patients had height that was below 5th percentile. In our study the facts & figures also verify the other studies.

Anemia is a predictable consequence of CRF and
generally develops long before end stage renal disease and its severity is directly related to the severity of CRF. Inadequate erythropoiesis due to insufficient erythropoietin synthesis is the main cause of anemia. A study conducted in Karachi showed that 94% of the patients found with anemia. A study in Lahore shows that small increase in hemoglobin take place after dialysis. Pre-dialysis was 7.4 gm/dl and post dialysis hemoglobin was 8.3 gm/dl. And most of the patients anemia treated with blood transfusion or erythropoietin injection. In our study, 80% of the patients had pallor clinically and 88% of the patients had hemoglobin level below 10gm/dl on investigation which was mostly corrected by blood transfusion.

Hypertension is also an important sign in CRF patients. The incidence increased upto 90% with progressive deterioration of renal functions. Most recent data from USA shows that 38% children are taking anti-hypertensive medicines. Other studies in Pakistan also shows that 50% cases of CRF are hypertensive. In our study, at least 50% of the patients had both systolic and diastolic blood pressure above 95th percentile.

Bone disease is common in patients with renal insufficiency and can result in substantial morbidity. Renal osteodystrophy involves a complex interrelationship of loss of divalent mineral homeostasis, hyper parathyroidism and gene modulation. The renal bone diseases are a heterogenous group of disorders that can be divided into 3 groups: those with high bone turnover, or osteitis fibrosa, caused by secondary hyperparathyroidism; those with low bone turnover, or adynamic bone; and those that exhibit features of both these abnormalities, also termed mixed renal osteodystrophy. In our study, signs of renal osteodystrophy were present in 60% of the patients which show that bone disease is the important consequence of CRF.

During our study period, three patients (8%) expired while they were in hospital. 1(2.5%) patients died due to uremic encephalopathy, 1(2.5%) due to sepsis and 1(2.5%) due to intractable fits due to hypertension and hypocalcemia. Groothoff JW et al reported that common cause of death are cardiovascular and infections.

Patients with posterior Urethral valve require regular nephrologists assessment after birth. We recommend antenatal screening screening for beta2 microglobulin to detect obstructive uropathy, ultrasonography and routine roentgenography with first urinary tract infection in children.

We also recommend that early referral of the patient to pediatric nephrologist / urologist very important to preserve the renal functions.

CONCLUSIONS
Chronic renal failure is a disease entity, which is underestimated because of non-specific signs and symptoms early in the disease, so any child with pallor, acidotic breathing, growth failure, signs of renal osteodystrophy and hypertension should be evaluated for chronic renal failure. In our population treatable causes like urinary tract infections, obstructive uropathy, calculi and reflux nephropathy accounted for a significant number of patients. If recognized at a timely stage, complications of obstructive uropathy like hydronephrosis with progressive renal damage and urinary ascites may be prevented.

We should also promote awareness among physicians about early referral of children with chronic renal failure and have high index of suspicion when unexplained pallor, hypertension growth retardation and bony changes occur.

REFERENCES


The best way to get **Something** done is to begin.

*Unknown*